EFSUMB Course Book, 2nd Edition

Editor: Christoph F. Dietrich

Ultrasound of the spleen

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Acknowledgment:

The authors thank Vito Cantisani for peer review of the manuscript

Anatomic remarks

The spleen is an intraperitoneal organ located in the left-lateral upper quadrant, underneath the diaphragm and abutting ribs. It is attached to the retroperitoneum by fatty ligaments that also contain its vascular supply. The spleen is located close to the stomach, the left kidney, the splenic flexure of the colon and the tail of the pancreas. The splenic artery has a tortuous course and enters the hilum on the medial surface through the splenorenal ligament. The splenic vein drains through the central hilum and courses along the antero-superior part of the pancreas to its confluence with the superior mesenteric vein to form the portal vein.

The spleen consists of two parts: macroscopically, the red pulp can be differentiated from very small grey spots of 0.2-0.7 mm called the white pulp, which are both separated by the marginal zone. The white pulp consists of T and B lymphocytes. The red pulp forms a spongy reticular network that surrounds the blood sinusoids. The red colour is caused by the large number of erythrocytes in the sinuses. The sinusoids are the sites of cellular exchange located between the spleen and circulatory system. The splenic arteries enter the pulp within the trabeculae. From these trabecular arteries, the central arteries extend into white and then the red pulp. The arteries branch into the white pulp and are surrounded by a sheath of lymphocytes, mainly T cells, called periarterial lymphatic sheath or PALS. From the central arteries, small branches enter the red pulp or are connected directly to the sinusoids at the end of the arterioles. These sinusoids are part of the marginal zone. Blood from the sinusoids are collected in the pulp and trabecular veins. These trabecular veins merge to form the splenic vein leaving the spleen through the hilum.

Thus, an open circulation (mainly open-ended arterioles in the red pulp) can be differentiated from a closed circulation in which arterioles are directly connected to the sinusoids. The open circulation functions as a filter for red blood cells because only flexible (and younger) red blood cells can pass through the slits of the sinusoids and re-enter systemic circulation; older and worn-out red blood cells are destroyed and dissolved by phagocytosis. Open circulation is a relatively slow process and allows blood cells to be filtered when entering the sinusoids. In comparison, the closed circulation is rapid; blood cells traverse the sinusoids and are drained into the splenic veins.

Imaging the normal spleen

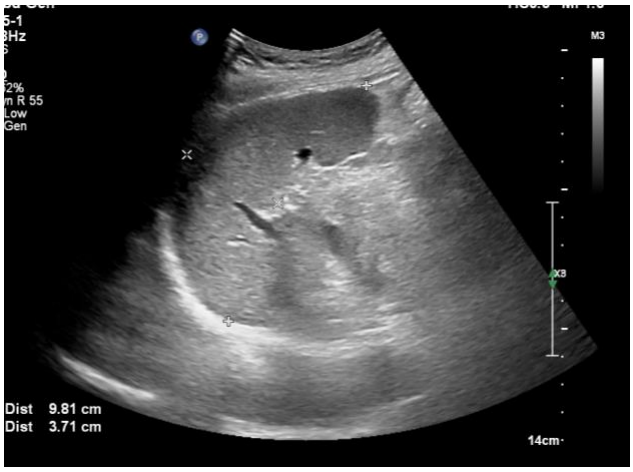
The spleen can be imaged from a left intercostal coronal approach in either a supine or right lateral decubital position. The probe should be placed between the ribs at the level of the ninth intercostal space.

To detect small intrasplenic lesions it is important to image the spleen completely. For the examination of the spleen a wideband 2-5MHz convex probe is usually used. In the case of lymphatic diseases a high-frequency linear probe is recommended.

Measurements should be taken from a longitudinal and transverse plane. A normal spleen weighs 150 g and is approximately 11-12 cm in craniocaudal length and is 3-4 cm thick. A normal-sized spleen is not usually palpable. But, that does not necessarily mean a clinically palpable spleen is pathological. An enlarged spleen is usually caused by extrasplenic diseases.

The spleen length in children correlates with age, weight, body surface area and length of a patient [(1)]. There is a wide range of normal spleen sizes, from very small to large organs. A normal spleen decreases in size and weight with increasing age. It also slightly increases during digestion and can vary in size depending on the nutritional status of the body [(2)]. As splenomegaly normally develops secondary to systemic or liver disease, it is important to know at which splenic size the organ is considered enlarged. Spielman reported that splenic length and width in young athletes correlates with length and gender [(3)]. Male athletes taller than 2 m had a mean spleen length of 13.2 cm (maximum 16.2 cm) and in females approximately 2 m in height had a mean spleen length of 11.2 cm (maximum 14.0 cm). A good correlation (r=0.86) between splenic length measured in the right lateral decubitus position and CT volume has been described by Lamb [(4)].

Figure 1 Measuring the splenic size.



In routine clinical practice, most radiologists and sonographers perform measurements on longitudinal scans only. Lamb's study concluded that the measurement of splenic length in routine clinical practice is a very good indicator of actual splenic size [Figure 1] [(4)]. As well as measuring diameter, it has been suggested that the largest area should also be calculated. A study describing portal hypertension in cirrhotic patients defined a normal sized spleen as having an area of <45 cm^2, a moderately enlarged spleen of 45-65 cm^2 and a marked splenomegaly having an area of > 65 cm^2 [(5)] [Figure 2].

Figure 2 Area calculation in a moderately enlarged spleen, with a longest diameter of 16.7 cm and a width of 5.5 cm, representing an area of 82.7 cm^2.

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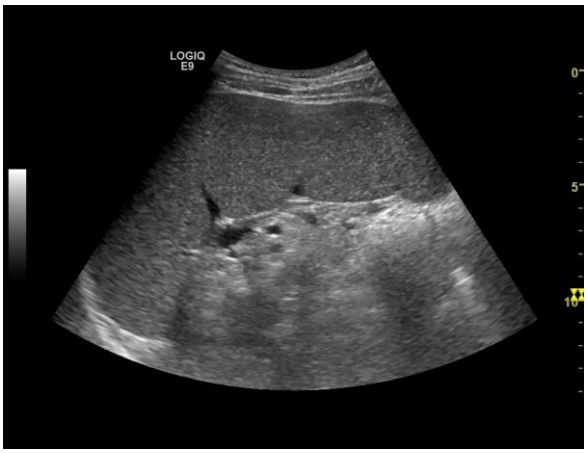

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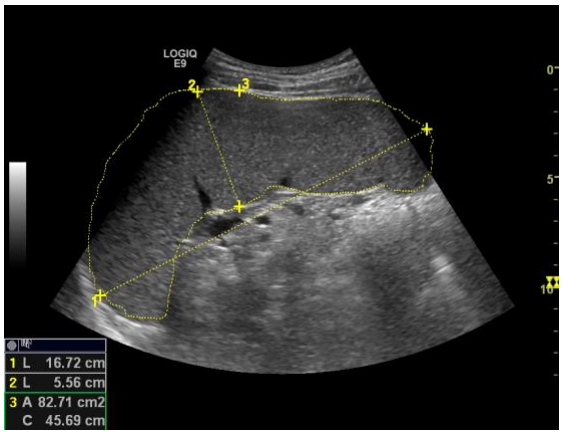

Several techniques are used to image the spleen by ultrasound: B-mode ultrasound, Colour, duplex and Power Doppler, as well as contrast-enhanced ultrasound (CEUS). The behaviour of the spleen at CEUS examination is similar to other imaging modalities such as contrast-enhanced CT or contrast-enhanced MRI and correlates with the anatomic particularities of the organ.

Imaging modalities such as contrast-enhanced CT or contrast-enhanced MRI shows heterogenous contrast filling during the arterial phase; after approximately 1 min the spleen shows a homogeneous enhancement. The same is true on contrast-enhanced ultrasound examinations during the first minute of contrast bolus injection. In contrast to the liver, the arterial phase of the spleen is not suited for the detection and characterization of splenic lesions.

MRI examination demonstrates different splenic circulations immediately after gadolinium breath-hold Tl weighted spoiled gradient echo (SGE) sequences. The most common pattern (79%) is arciform. This appears as a serpiginous pattern of high signal (closed circulation) and low signal (open circulation) stroma. This pattern becomes homogeneous and high in signal within 1 min post-contrast [(6-9)]. It has been observed in all healthy spleens and in some spleens of patients with inflammatory or neoplastic diseases. Two other different splenic enhancement patterns have been described on immediate post-gadolinium images. The second most common pattern (16%) is homogeneous high signal intensity enhancement. This was identified in patients with inflammatory or neoplastic disease, focal fatty liver infiltration or hepatic enzyme abnormalities. It is thought that a non-specific immune

response could be responsible for this pattern of enhancement. The third pattern is uniform low-signal intensity (5%). This was found in all patients who had undergone multiple recent blood transfusions. The T2 shortening effects from haemosiderin deposition in the reticuloendothelial system replace the Tl shortening effects of gadolinium [(6-9)]. Similar images are seen on contrast-enhanced CT.

Data have shown that a normal vascular pattern of spleen enhancement on contrast-enhanced ultrasound is close to contrast-enhanced-CT [Figure 3c] or contrast-enhanced-MRI. The splenic artery starts to become opaque at about 12 seconds after sulphur-hexafluoride filled phospholipid stabilized microbubbles (SonoVue™, Bracco, Italy) bolus injection. Heterogenous enhancement of splenic parenchyma occurs in the arterial phase, which resembles the well-known zebra-striped pattern seen on dynamic CT or MRI [(10)]. During the first minute following injection, small arteries are seen radiating from the splenic artery. Approximately 1 min after the injection, the splenic parenchyma becomes homogeneously enhanced and shows a dense persistent enhancement for at least 7-10 min [Figure 3 a,b]. It is thought that closed circulation is enhanced much faster than the open circulation. But, this assumption has not been proven. It is important to note that SonoVue produces spleen-specific enhancement longer than the blood pool phase due to parenchymal uptake [(11)]. In comparison with the contiguous left kidney that shows intense but transient enhancement, the spleen appears as hypoechoic during the early opaque phase and hyperechoic during the late phase [(12)]. The other two enhancement patterns described before at MRI examination can also be found on CEUS. Although there are no studies, homogenous enhancement has been found in some cases of liver diseases and inflammatory disorders [Figure 4].

Figure 3 **Contrast images of the spleen 18 (a) and 64 (b) seconds after bolus injection of Sonovue. An arciform-like enhancement pattern of the normal spleen quickly develops during the arterial phase with the closed circulation enhancing later. After one minute the spleen is homogeneously enhanced. Contrast images of the spleen during arterial and venous phase on CE-CT. Images are similar to CEUS (c,d).**

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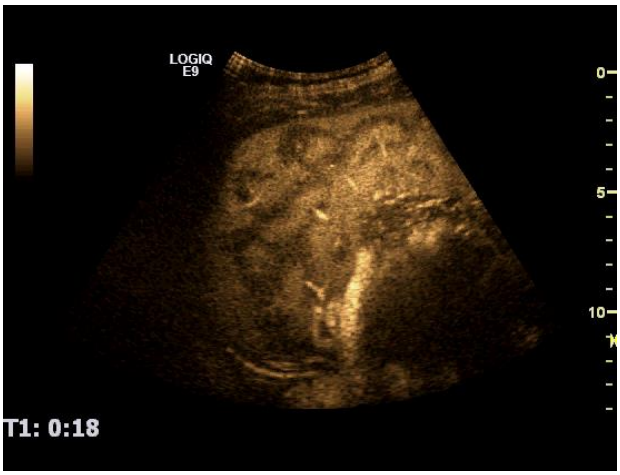

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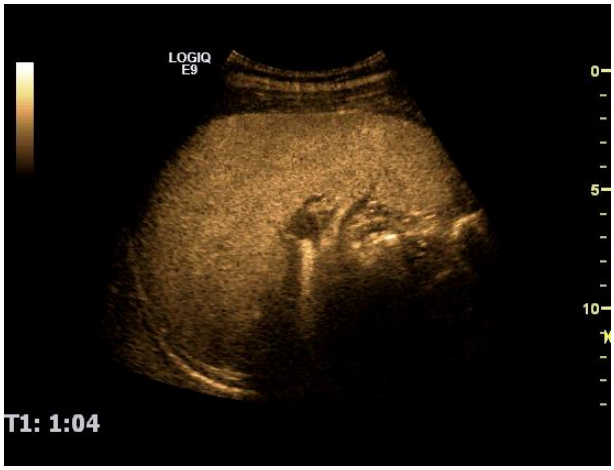

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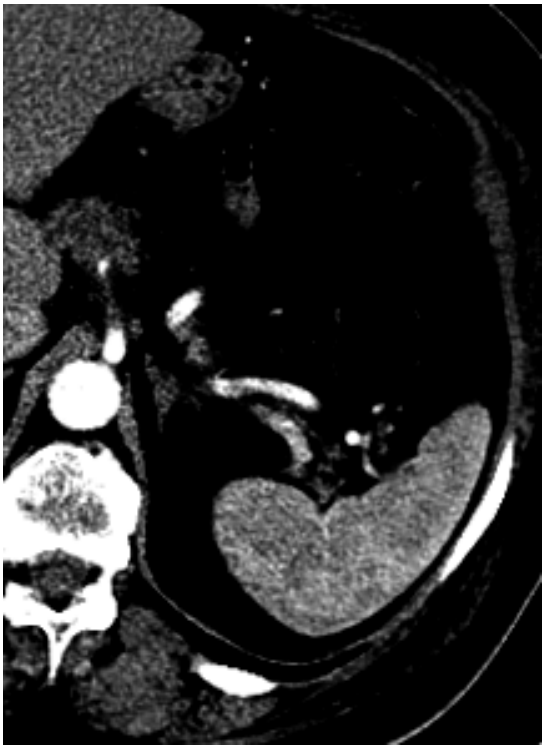

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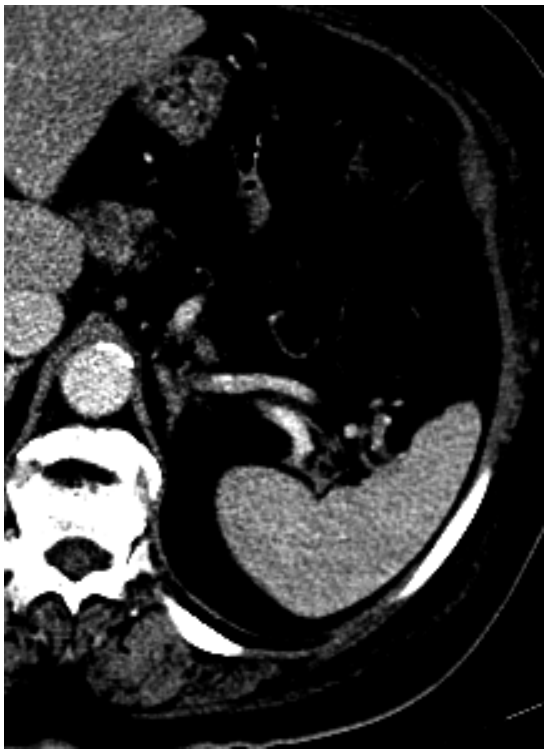

Figure 4 **Contrast images of the spleen 24 (a) and 35 (b) seconds after bolus injection of Sonovue. Homogenous enhancement pattern during the arterial phase in cirrhotic patient, HCV ethiology with marked splenomegaly. Note that the intra-splenic circulation misses the arciform enhancement pattern, normally seen during the first minute after contrast injection.**

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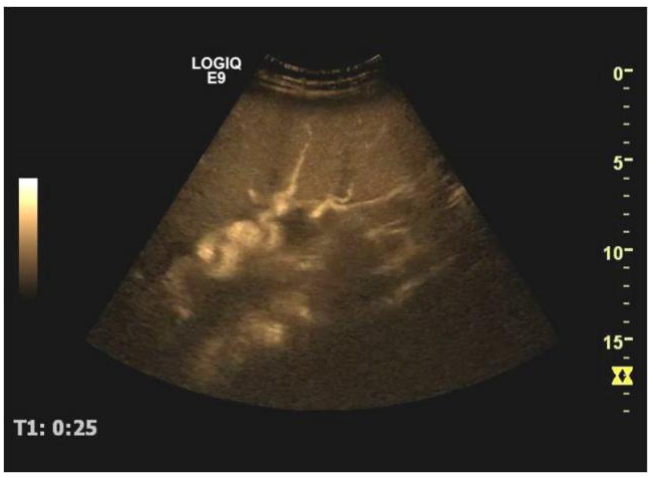

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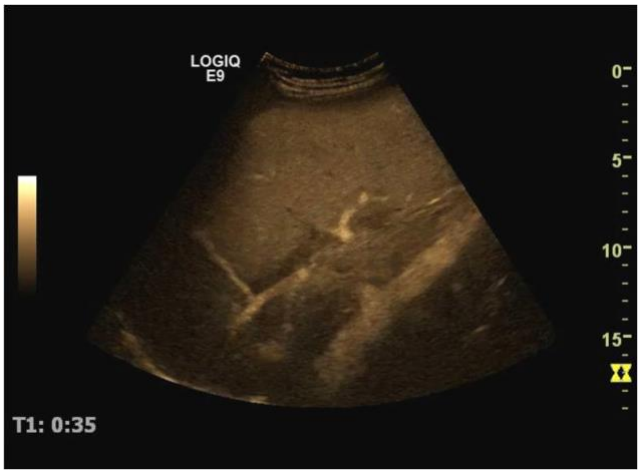


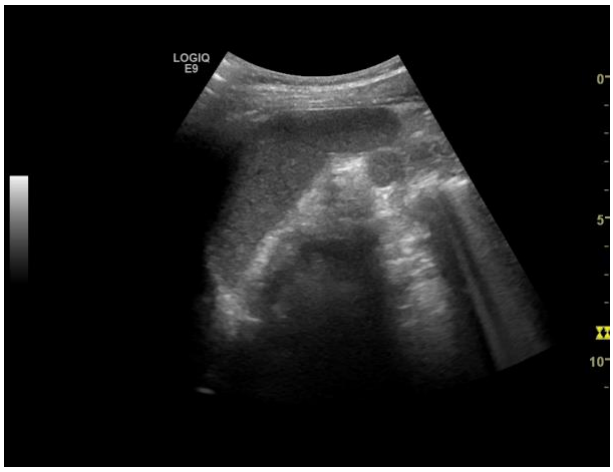
Congenital and acquired splenic variations

An accessory spleen is usually found incidentally in abdominal imaging (10-15%) and in up to 30% of cases at autopsy examination [(13, 14)]. Commonly, it is located near the hilum or at the lower pole of the spleen. An accessory spleen can mimic an enlarged lymph node as well as a tumour in the adrenal gland, pancreas, stomach or intestine. Most appear as well-delineated, round or oval masses, usually not larger than 2 cm, with a B-mode ultrasound appearance similar to the adjacent spleen and with a similar enhancement on contrast-enhanced imaging [(12)]. An accessory spleen is characterized by a tree-like architecture of its vessels entering from its hilum [Figure 5]. Its enhancement lasts as long as it does in the spleen; in an enlarged accessory spleen this can be for more than 5 min [Figure 6].

An accessory spleen below 1 cm may be misinterpreted as pathological on CT because a partial volume effect, which may demonstrate a weaker enhancement than the normal spleen.

Figure 5 Accessory spleen in B-mode (a) and in Power Doppler (b). The normal vessel architecture of an enlarged accessory spleen after splenectomy are shown by using B-Flow technique (c).

a



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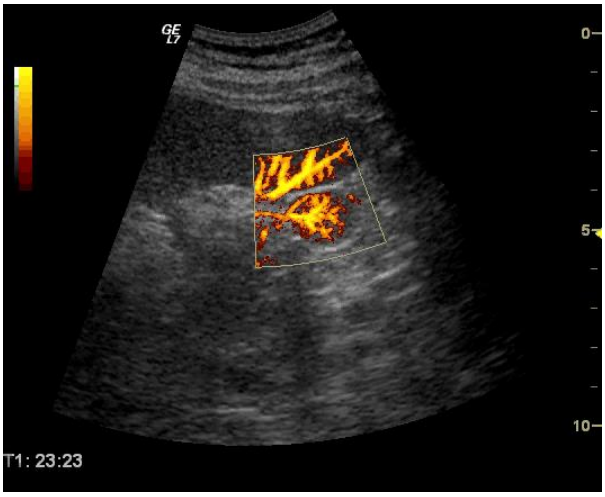

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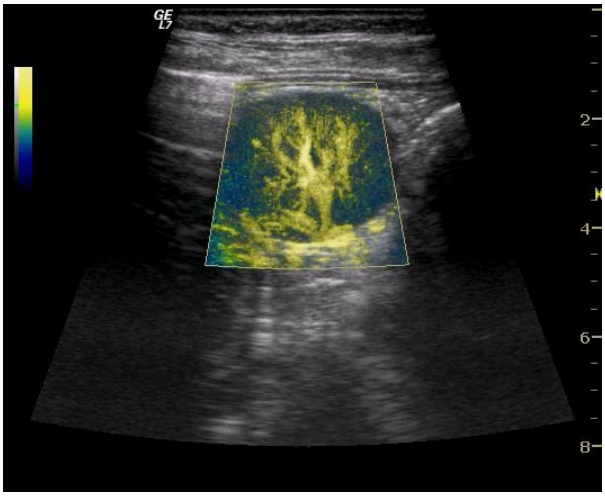

Figure 6 Two enlarged accessory spleens after posttraumatic splenectomy (a). The contrast study shows a long lasting enhancement and thus proves this tissue to be splenic (b).

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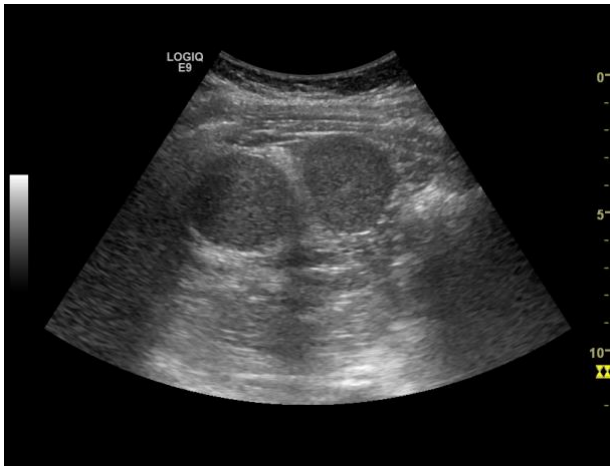

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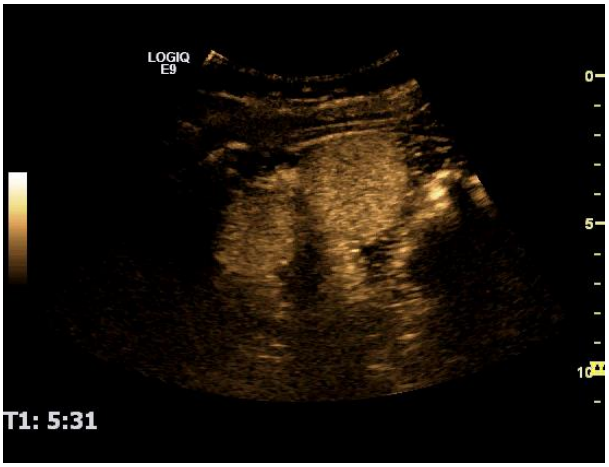


Sometimes the spleen is not found in the normal position. The "wandering" spleen is due to a failure to fuse between the dorsal mesentery, which causes the posterior peritoneum and the mesentery to be mobile. In this situation, the spleen can be found in unusual positions and can be misinterpreted as a mass. It may undergo torsion and result in acute or chronic abdominal pain [(15-17)]. In these cases, colour Doppler ultrasound that shows the absence of the blood flow can be helpful.

Asplenia (congenital absence of the spleen) and polysplenia (congenitally multiple spleens) syndromes are part of the spectrum of anomalies known as visceral heterotaxy. Polysplenia

should be differentiated from post-traumatic splenosis. Following splenic rupture, splenic cells can implant thorough the peritoneal cavity and increase in size, which results in multiple ectopic splenic rests [(18-20)]. In cases of congenital or post-traumatic ectopic spleen, the most sensitive imaging technique for diagnosis is technetium labelled heat-damaged autologous erythrocytes [(21-23)]. CEUS is useful in such cases of ectopic accessory spleen diagnosis showing similar enhancement to the spleen and no further investigations are necessary [(24, 25)].

Splenic atrophy is found in healthy individuals, but also in some pathological situations such as chronic haemolytic anaemia, particularly sickle-cell anaemia or wasting diseases. Owing to multiple infarctions, increasing fibrosis, loss of pulp, and iron and calcium deposits, the spleen can become hardly recognizable. In a small or enlarged spleen, such as in sickle cell anaemia, hypo- or functional asplenia can be seen [(26)]. Functional asplenia and hyposplenia can be seen in homozygous sickle cell anaemia, autoimmune diseases, inflammatory bowel diseases, after septicaemia or after bone marrow transplantation. Colour Doppler ultrasound demonstrates a diminished vascularization and CEUS shows only a short enhancement in functional hyposplenia or asplenia.

Splenomegaly

The spleen is involved in many systemic disorders but is rarely the primary site of disease. Splenomegaly can be caused by diffuse diseases or focal lesions such as splenic cysts. Diffuse splenomegaly is associated with many clinical conditions. The most common ones are:

- Immune response of the spleen during bacterial infections such as endocarditis, virus infections such as mononucleosis, or parasitic infections, such as malaria.
- Increased red blood cell destruction, such as sickle cell anaemia, hereditary spherocytosis, thalassemia, other haemoglobinopathies.
- Systemic neoplastic diseases, such as leukaemias, lymphomas (Hodgkin's and non-Hodgkin's disease), myeloproliferative disorders, polycythaemia rubra vera, metastatic tumours (commonly melanoma), and histiocytosis X.
- Acute or chronic congestion of spleen: splenic or portal vein obstruction, portal hypertension in cirrhosis, heart failure and Budd-Chiari syndrome.

- Disordered immunoregulation, such as sarcoidosis, rheumatoid arthritis, systemic lupus erythematosus and drug reactions.
- Metabolic diseases, such as amyloidosis, Gaucher's disease, Niemann-Pick disease, Hurler syndrome and other mucopolysaccharidoses.

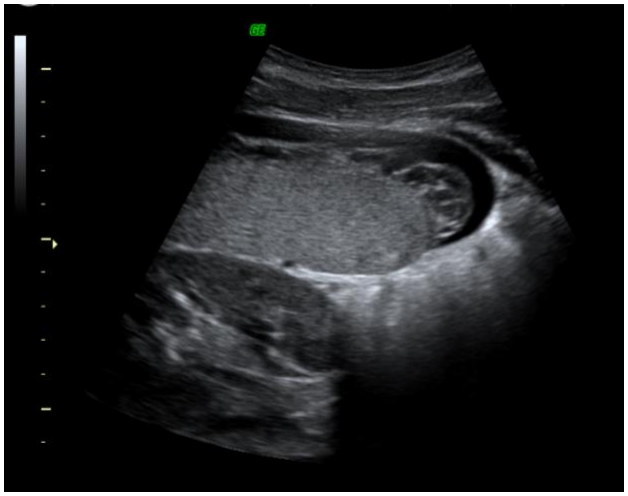
Generally, mild-to-moderate splenomegaly is a result of infection or portal hypertension, marked splenomegaly is found in haematological disorders (leukaemia, lymphoma and infectious mononucleosis) and massive splenomegaly can be seen in myelofibrosis.
There are studies that have attempted to quantify the degree of splenic fibrosis or tumour infiltration by analysing different ultrasound signal parameters for speed or attenuation, but the results were inconclusive [(27-29)]. Quantitative studies have also been performed on CEUS enhancement [(11)].
On CEUS examination changes in enhancement of the splenic parenchyma are neither constant nor specific. In some cases with marked splenomegaly a slightly delayed global enhancement can be seen, with a less-intense opacification of splenic parenchyma and a prolonged early-phase inhomogeneity [(10)].

Infectious diseases

Splenic involvement in infectious diseases is mostly diffuse and mild to moderate splenomegaly is usually seen. But there are clinical situations when focal splenic lesions are found, especially in immune compromised patients.
In a study of 20 patients with infectious mononucleosis the spleen was found enlarged by up to approximately 33% in the longitudinal diameter, reached the peak value after 12 days and decreased continually thereafter [(30)]. Most patients with infectious mononucleosis develop splenomegaly within the first 2 weeks of disease onset Very small echo poor lesions can sometimes be seen when using high frequency probes. Parenchymal bleeding and rupture of the organ are rare [Figure 7].

Figure 7 17 years old male 2 weeks after onset of symptoms of mononucleosis. Subcapsular bleeding of the mid and lower third of the spleen could be treated conservatively without surgery (a). Topographic ultrasound imaging (b).

a



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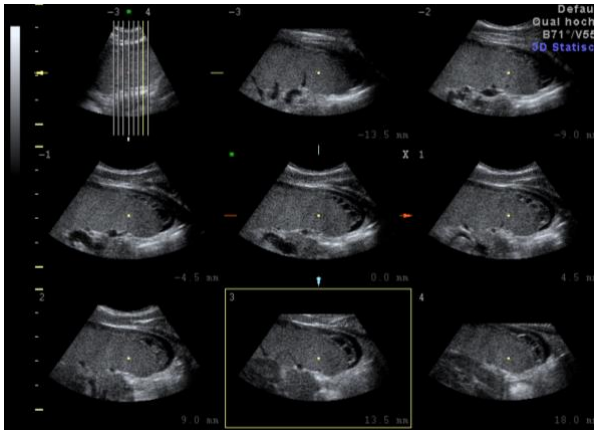
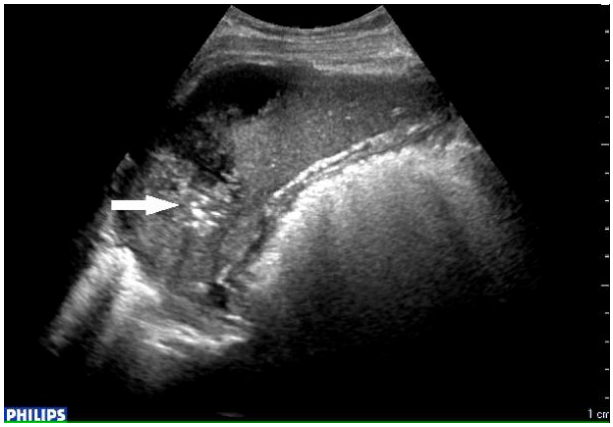


Splenic abscesses have been found in 0.14-0.7% of cases on autopsy [(31)]. Endocarditis, pancreatitis, sepsis and complication after surgery are the most common reasons for a splenic abscess [Figure 8].

Figure 8 Abscess caused by septic emboli in endocarditis, white arrow points to air bubbles within the spleen (a). The CEUS image demonstrates the perfusion defect and a big air bubble within the abscess (b).

a



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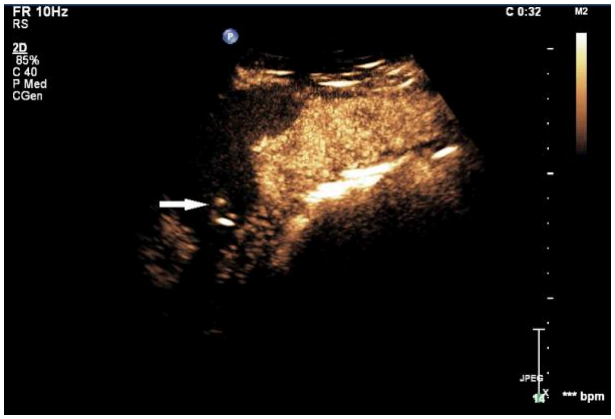


Spontaneous rupture of the organ is rare and in most cases is a complication of a splenic abscess.

Acquired Immune Deficiency Syndrome (AIDS)

Usually splenomegaly is the most common abnormal splenic finding in HIV infected patients. Data from literature shows more than a 50% frequency of splenomegaly on ultrasound examination [(32, 33)]. But focal splenic lesions can be also identified, caused by opportunistic infections (candida, mycobacterium tuberculosis, pneumocystis carinii) or due to non-Hodgkin's lymphoma (NHL), Kaposi sarcoma (KS) and cervical cancer [(34)].

On ultrasound examination focal splenic lesions are usually multiple and may appear as small, rounded hypoechoic and well-defined masses, or as tiny calcifications throughout the spleen. In candidiasis lesions may have bull's eye appearance [(35)]. In many cases patients may have multiple organ involvement (liver, spleen, kidneys).

Focal splenic lesions

Focal splenic lesions are rare. In comparison to the liver, only a few studies on CEUS in splenic lesions have been published. The most comprehensive study was published by Neesse et al [(36)] and reported between January 2004 and March 2009 about 50,000 abdominal ultrasound examinations performed, and only 279 (<0.6%) focal splenic lesions detected. The 279 patients (0.6%) with focal splenic lesions were diagnosed on B-mode sonography as follows: 72 cases (25.8%) splenic infarction, 57 cases (20%) non-Hodgkin's lymphoma, 51 cases (18.4%) splenic incidentaloma (incidentally detected focal splenic lesion, no history of tumour, infection or trauma, stable on follow-up examination), 35 cases (12.6%) splenic rupture, 7 cases (2.5%) splenic abscess, 25 cases (9.1%) miscellaneous splenic lesions (i.e., haemangioma, hamartoma) and 32 cases (11.5%) splenic metastases of solid tumours.

Besides the low number of cases, another limitation in the evaluation of splenic lesions is the difficulty in obtaining a histological confirmation of the CEUS diagnosis. In many cases the only references are radiological investigations (contrast-enhanced CT and contrast-enhanced MRI) and clinical evolution. Malignant splenic lesions mostly develop late in metastatic disease and are not usually an indication for puncture or surgery. In an autopsy study on 8,563 cases, 1,898 had a malignant disease (1,774 carcinomas, 36 sarcomas and 27 malignant melanomas). Metastasis to the spleen occurred in only 57 cases. Lung cancer, cutaneous malignant melanoma and breast cancer were the most frequent primary tumours, which accounted for 24.6%, 15.8% and 12.3% of all spleen metastases, respectively [(37)].

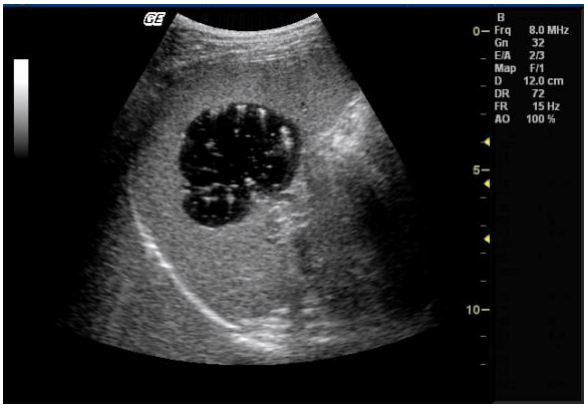
Focal splenic lesions can be single or multiple and occur in a normal or an enlarged spleen. They may have a benign (cysts or solid masses) or a malignant character (primary or secondary splenic lesions). The differentiation between benign and malignant focal splenic lesions can be difficult, even when using US contrast agents. The accurate diagnosis is very

important, because there are studies showing that hyperechoic incidentally found lesions are mostly benign, but the iso-hypoechoic lesions have a risk of being malignant in 34.3 % of cases [(38)]. CEUS is therefore of only limited benefit in these cases. According to the EFSUMB Guidelines, benign splenic lesions usually have no or a rapid wash-in in the arterial phase, followed by persistent enhancement lasting up to the late phase, while malignant nodules typically show a iso to weak diffuse or peripheral wash-in followed by rapid and marked wash-out [(39, 40)]. Just like in some hepatic haemangiomas, some benign splenic lesions as haemangiomas, hamartomas, granulomas and other more uncommon benign lesions may show a wash-out in late phase [(39)]. The EFSUMB consensus on this subject was published in the latest Guidelines on non-liver applications. CEUS is recommended for the triage of patients with focal splenic lesions. Lesions showing low-level arterial enhancement and progressive late-phase contrast washout usually require further investigations, imaging or biopsy, particularly in patients at risk for splenic metastases or malignant infiltrations from lymphomas [(40)].

Benign focal splenic lesions

Simple congenital splenic cysts (true epidermoid or false posttraumatic cysts) are rare and defined by the presence of an inner endothelial lining [(41)]. Congenital cysts include lymphangiomas and, very rarely, cystic haemangiomas [(42)], post-traumatic cysts (also called pseudocysts) have no cellular lining [(43)]. The walls of these cysts can become calcified. The cysts can contain low level echoes that can be cholesterol crystals or debris [Figure 9] [(44)]. Haemorrhagic cysts are partially or completely filled with very small echoes that may be disturbed when the patient changes position. Ultrasound cannot make a reliable differentiation between true cysts and pseudocysts [(2)]. There is no indication for CEUS in diagnosing cysts except when they appear as complicated. CEUS can then be used to prove the cystic nature by demonstrating the non-enhancement and further investigation is not needed.

Figure 9 Splenic cyst with internal echoes and calcification of the wall. Histology ruled out a hydatid cyst.



In addition to splenic cysts, there is a spectrum of lesions that have a predominantly cystic appearance at imaging. Cystic splenic masses may be congenital (true cyst) inflammatory (abscesses or hydatid cyst), vascular (infarction or peliosis), post-traumatic (haematoma or pseudocyst) or neoplastic (benign, haemangioma or lymphangioma; or malignant, lymphoma or metastasis) [(41)].

Isolated splenic peliosis is extremely rare [(45)] and occurs in less than 1% of autopsy cases [(46)]. It is characterized by the presence of multiple cyst like, blood-filled cavities within the splenic parenchyma. These cysts vary in size and may or may not contain an endothelial lining. Thrombosis within the blood-filled spaces can also occur [(47)]. The aetiology of splenic peliosis is unknown, although it may be associated with malignant haematological diseases (such as Hodgkin's disease and myeloma), disseminated cancer, tuberculosis, use of anabolic and contraceptive steroids and certain viral infections [(48)].

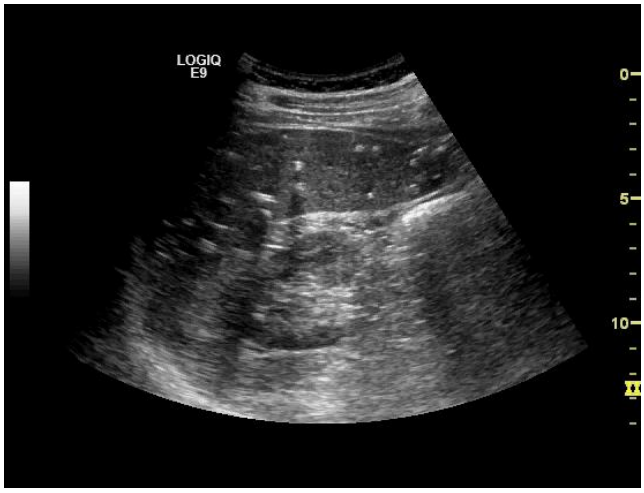
Ultrasound examination shows multiple hypoechoic or hyperechoic lesions without sharply demarcated borders; these lesions may occupy the entire spleen [(41)]. CT similarly shows multiple low-attenuation foci. The enhancement pattern is similar to that of haemangiomas [(49)].

Patients with splenic peliosis are usually asymptomatic and the disease is detected incidentally from imaging studies or at autopsy. Complications arise when peliotic lesions rupture. This can occur spontaneously, probably due to intrinsic pressure effects, or because of extrinsic trauma. The resulting intraperitoneal haemorrhage can be fatal [(47, 50, 51)],

Parenchymal calcifications are a quite common and non-specific finding. Their size may vary [Figure 10 and 11]. Splenic calcification can be secondary to splenic metastases, chronic infarction, tuberculosis and granulomas.

Figure 10 Splenic calcification without finding a clinical explanation (a). The contrast image demonstrates a normal splenic circulation during the wash in phase (21 s post bolus injection) (b).

a



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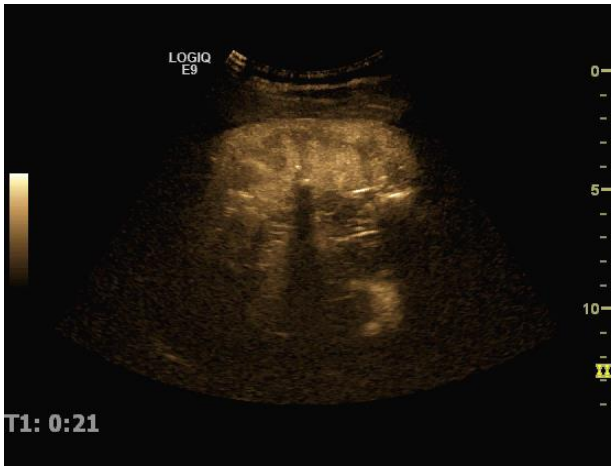
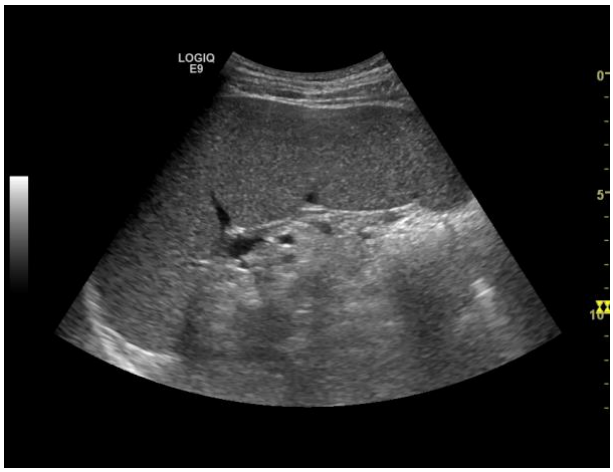


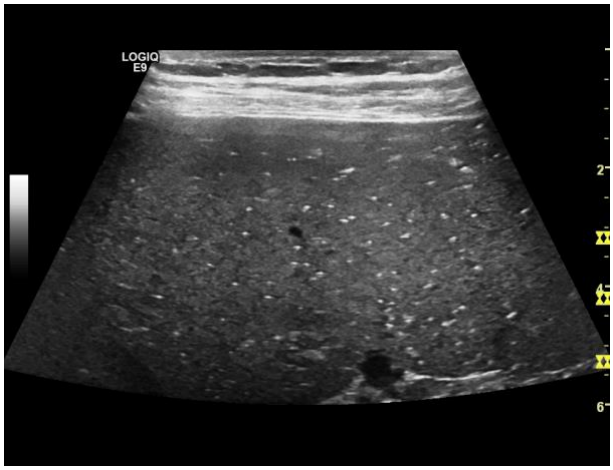
To detect small splenic lesions it is also recommended to use a linear high frequency probe [Figure 11 and 24].

Figure 11 Moderate splenomegaly with tiny calcifications (a), best seen when using a high frequency probe (9MHz linear probe (b)).

a



b



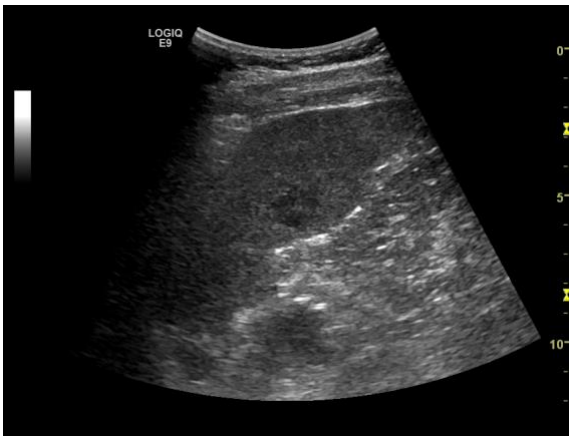
In B-mode ultrasound splenic lesions can be described as hyper, iso or hypoechoic when compared with the surrounding normal tissue.

Benign primary tumours of the spleen are rare and include hamartoma, haemangioma and cystic lymphangioma. Splenic haemangiomas have been reported in up to 14% of autopsy studies [(52, 53)]. They can appear isolated or can occur in the Klippel-Trenaunay-Weber syndrome [(54)]. There is no specific finding for haemangiomas. The majority are homogeneously echo rich, less than 2 cm and well defined. On CEUS haemangiomas consistently homogeneously iso-enhance. An hyperechoic lesion on baseline images that becomes undetectable on enhanced scans is diagnosed as a haemangioma [(10)].

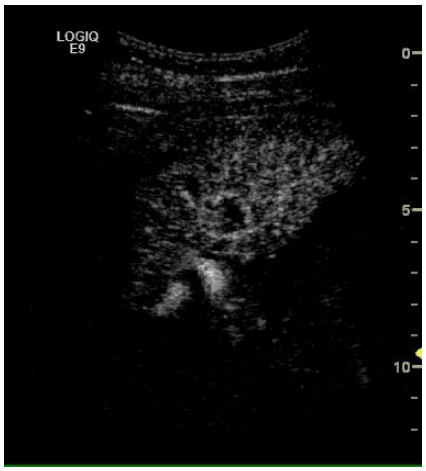
Larger, cavernous haemangiomas (> 3 cm) can appear as iso to hypoechoic and with cystic changes or calcification [(55)]. They show more enhancement, with rapid or slow opacification. Filling can be centripetal or diffuse. Contrast enhancement is very pronounced and prolonged, with possible shadowing in larger haemangiomas [(12)]. Occasionally spoke-wheel enhancement or lower uptake in the parenchymal phase can be seen [(55)]. In a minority of cases haemangiomas rapidly enhance with a centripetal direction of enhancement [Figure 12].

Figure 12 Echo-poor 14 mm splenic lesion (a). Typical contrast kinetics of a splenic haemangioma (b-d). The centripetal filling starts at 18 seconds and is finished 10 seconds later.

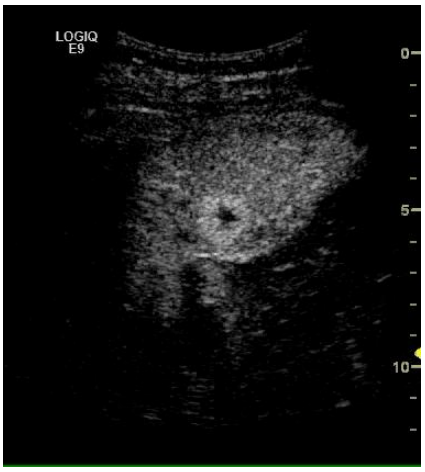
a.



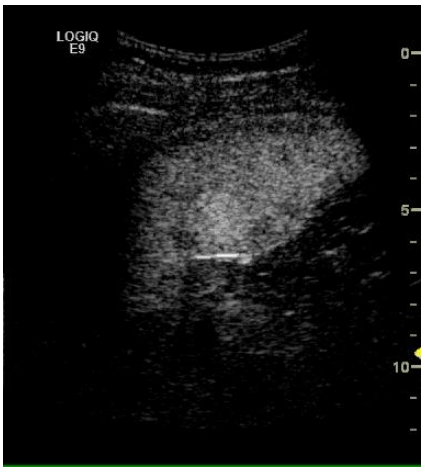
b.



c.



d.



Benign lesions are usually echo rich. Lesions that do not washout or only do so a little can be regarded as benign. The most common causes are previous granulomatous infections, such as histoplasmosis, tuberculosis or sarcoidosis [(56, 57)]. Usually multiple hyperechoic foci can be seen diffusely throughout the spleen and can be associated with calcification in the splenic artery [(2)].

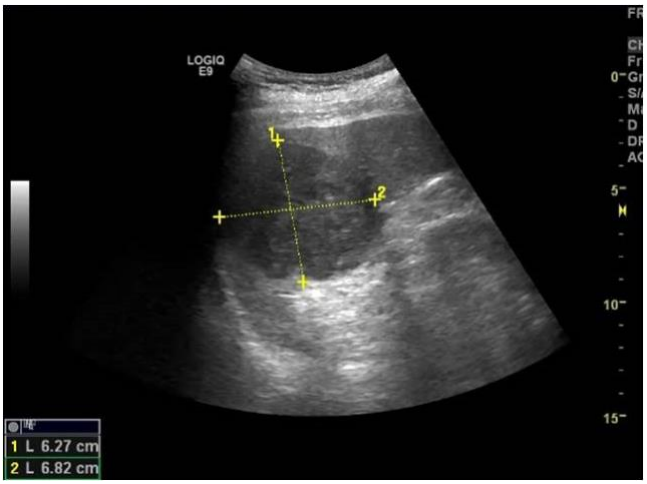
In active tuberculosis multiple, small, hypoechoic splenic lesions or small cystic lesions, which represent tuberculous abscesses can be seen [(2)]. On CEUS, the lesions progressively enhance less and lesion-to-parenchyma contrast increases in the parenchymal phase [(55)].

Splenomegaly in sarcoidosis can be correctly described by B-mode ultrasound in more than 50% of cases, whereas clinical examination identifies only a small percentage of cases [(58)]. Sarcoidosis may cause multiple, echo-poor, round infiltrations that progressively washout

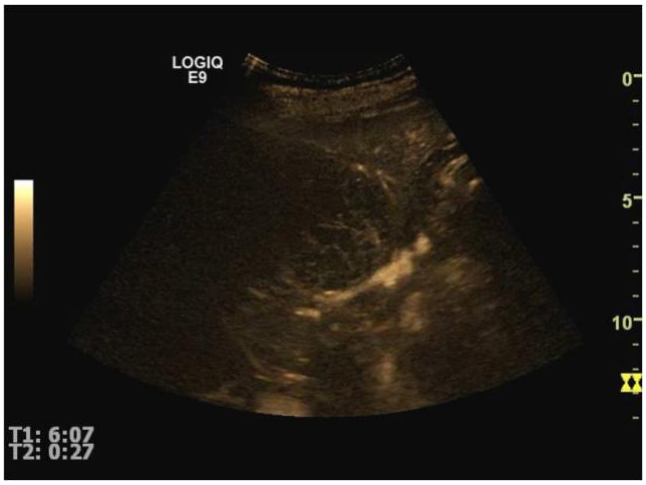
like malignant tumours [(58, 59)]. In granulomas of the spleen no specific findings on B-mode ultrasound or CEUS can be seen [Figure 13 a-d].

Figure 13 Echo-poor unique heterogenous 6.5 cm splenic lesion, incidental finding (a). Diffuse arterial enhancement, with anechoic areas inside (b). Marked venous washout, suggesting a malignant lesion (c). Histological exam after splenectomy diagnosed rare nonspecific inflammatory granuloma (d).

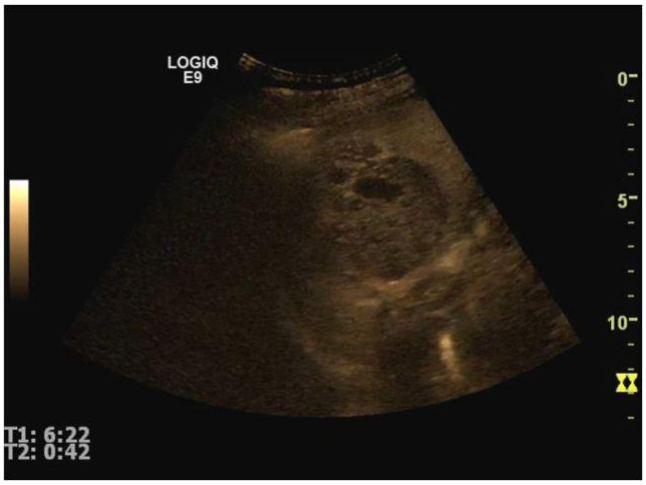
a



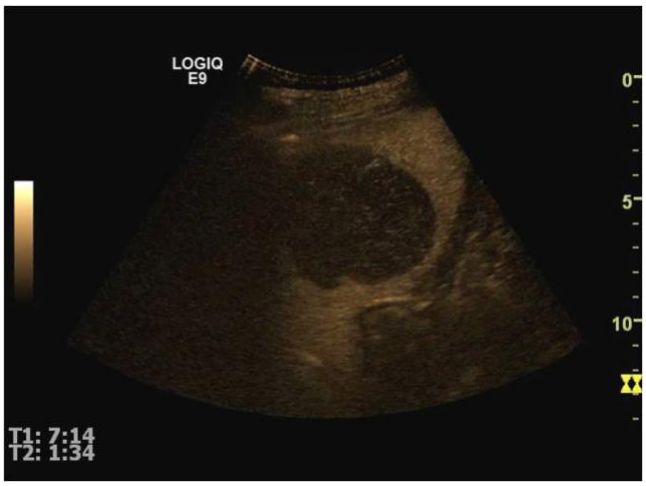
b



c



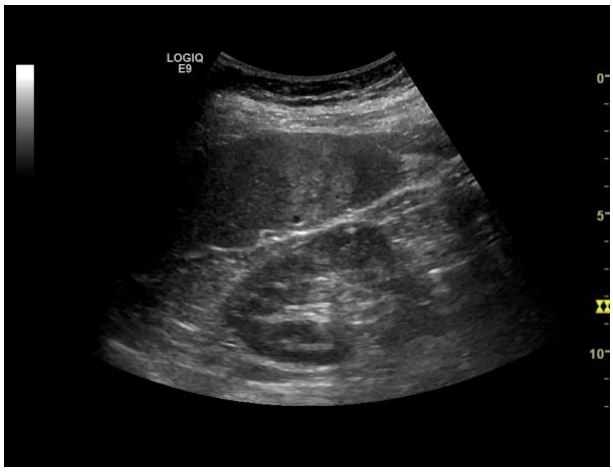
d



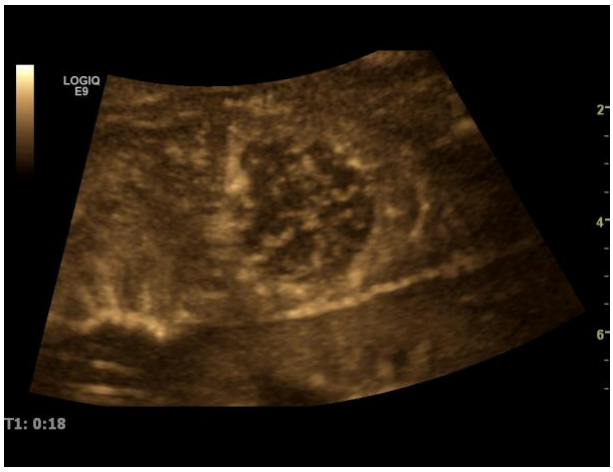
On ultrasound examination, hamartoma has both solid and cystic components, and generally appears hyperechoic [(60)]. Splenoadenomas (or harmatoma) of the spleen may show the typical stellate pattern on CEUS [Figure 14].

Figure 14 Splenoadenoma: echo-rich lesion in B-mode (a), stellate vessel architecture in the arterial phase, reminding on FNH of the liver (b). Later wash out (healthy 35-year-old female, incidental finding).

a



b



Ultrasonographic appearance of lymphangioma is shown as a multicystic mass that replaces splenic parenchyma [(57)].

Hydatid disease

Hydatid disease primarily affects the liver and secondary involvement as a result of haematogeneous dissemination may be seen in almost any anatomical location. Thus, splenic involvement is uncommon in patients with hydatid disease [(61)] and baseline ultrasound shows a similar appearance regardless of the location of the hydatid cyst. On CEUS the lesion is constantly non-enhanced.

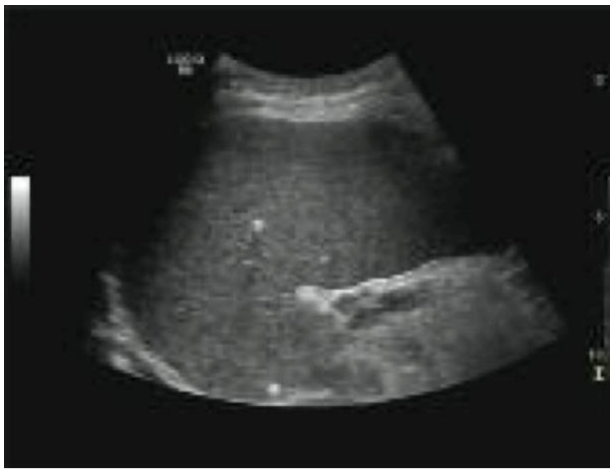
Malignant splenic lesions

Lymphomas

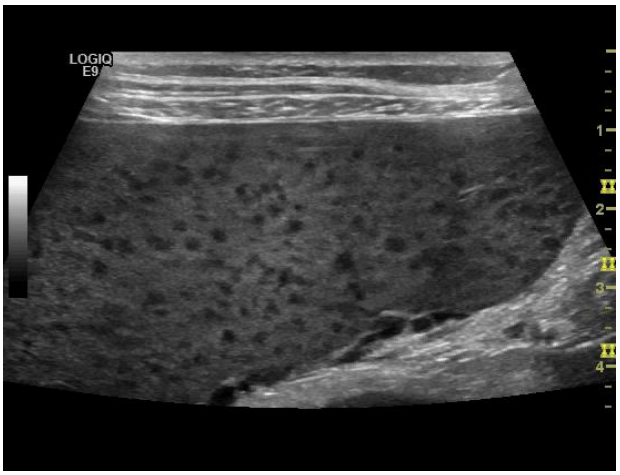
Splenic involvement in Hodgkin or non-Hodgkin's disease is the most common cause of focal splenic lesions. Gorg published a retrospective study in 2009 and found that in 41 of 250 cases with a variety of lymphatic diseases the spleen was involved, but CEUS did not increase the number of detected focal splenic lesions and was therefore not superior to B-mode imaging [59]. In contrast to this study, Picardi found, in a study of 100 patients with Hodgkin's disease, that CEUS was the most sensitive imaging modality to detect splenic involvement and was superior to CT and FDG-PET. The lesions were described as echo-poor and mostly hypo-enhancing on CEUS, a small number were iso-enhancing during the arterial phase, but washed out over time [(62)]. The size of the lesions can vary; they are often multiple, with small lesions less than 1cm [Figure 15]. This is why very small lesions can be detected most effectively by using high linear frequency probes.

Figure 15 Small leukemic infiltrations of a moderately enlarged spleen (a), best seen when using a high frequency probe (9 MHz) (b).

a

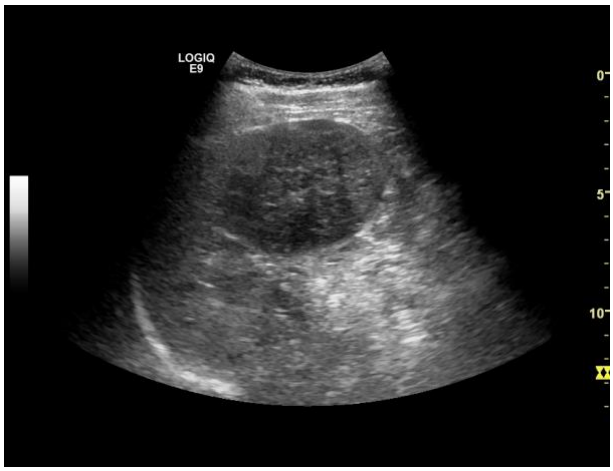


b



The detection of splenic involvement in this disease is of clinical relevance because it may change the therapeutic approach. Small lesions in non-Hodgkin's lymphoma can be overlooked even on CEUS because the microvasculature does not differ from the non-infiltrated tissue. In other cases, the lesions are hypovascularised even during the wash-in phase and may completely wash-out overtime [Figure 16].

Figure 16 Mantle cell lymphoma causing a large infiltration of the lower splenic pole.



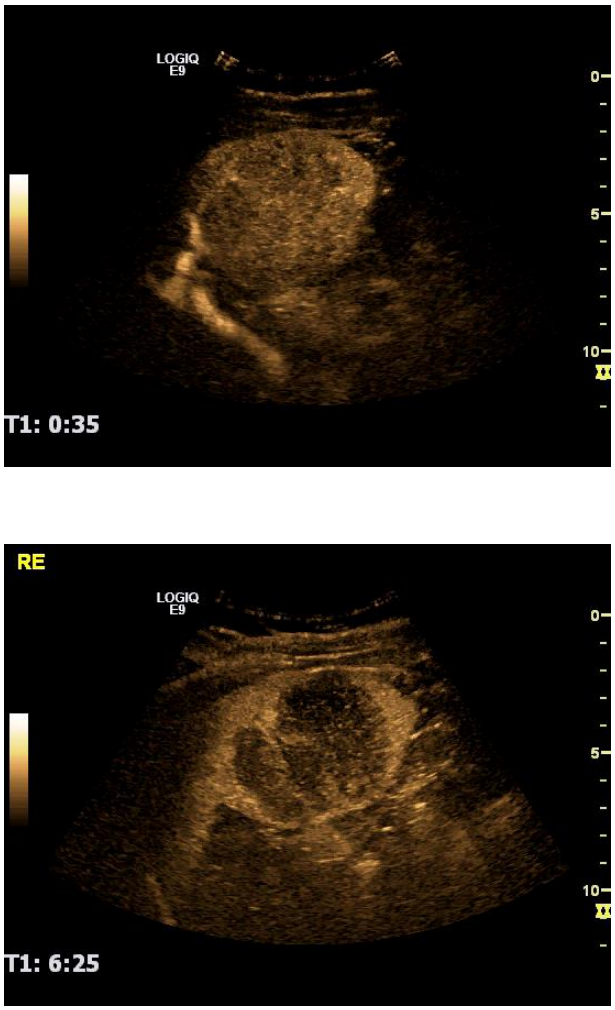
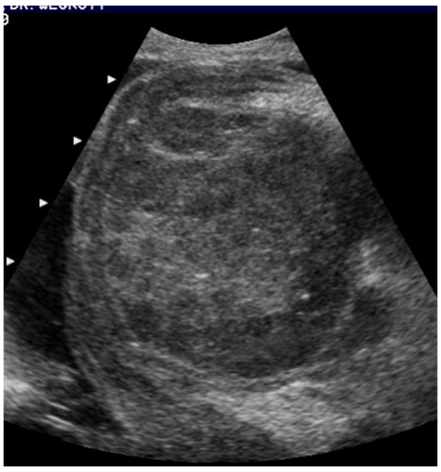
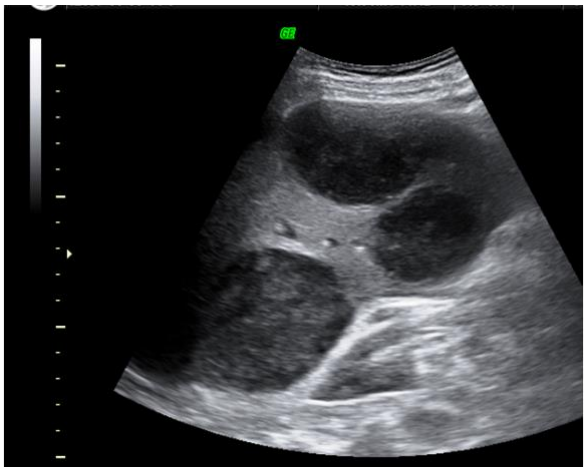
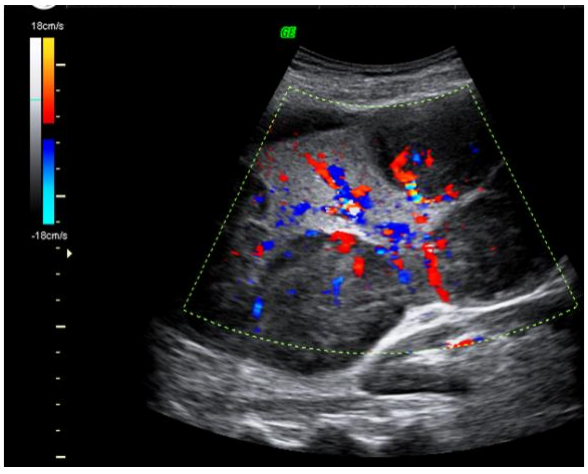


Figure 17 a shows a more diffuse type of a Burkitt lymphoma infiltration, (b) and (c) are large infiltrations in a B-non-Hodgkin's lymphoma.

Figure 17 More diffuse infiltration of the spleen in a patient with far advanced Burkitt lymphoma (a). Large echo-poor infiltrations in a B-NHL (b). Same patient, colour Doppler image (c).






18cm/s
-18cm/s

Primary neoplasm of the spleen

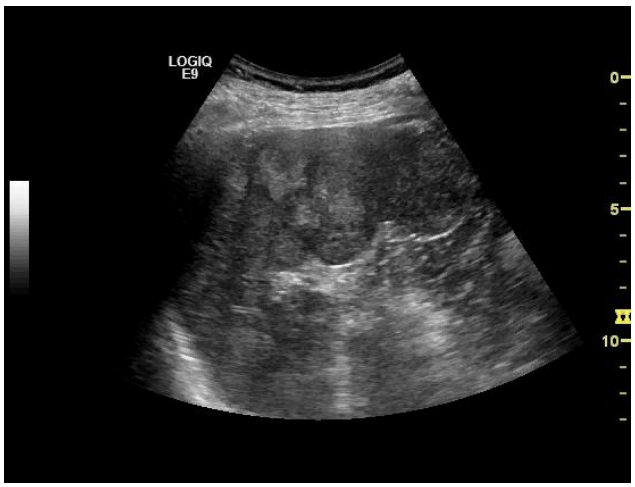
Primary splenic tumours, like haemangiosarcomas, are very rare.

Metastases

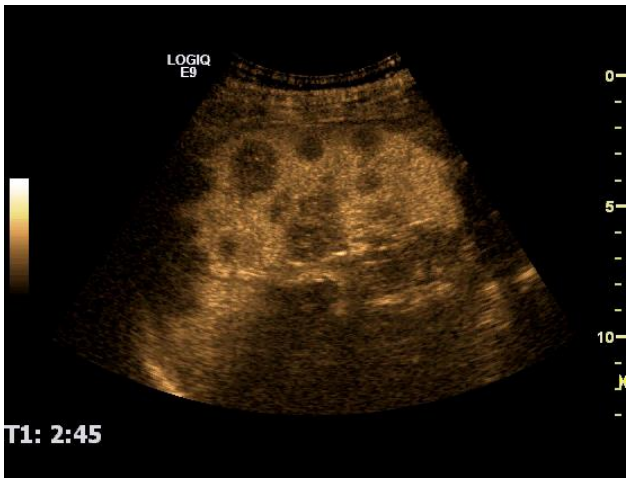
Splenic metastases are usually seen in very advanced malignant diseases, except in patients with testicular germ cell tumours and small cell lung cancer in which the spleen can be the only abdominal organ showing a metastatic spread [Figure 18].

Figure 18 Multiple echo rich splenic metastases with an echo-poor halo (malignant melanoma) (a). The spleen was the only solid organ in which metastases were found at that time, CEUS (b).

a

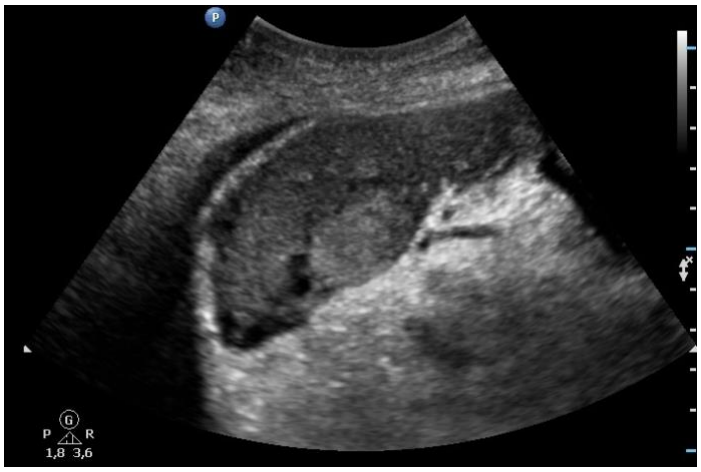


b



Mostly splenic metastases have an echo-poor appearance, but echogenicity alone is not a reliable sign for the lesions character [Figure 18]. In patients with testicular germ cell tumours, 4 of the 9 patients had splenic metastasis; in malignant melanoma patients, 9 of 27 had spleen metastasis; and 8 of 106 small cell lung cancer patients had spleen metastasis [(37)]. In the majority of cases a biopsy is not required because proof will not change the clinical management of these patients. Metastases are usually echo poor with no or only a little tumour vasculature on colour flow imaging. On CEUS the lesions are hypo enhancing and washed out quickly [Figure 19].

Figure 19 Hypovascularised echo-rich metastasis of an advanced liposarcoma in B-mode, CFI and CEUS (at 1.30 min).



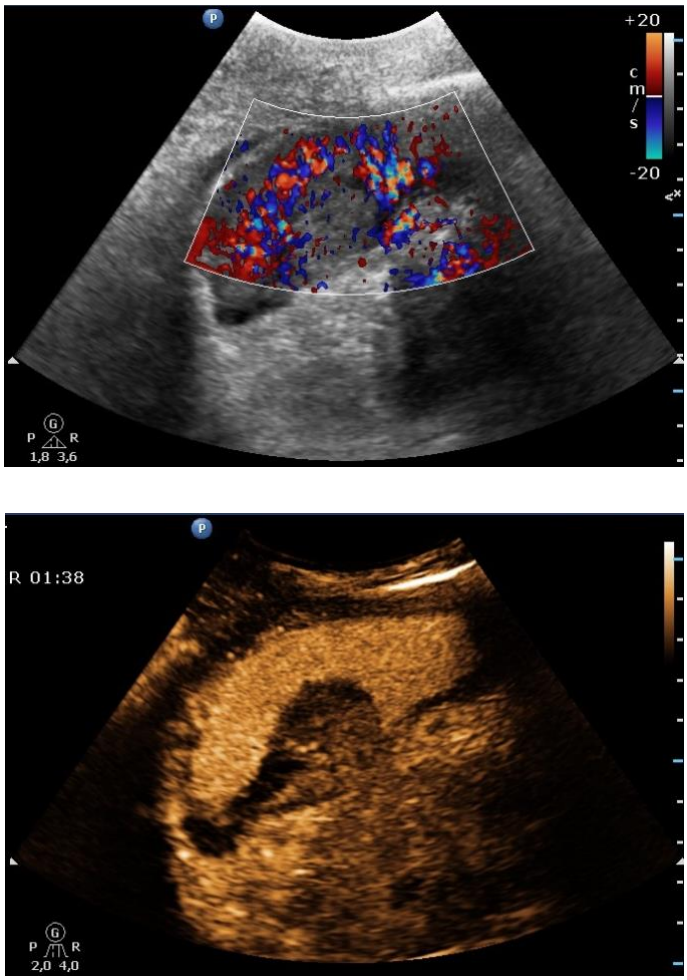
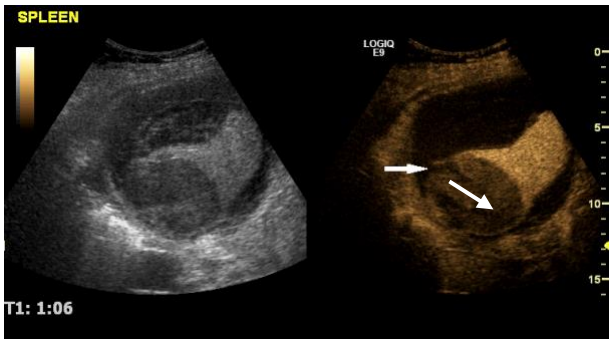


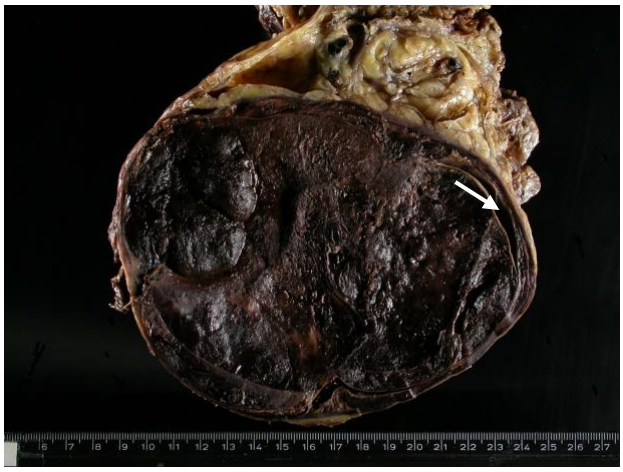
Figure 20 shows the CEUS finding of a patient with spontaneous rupture of an intra-splenic metastasis of malignant melanoma. A spontaneous rupture is an extremely rare event. It is associated with a high mortality rate within 30 days in patients with malignant disease. Sonomorphological grading is helpful for treatment decisions. A 30-day mortality rate is correlated with neither ultrasound grade nor surgical treatment rates [(63)].

Figure 20 Acute onset of left flank pain due to a ruptured metastasis of a malignant melanoma (a). Arrow points to the site of tumour rupture. The gross specimen is shown as well (b).

a



b

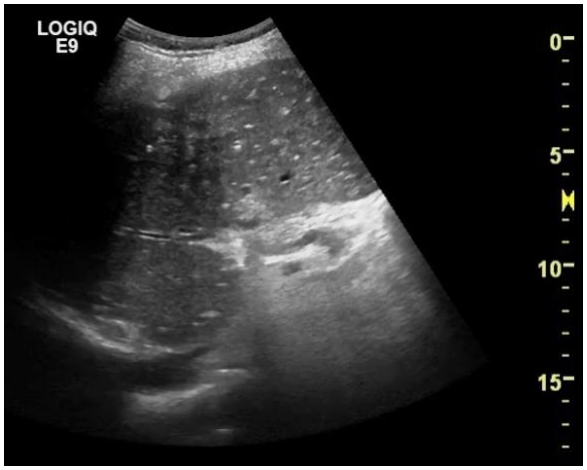


Vascular disease

Infarctions of the spleen are common. These are caused by embolic or thrombotic occlusion of splenic branches. Splenic infarction can have variety if aetiologies; most are caused by embolism or dissection of its supplying arteries. Pancreatitis, leukaemia, lymphomatous disorders, sickle cell anaemia, sarcoidosis or polyarteritis nodosa may also cause splenic infarctions [(64, 65)]. Multiple small splenic infarctions have been found in patients with systemic lupus erythematosus with long history of disease [Figure 21 a,b].

Figure 21 **46 year old female with SLE, with 21 years history of disease. Multiple small hyperechoic foci (calcifications) and a typical old infarction in the median part of the spleen can be seen (inhomogeneous, ill-defined area, capsular retraction) (a). Colour Doppler examination (b).**

a



b

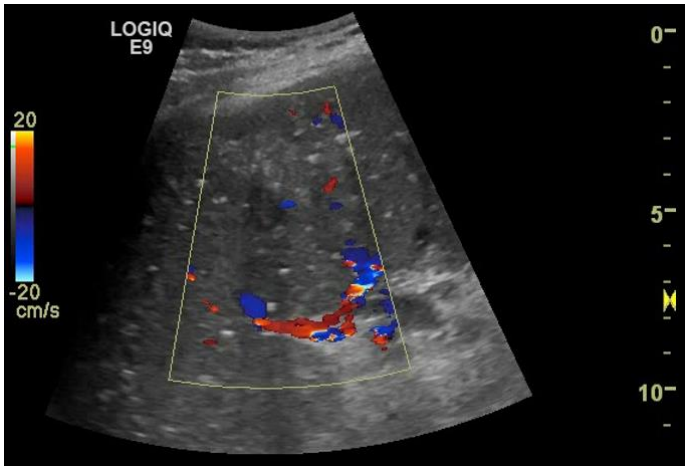
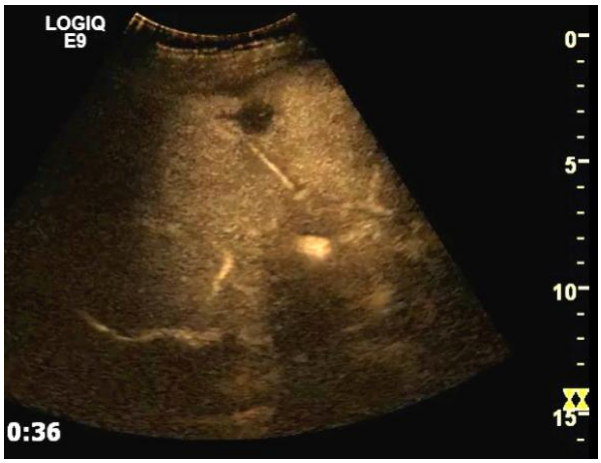
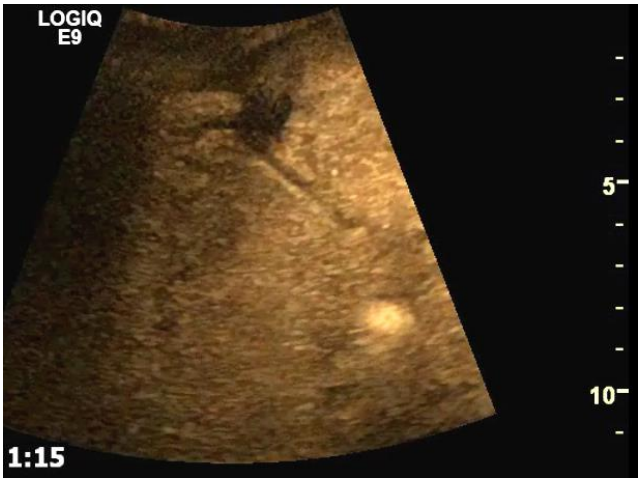


Figure 22 **Same patient as in Figure 21, CEUS exam shows the artery abruptly interrupted, in relation with the infarction apex. Arterial phase (a); venous phase (b).**

a



b

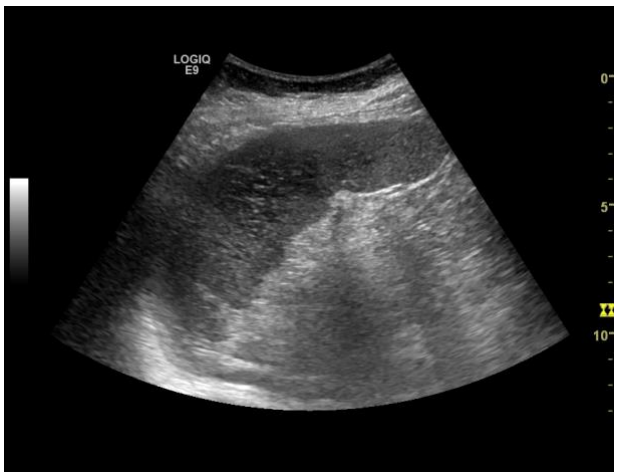


The sonographic appearance of splenic infarction can vary depending on the time of examination. Acute splenic infarctions differ in size, but these echo-poor lesions within the tissue always reach the capsule. In B-mode or CFI, arterial infarction of the spleen, especially if small, is not always seen and its volume is often underestimated [Figure 23]. Infarcted areas appear on B-mode as slightly echo-poor and are not always sharply delineated. Over time, fibrosis progresses and the lesions become hyperechoic, have a wedge-shaped appearance, with the base toward the sub-capsular surface of the spleen and capsular retraction, or are nodular. It has been proven that the echogenicity of the infarction is related to the age of infarction [(66-68)]. Acute or chronic, on baseline examination the lesions appear ill-defined and their real extension is difficult to appreciate. Occasionally, only an inhomogeneous area inside the spleen is found.

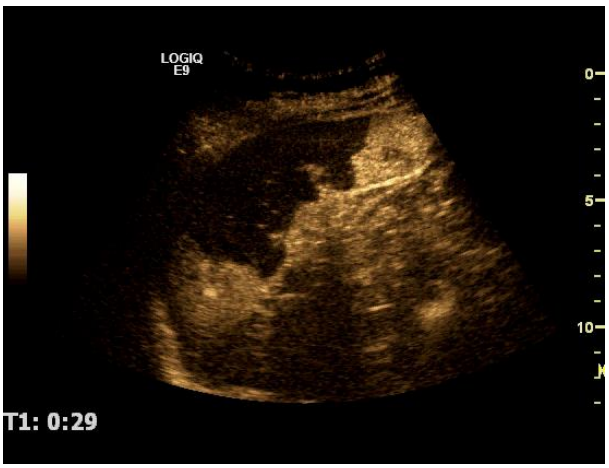
CEUS examination significantly improves the diagnosis. The infarcted areas are avascular after contrast injection [Figure 23]. The margins can be well- or ill-defined, and the structure can be homogeneous or inhomogeneous. No enhancement can be seen within the lesion. Sometimes an abruptly interrupted enhanced artery can be seen on early phase scans in relation to the infarct apex, whereas a small enhancing rim can be noted on avascular area margins [Figure 22]. Atypical infarcts, sometimes resembling focal lesions on baseline scans are readily diagnosed because of absent enhancement.

Figure 23 Typical B-mode appearance of a splenic infarction (a), in CEUS the avascular volume is much bigger than expected (b).

a



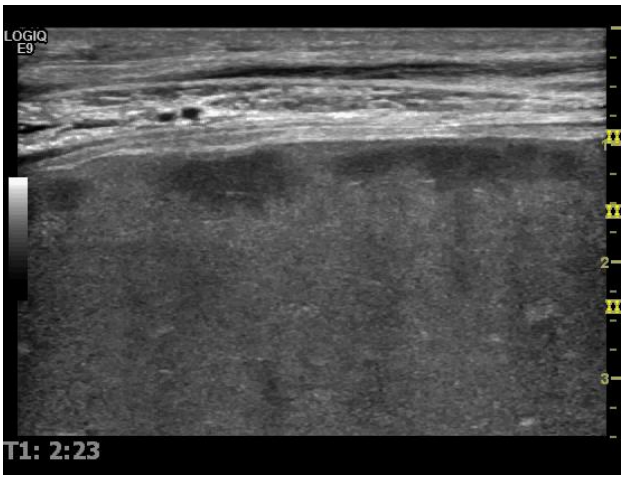
b



In splenomegaly of patients with systemic diseases subcortical infarctions will cause a sudden onset of pain and CEUS will demonstrate regional perfusion defects [Figure 24].

Figure 24 72 year old male with leukaemia and a severe splenomegaly of 25 cm. The patient could navigate the transducer to the site of maximum pain and thus the subcapsular infarction.

a



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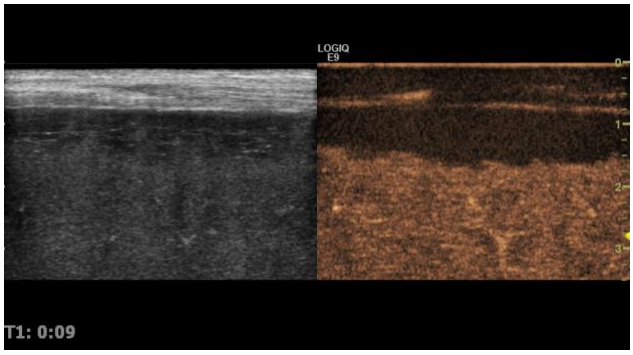
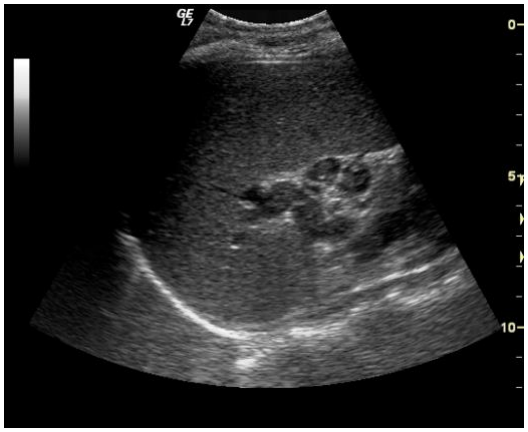


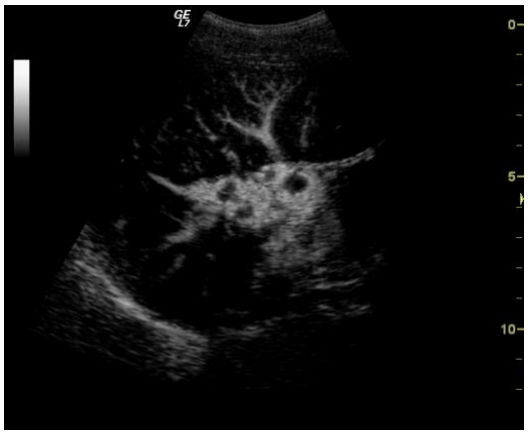
Splenic vein thrombosis is common in patients with pancreatic disease or in sepsis [Figure 25]. B-mode ultrasound and colour Doppler often fail to reliably diagnose a partly or complete occlusion of the splenic vein. In comparison, CEUS has much higher diagnostic confidence.

Figure 25 24 year old drug addict female with thrombosis of the portal and splenic vein. The spleen is moderately enlarged - B-mode appearance (a). The veins in the hilum show clot still surrounded by flowing blood - B-flow image (b).

a



b



Trauma

After studies that showed the efficiency of emergency ultrasound scans in blunt abdominal trauma patients, performed by physicians of different levels of training [(65, 69-72)], the FAST protocol (Focused Assessment of Sonography in Trauma) is now commonly used to detect or exclude the presence of free fluid in the pericardium or in the abdomen in cases of trauma.

In clinically stable patients, the role of the FAST technique is controversial [(73-76)]. In these cases, contrast-enhanced CT is the modality of choice for evaluation of parenchymal lesions. But the specificity of contrast-enhanced CT decreases in lower trauma, contusions, oedema or thin lacerations that can be missed or exaggerated on CT. The use of CEUS may partially overcome this limitation [(73, 77-80)].

Although a CT scan is particularly useful in trauma because more upper abdominal pathology can be identified in a single examination [(81, 82)], ultrasound proves its efficacy and accuracy to exclude or prove parenchymal damage in blunt trauma, especially when using CEUS. Ultrasound is fast, portable and easily integrated into the resuscitation of the patients with trauma without delaying therapeutic measures [(71)]. Routine abdominal ultrasound can be performed at the bedside in trauma centres. The use of screening ultrasound can improve clinical-decision making for the use of emergency laparotomy [(64, 65)].

In the same way as in other solid organs, the sonographic appearance of the spleen depends on the amount of tissue damage and the time delay between the trauma and the first ultrasound examination. Immediately after a trauma incident, the haematoma appears hypoechoic and can be easily differentiated from splenic parenchyma. But, within the first few hours, an intrasplenic haemorrhage may not be visible at all; haematoma develops a nearly isoechoic appearance with inhomogeneous areas within. Depending on the volume of haemorrhage, the spleen can be enlarged and cause local pain. Over the following days, haematoma becomes slightly hypoechoic due to reliquefaction. Finally, subcapsular or pericapsular haematoma can be differentiated as clearly hypoechoic areas. Because the splenic capsule is very thin, important information about the integrity of the capsule can be collected by analysing the form of the fluid collection. If the collection is crescent and conforms to the contour of the spleen, it can be presumed that the haematoma is subcapsular. If the collection is irregularly shaped, perisplenic haematoma is likely [(83)] [Figure 26 and 27].

Figure 26 B-mode image of a patient with atrial fibrillation and warfarin treatment. Acute intrasplenic bleeding after a minimal blunt trauma.

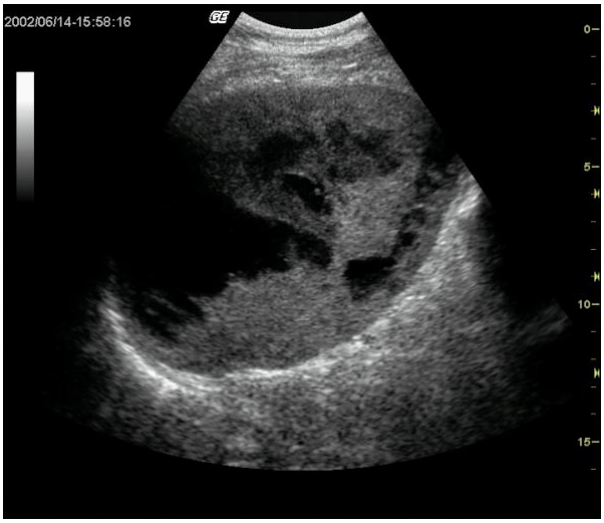
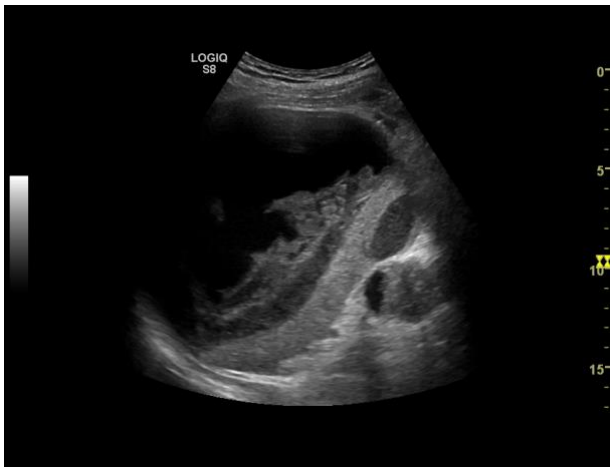
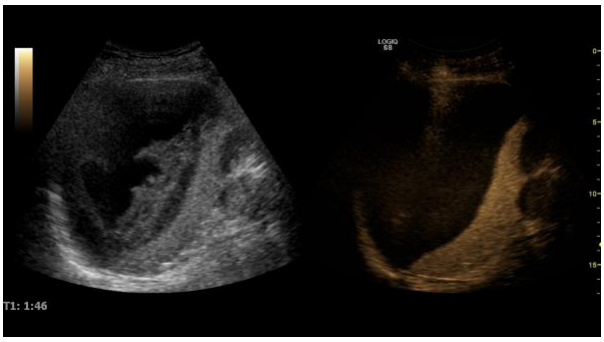


Figure 27 CEUS can evaluate the viable part of the spleen and can exclude active bleeding (B-mode (a) and CEUS (b)).

a

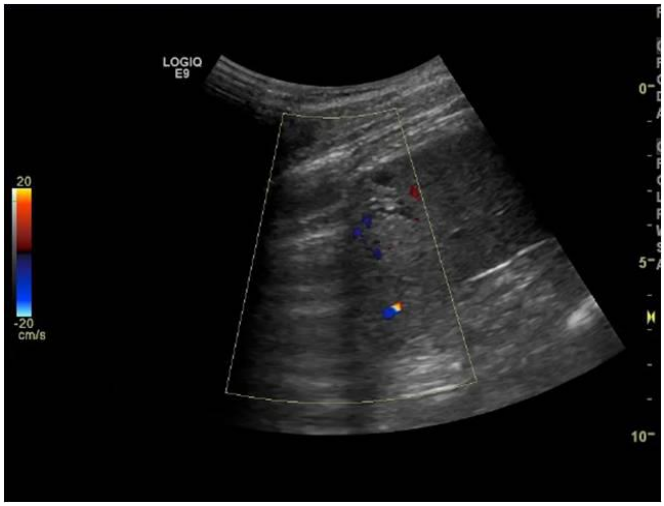


b



When the spleen recovers, it may contain small irregular foci or the parenchyma may have a homogeneous B-mode appearance again. Occasionally at a later scan, a cyst can be seen at the site of the haematoma. CEUS is the most sensitive ultrasound technique to show minor defects during the follow-up of splenic trauma [Figure 28].

Figure 28 B-mode and colour Doppler image of old trauma in young patient. Peripheral "wedge-shaped" image and small cysts.



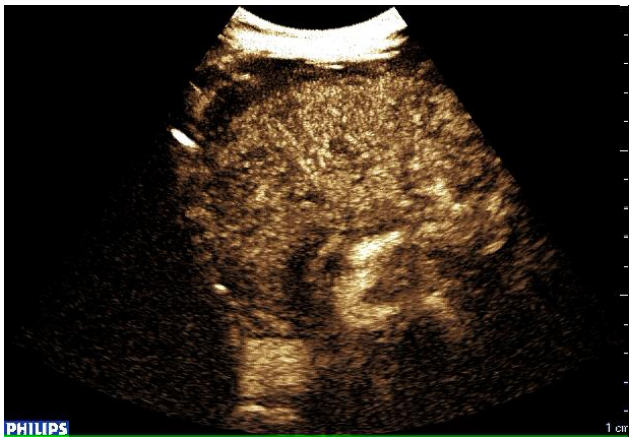
B-mode ultrasound has a poor detection rate in blunt splenic injury, especially when imaging minor tissue damage. In a report of 162 patients with blunt splenic injury, ultrasound could detect only 19% of cases [(69)]. Other data have reported up to 40% of patients without free fluid have parenchymal damage. B-mode ultrasound is therefore not recommended in assessment of stable trauma patients [(84)].

It has been reported that patients who have suffered low energy blunt trauma may have undetected injuries on contrast-enhanced CT [(85)]. In these cases, considering the disadvantages of contrast enhanced CT (exposure to ionising radiation and injection of iodinated contrast material), especially in children, CEUS should be considered as a diagnostic alternative. To avoid unnecessary contrast enhanced CT to be performed for follow-up during conservative treatment of splenic trauma, CEUS is a reliable alternative [(85)].

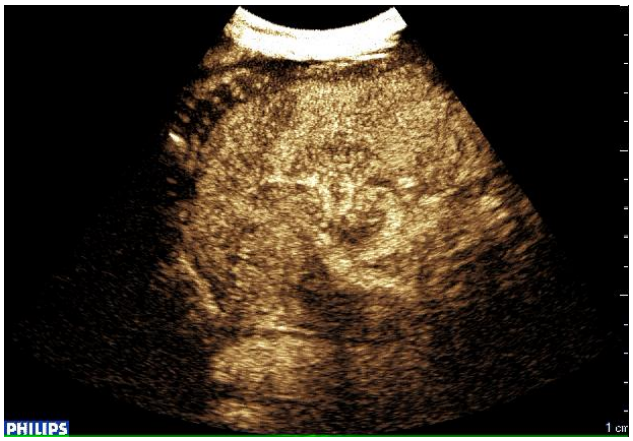
Blunt parenchymal trauma can cause various injuries, such as lacerations, contusions, haematomas, capsule rupture and vessel tears of varying severity [(84)]. They appear as opacification defects visible in all circulatory phases of the organs. Necrotic parenchymal areas appear non-enhanced and sharp-edge delineated. Lacerations appear as clearly hypoechoic bands linear or branched, which are usually perpendicular to the spleen surface [(73)]. Contusion appears as ill defined, slightly hypoechoic areas, with varying degrees of decreased perfusion due to crushing rather than tearing of the parenchyma. Presumably, the less intact the perfusion, the worse and more vulnerable is the contusion injury [(73, 84)]. Lacerated areas and parenchymal haematomas appear without mass effect or vessel displacement [(Catalano, 2004 #87)]. Haematomas appear, after the bleeding has stopped, as non-enhanced sharp-edge delineated areas. In cases of active bleeding, contrast extravasations can be seen as an early-phase hyperechoic pool or a jet within the splenic parenchyma or perisplenic haematomas [(73)] [Figure 29]. Partial hypoperfused areas (post traumatic infarctions) appear as wedge-shaped or polar hypoechoic tissue segments. In cases of pedicle avulsion or severe hypovolaemia (or "shock spleen") total or subtotal lack of enhancement is detectable. In cases of shock spleen overall parenchymal enhancement is poor, less than expected and less than the adjacent left kidney.

Figure 29 CEUS in acute bleeding. During the early arterial phase the small echo-free peri-splenic space starts to take up a few bubbles (b), indication a perforation.

a



b

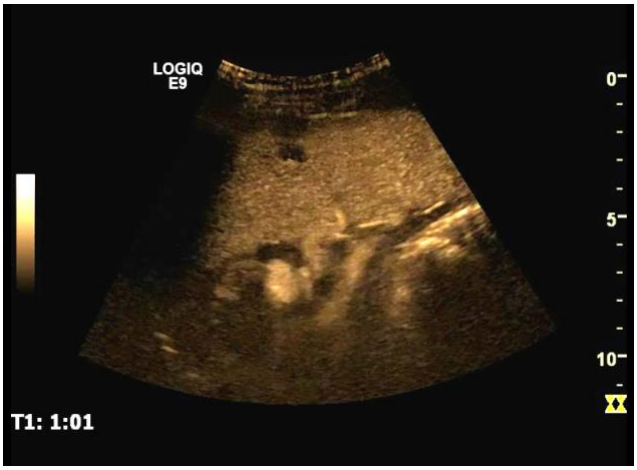


For the left side trauma, smaller doses of ultrasound contrast agents than in regular liver studies (half to a quarter) are recommended [(85)]. After the bolus injection the left kidney is examined immediately and continuously until the end of the homogeneous phase, that lasts 3 min. The transducer is then moved for scanning the spleen. For the spleen, the homogeneous phase lasts more than 5 min. Owing to the parenchymal uptake of the spleen, there is enough time for an extensive examination and a second injection of CA is rarely necessary. The second dose, if necessary, should be lower than the first.

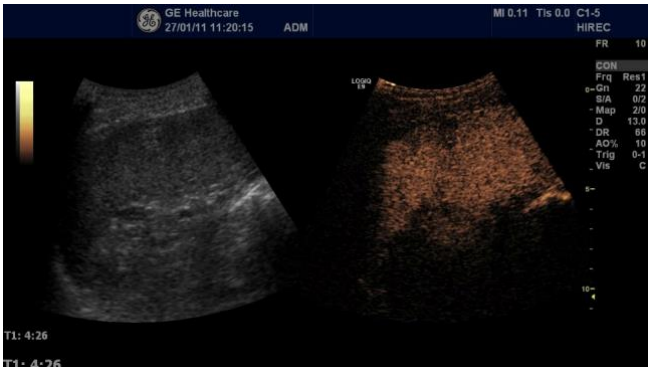
Excessive CA dose creates over saturation with attenuation in the deeper parts of the spleen that may hide thin traumatic fissures. A so called "glare artefact" may appear distal to the spleen, which creates stable enhancement within renal cysts located distal to the spleen. It can therefore mimic a diffuse zone of "bleeding" of the contrast echo into structures immediately adjacent to enhanced parenchyma.

Figure 30 Late posttraumatic follow up in a young patient, a. CEUS exam, homogenous phase: anechoic peripheral "wedge shaped" area. b. After "flash" another hypoechoic peripheral "wedge shaped" area can be seen closely the first area, suggesting posttraumatic hypo-vascularised area.

a



b



The doses have not been established in children and depend on the machine used; however, we recommend the following formula:

Dose (millilitres) = patient age (years)/10 for the liver

and half that dose for the spleen and kidneys, but not below 0.1 ml [(84)].

In detection of perisplenic fluids the sensitivity of CEUS is less than contrast enhanced CT and only slightly superior to ultrasound, especially for small amounts of fluid. In a preliminary study, Catalano et al reported a detection rate of 73% with CEUS, which is lower than for other organ injuries and not different from the ultrasound detection rate [(73, 86)].

The most recent published study (2011), reported a good detection rate of perisplenic fluids, but inferior to contrast-enhanced CT (11 from 13 patients detected on contrast-enhanced CT). The reasons for these failures were thought to be the minimal amount of fluid and the deep localisation that caused it to be confounded with intra-abdominal fat due to the limited penetrability of low-mechanical index ultrasound that make the deep lesions to be difficult to detect [(86)]. These two factors were also reported by other CEUS trauma studies of retroperitoneal lesions in which the detection rate of perisplenic fluids was reduced to 69% [(87-89)]. On the other hand, owing to its relatively low perfusion, fat appears almost anechoic on CEUS in the same way as free fluid or haematomas [(86)], the reference image or baseline B-mode helps to differentiate fluid from fat.

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