Contrast-Enhanced Ultrasound (CEUS) in Non-Traumatic Abdominal Emergencies

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ABSTRACT

Conventional ultrasound imaging (US) is the first-line investigation in acute non-traumatic abdominal emergencies, but sometimes it needs further examinations, such as computed tomography (CT), to reach a certain diagnosis. Contrast-enhanced ultrasound (CEUS), through injection of contrast medium, may provide the radiologist with additional information that could not be investigated with baseline US. It could help reach a diagnosis and rapidly determine the proper therapy in an emergency setting. The purpose of this review is to explain and illustrate the various possibilities and limitations of CEUS in acute non-traumatic abdominal diseases, in particular acute inflammation, parenchymal infarcts, and hemorrhages.

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In an emergency setting, ultrasound (US) imaging is the first-line approach, and it has a fundamental role in detecting and diagnosing various acute abdominal pathologies [1–3]. The many applications of US imaging in the study of abdominal diseases make US examination a versatile modality. Nevertheless, standard US imaging has several limitations in characterizing anatomic structures and vascularized lesions. Contrast-enhanced ultrasound (CEUS) is a technique that uses specific contrast agents that can improve the characterization of anatomical structures through the visualization of small vessels and microcirculation [4–7].

CEUS contrast agents are microbubbles made of a gas core and a stabilized biological shell. The second generation of sonography contrast media is a solution prepared very quickly and it is immediately administrable. CEUS has the benefit of a high temporal resolution and the operator can detect the contrast transit in the arterial, portal-venous, and late phase. The arterial phase starts 10 sec after injection and lasts 25 – 30 sec. The portal-venous phase starts immediately after the arterial one. Furthermore, these contrast agents have a short half-life, are excreted rapidly from the lungs, and are very well tolerated. In fact, they can be injected into patients with renal insufficiency, hypotension, shock, without further preliminary laboratory tests, and are also indicated in critical patients [4, 5, 8]. CEUS contrast media are safe with a very low incidence of side effects. There are no cardio-, nephro- or hepato-toxicities and life-threatening anaphylactic reactions in abdominal applications have been reported with a rate of 0.001 % in the study of O'Connor et al. [9]. In Europe, CEUS has only been approved for a

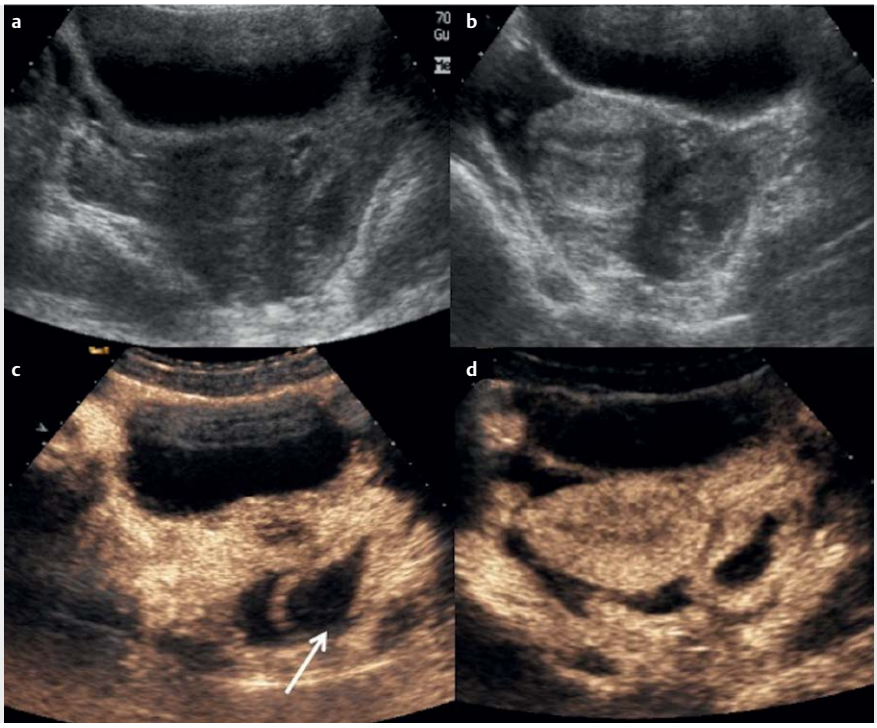
limited number of non-traumatic abdominal pathologies in adults, focusing especially on liver disease. Various studies have shown it to be an excellent imaging technique also for non-hepatic applications. A fundamental practical approach is described in the EFSUMB Guidelines [10–12]. CEUS application in children is currently still "off-label" except for a few indications including vesico-uereteral reflux, but it could be a very useful method in the non-ionizing imaging of young patients [6, 13–17].

Today, in the emergency setting, CEUS is used predominantly in the study of blunt or penetrating traumatic lesions, especially for the diagnosis and follow-up of the solid parenchymal organ (so-called "non-operative management") [8, 18–22]. Often CEUS is used after a baseline US examination, in an attempt to avoid radiation exposure a computed tomography (CT) examination, especially in hemodynamically stable minor trauma. Furthermore, CEUS is a valid method that can help the radiologist make rapid decisions in case of an unstable major trauma that cannot be moved to the radiology emergency department and needs immediate surgical treatment [8, 19, 20, 23, 24].

The experience with CEUS in abdominal non-traumatic pathology is still limited. In fact, the purpose of this article is to review the possibilities and limitations of CEUS in the acute abdominal setting, focusing on various scenarios (inflammation, ischemia, and hemorrhage) and their related radiological images.

Intra-abdominal hemorrhage

Intra-abdominal hemorrhage can be caused by spontaneous bleeding, for example during anticoagulant therapy, spontaneous rupture of a solid mass, a hepatocellular carcinoma, an aortic aneurysm, or a hemorrhage within cystic lesions (▶ **Fig. 1**) [5, 25]. It can be secondary also to diagnostic procedures or therapies such as biopsy or femoral artery puncture in interventional maneuvers. Baseline US can detect the collection of bloody in the peritoneal or extraperitoneal space. Performing CEUS exam helps to recognize the real site of bleeding, through the direct visualization of the contrast leakage (similar to in angiography or during CT exam after contrast injection) [26]. On CEUS, the operator sees active contrast extravasation directly from a vessel (in a continuous or pulsatile form), like in the case of a spontaneous rupture of an abdominal vessel. The extravasation is seen as enhancing blood passing through the arterial wall defect and adjacent pooling [27]. CEUS may have difficulties in differentiating active free bleeding from a pseudoaneurysm. In this case, the differential diagnosis must be made through angiography or CT (▶ **Fig. 2**) [26, 28–30]. In the case of a ruptured abdominal mass, CEUS examination can detect the contrast bleeding within the tumor or into the adjacent hematoma (▶ **Fig. 3**) [31]. Also, in the case of patients with a complicated abdominal cystic mass or a vesical hemorrhage, CEUS can depict the bleeding site and differentiate it from active contrast extravasation or endoluminal clots (for example, in the case of massive hematuria). However, CEUS exam cannot depict small, deep, and multiple hemorrhages, especially those located outside the scanned area. In these cases, CT with contrast media injection is the main radiological examination to be performed, because of its panoramic and direct visualization of the exact bleeding vessel [32]. Moreover, it has to be remembered that clinical evaluation is fundamental. For example, with both B-mode and CEUS it is not possible to differen-



▶ **Fig. 1** Hemorrhagic corpus luteum. A young girl 14 y.o. with pelvic pain arrives at the emergency department and the US examination shows the presence of an enlarged left ovary compared to the contralateral. The CEUS exam shows the presence of anechoic (internal) cystic formation with an enhancing wall and an interruption of the peripheral profile (white arrow), findings compatible with rupture of the corpus luteum. It is also associated with free fluid in the pelvis.

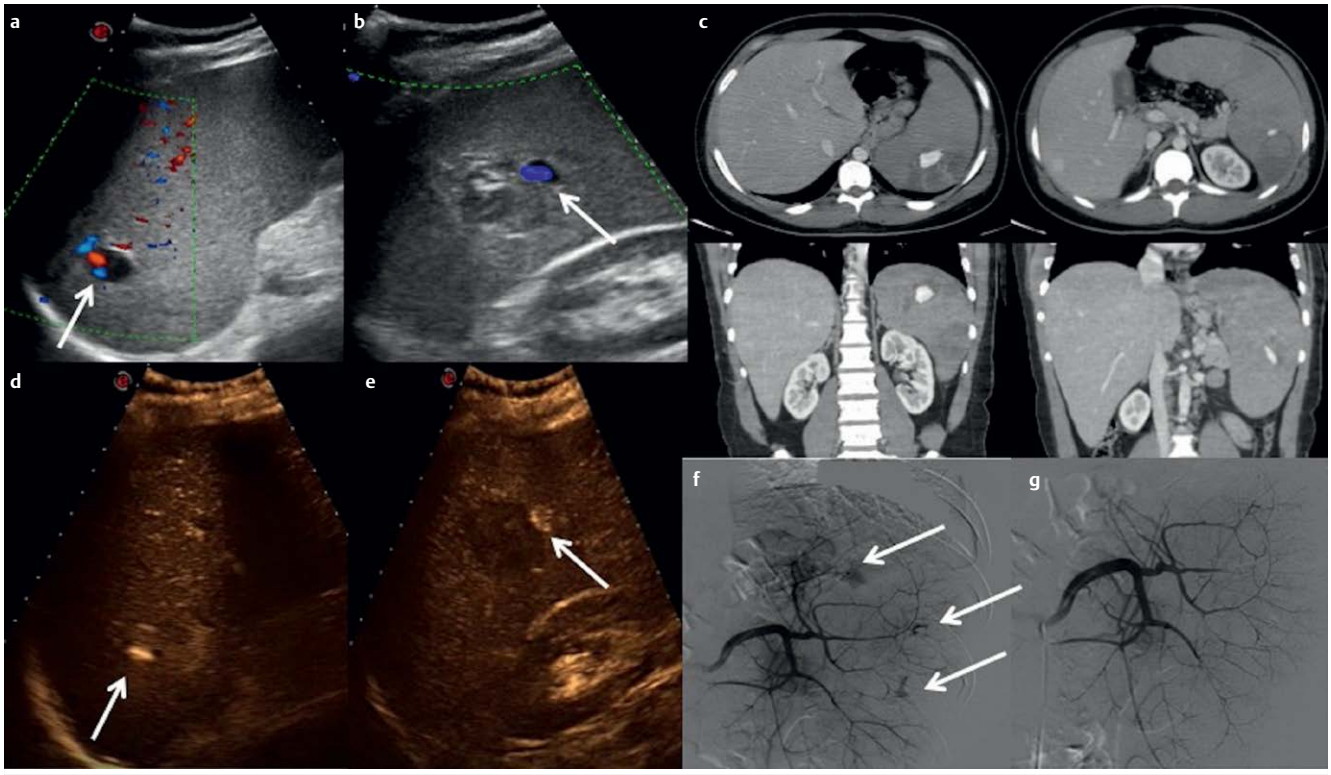
tiate between a spontaneous or traumatic splenic rupture, because the imaging findings are the same [33, 34].

Parenchymal ischemia and infarction

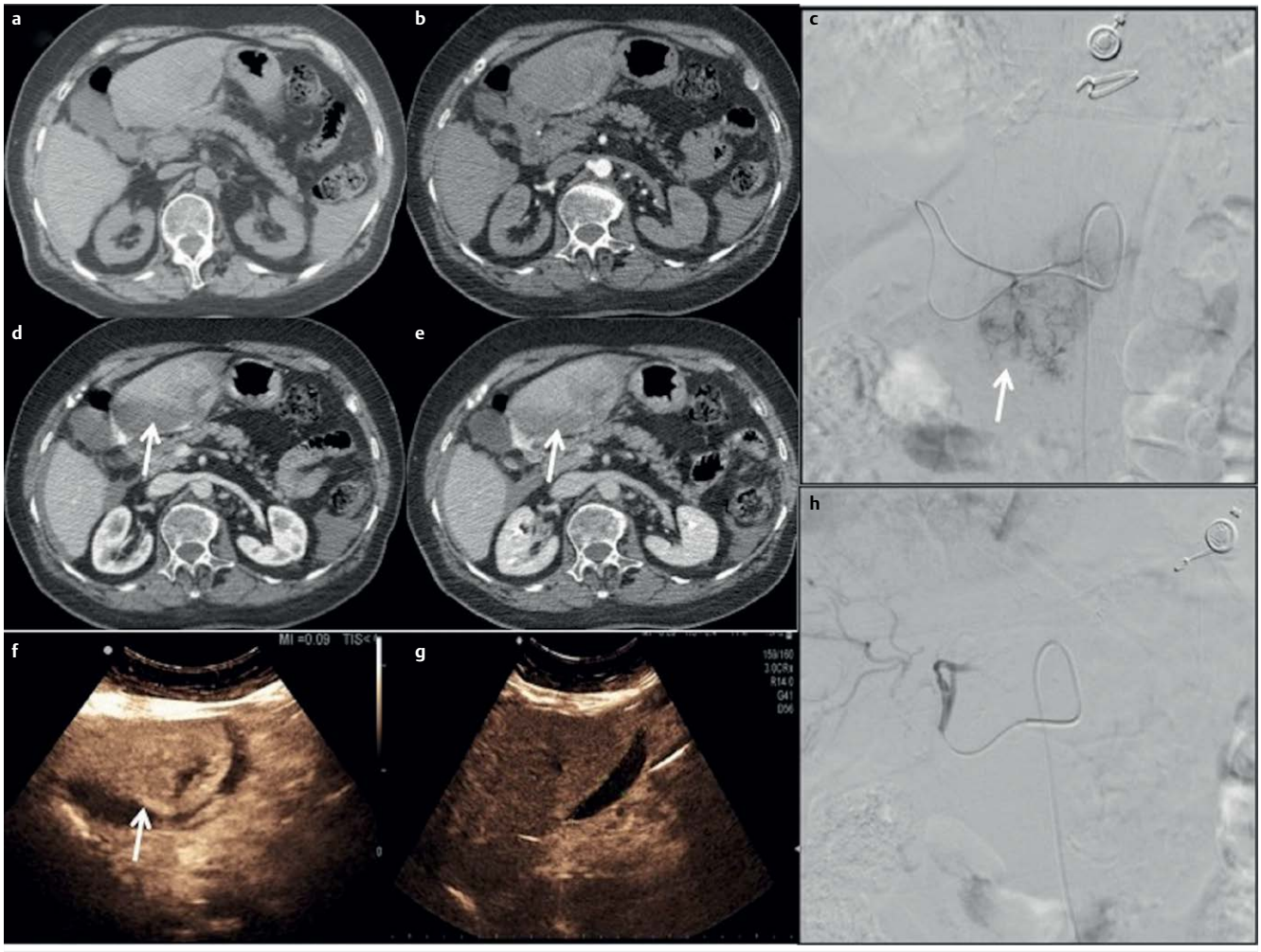
In the case of parenchymal ischemia and infarction, CEUS can easily demonstrate the non-vascularized area, especially in solid organs like the spleen, liver, and kidney (that are also effectively examined by ultrasonography examination) [33, 34]. Suspected hypoechoic areas due to hypoperfusion already detected on baseline US can be confirmed with CEUS, which effectively shows the presence of microcirculation alterations. In fact, the alterations in perfusion after the administration of the ultrasound contrast medium appear as clearly visible hypoperfused areas due to the high intrinsic lesion-to-parenchyma contrast of CEUS [5]. In these cases, CEUS can be used instead of CT to reach a correct diagnosis and evaluate the extent of the damage. It is a valid method to perform noninvasive follow-up especially if the infarction is treated conservatively. A recent review by Tedesco et al. shows the diagnostic approach of CEUS in infarctions of the kidney, spleen and pancreas. This affirms that CEUS can replace CT in specific situations [10, 35, 36]. Furthermore, the study by Setola et al. describes the important role of CEUS in confirming suspected renal infarction on baseline US (▶ **Fig. 4**) [37]. The same CEUS semeiotics can be seen in testicular or ovarian torsion and infarction, torsion of the spermatic cord and epididymis, as described in the study by Badea et al. (▶ **Fig. 5, 6**) [12, 38–41]. An advantage of CEUS in the pediatric population is the lack of radiation exposure. CEUS has also been reported useful in evaluating intestinal ischemia and small bowel infarction [42, 43]. Hata et al. reported a sensitivity of 85–100 % and a specificity of 98–100 % in diagnosing intestinal infarction with CEUS, from various etiologies [44].

Abdominal inflammation

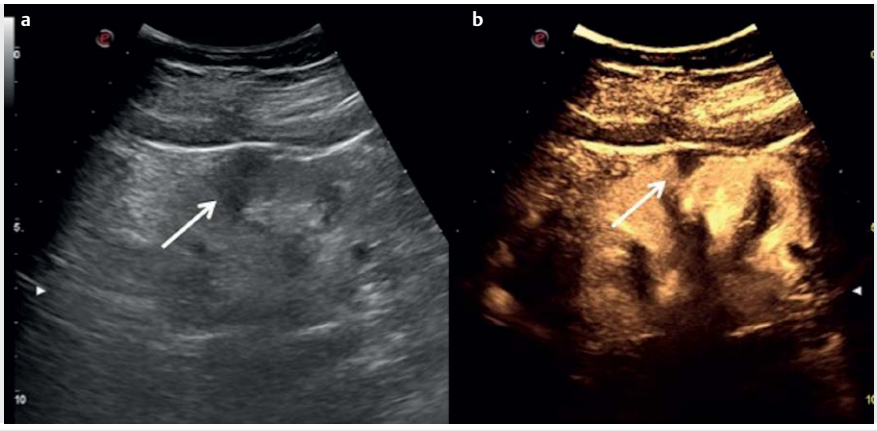
Similar to ischemia and infarction, in inflammation and phlogosis, there is a higher lesion-to-parenchyma contrast ratio in CEUS examination where the hyperemia corresponds to increased parenchymal microcirculation. CEUS in inflammatory disease has a key role in differentiating between an acute phlogosis and a real abscess or phlegmon or inflammation from a gangrenous evolution [10, 45, 46]. This principle is applied to any acute abdominal inflammatory disease from cholecystitis to appendicitis, pancreatitis, pyelonephritis, or diverticulitis. In particular, in acute cholecystitis, CEUS can very easily detect the evident mural enhancement and any possible gangrenous evolution. In the last case, the lack of mural enhancement is a sign of perforation indicating the need for immediate surgical treatment (▶ **Fig. 7**) [47, 48]. Similarly, in acute appendicitis, CEUS improves the detection rate of the disease achieving 98 % accuracy and 100 % sensitivity in the diagnosis, as reported by Incesu et al. [49]. This method can be used especially in the pediatric population after baseline US, avoiding a CT examination. CEUS has been shown to have sufficient accuracy to determine complications (such as perforated or phlegmonous



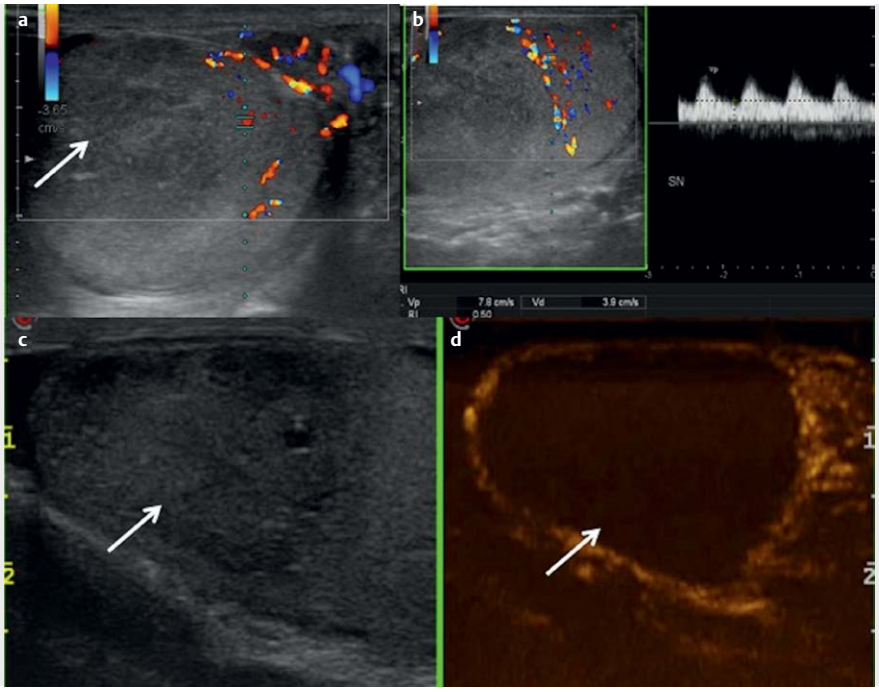
▶ **Fig. 2** Splenic pseudoaneurysm. Young male patient 18 y.o. arrives at the emergency department with upper-left quadrant pain. Baseline US (arrows in **a–b**) demonstrates the presence of at least two parenchymal anechogenic lesions with peripheral vascular signal at Doppler exam. CEUS (**d–e**) and CT (C) confirm the presence of two vascular lesions within the splenic parenchyma referable to pseudoaneurysm. The diagnosis of certainty and treatment were then made with angiography and embolization of pseudoaneurysms (**f**).



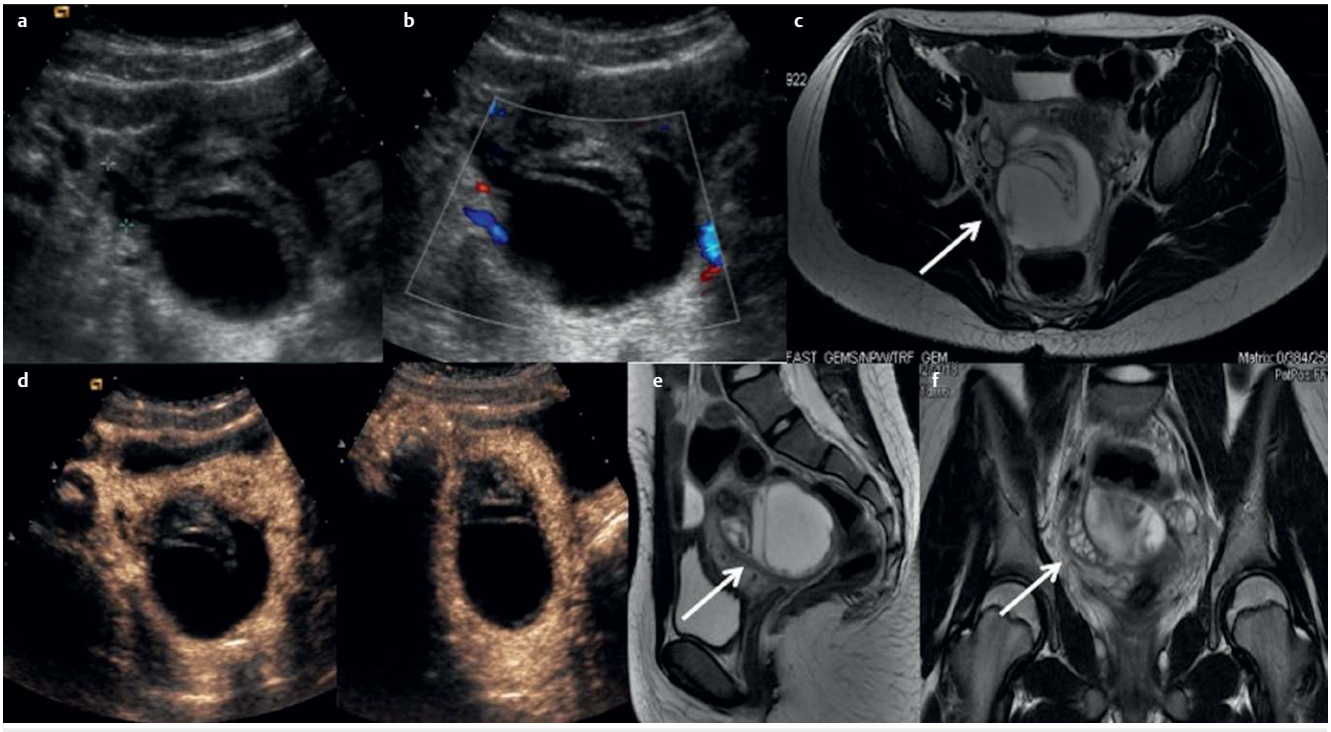
▶ **Fig. 3** Spontaneous HCC rupture. Case of spontaneous bleeding from an unknown liver lesion in a patient without additional comorbidities, which turned out to be hepatocellular carcinoma. CT with contrast medium (**a–b–d–e**) highlights the bleeding lesion in the left lobe, then confirmed by the CEUS examination (arrow in **f**) where there is a subcapsular arterial blush indicative of bleeding in progress, which also extends into the adjacent peritoneal cavity. Angiography confirms the presence of active bleeding (**c**), embolized and no longer evident in angiographic (**h**) and CEUS controls (**g**).



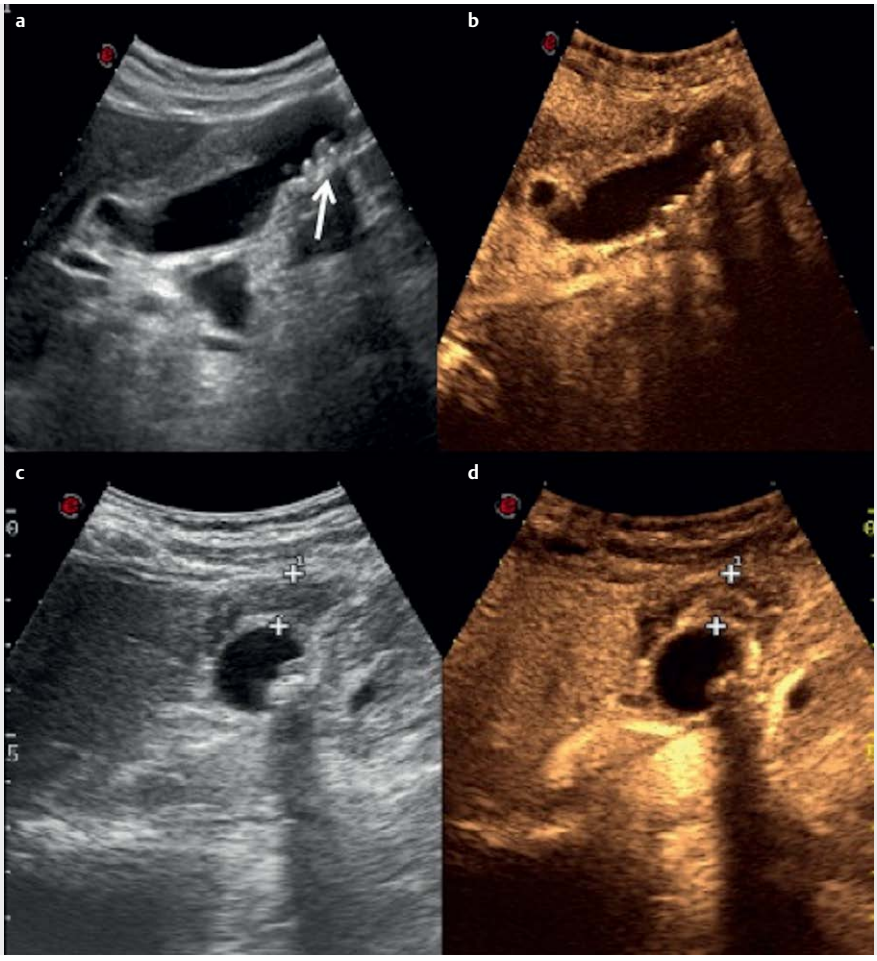
▶ **Fig. 4** Kidney infarct. Right cortical mesorenal infarction with triangular morphology, poorly visualized at baseline US (**a**) but without enhancement at CEUS (white arrow - **b**) compared to the remaining vascularized parenchyma.



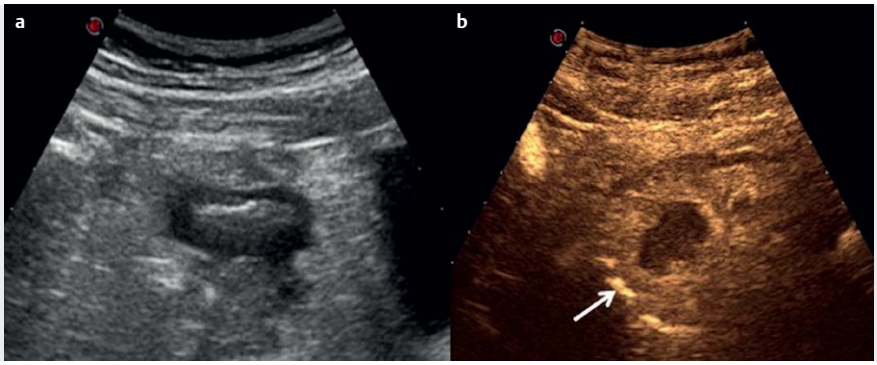
▶ **Fig. 5** Acute testicular infarct. Segmental ischemia of a testicle visualized as a diffusely hypoechoic area with poor Doppler representation (white arrow in **a–b–c**). The infarcted part of the testicle is not vascularized or enhanced on CEUS (**d**).



▶ **Fig. 6** Acute ovarian torsion. Young girl 10 y.o. comes to the emergency department complaining of constant pain during defecation. The first US examination (**a–b**) demonstrates the presence of a coarse cystic mass within the right ovary, with slightly thickened walls with poor peripheral vascularization. CEUS (**d**) demonstrates the presence of a cystic lesion with poorly enhanced walls and with solid endoluminal parietal projections. The patient completed the diagnostic procedure with MRI (axial **c**, sagittal **e** and coronal **f** T2-weighted scans) which confirmed the presence of the adnexal lesion (arrow). Note the perfect agreement between the ultrasound images, CEUS, and MRI. The lesion turned out to be a cystic teratoma.

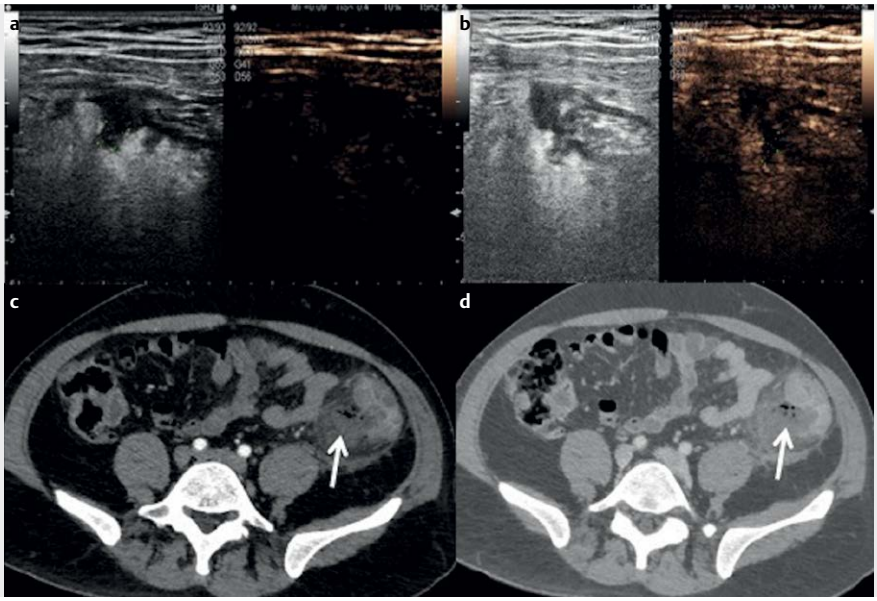


▶ **Fig. 7** Acute complicated cholecystitis. On the baseline US images (**a** and **c)** there are recognizable signs of cholecystitis with a gallbladder filled with sludge and microcalculi (arrow). CEUS highlights the evident enhancement of the gallbladder wall, which appears very thickened (**c** and **d**), without showing signs of complication such as an abscess or perforation.

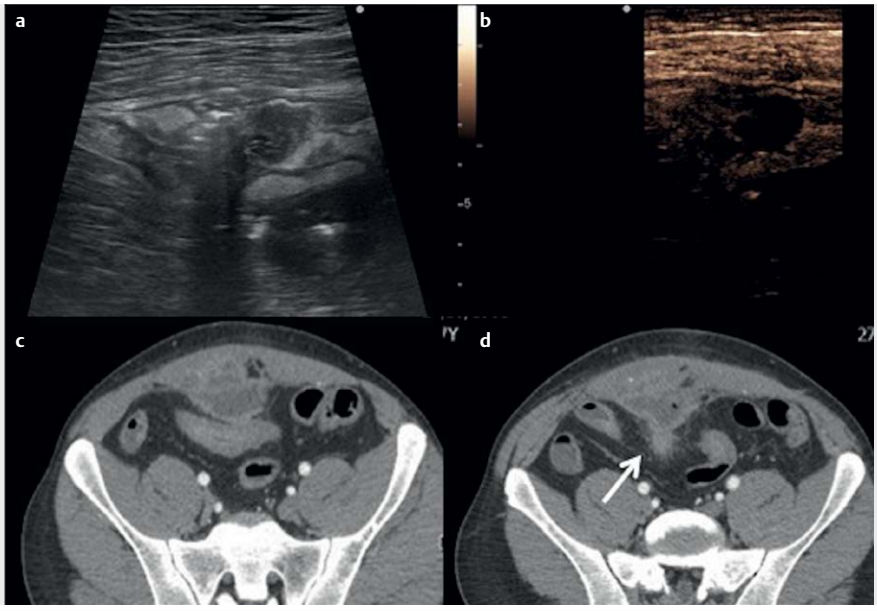


▶ **Fig. 8** Acute diverticulitis. In **a**, the intestinal wall is visualized an axial scan, highlighting a hypoechoic exophytic lesion suggestive of a diverticulum. After administration of US contrast medium **b**, the evident enhancement of the inflamed intestinal wall, in the arterial phase (arrow).

and gangrenous appendicitis) [13, 49]. Another cause of abdominal pain that can mimic appendicitis is epiploic appendagitis. Also, in this case, CEUS may help the diagnosis by highlighting rounded enhancement in the abdominal fatty tissue within a necrotic center, which is a typical finding in the disease [50]. In the case of acute pancreatitis, CEUS could be used to define the area of higher vascularization within the parenchyma. This technique is not used in routine daily work, first of all, because patients with acute pancre-



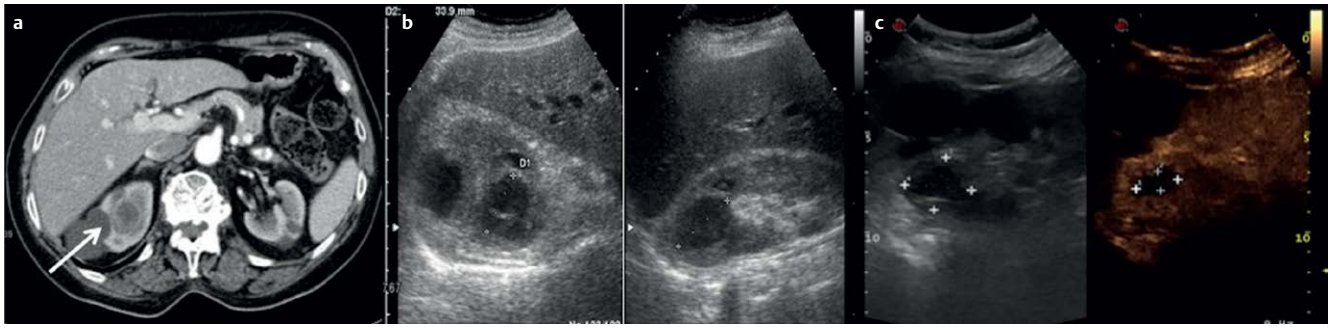
▶ **Fig. 9** Abscess in diverticulitis. Pain in the left iliac fossa in a man without further comorbidity. In the clinical suspicion of an abscess, a CEUS (**a–b**) examination was performed directly: it shows a nonhomogeneous constantly anechogenic fluid collection with marked peripheral arterial enhancement, typical of an abscess. The finding was confirmed by CT (**c–d**) which also makes small air bubbles stand out better, in the context of a peri-diverticular abscess.



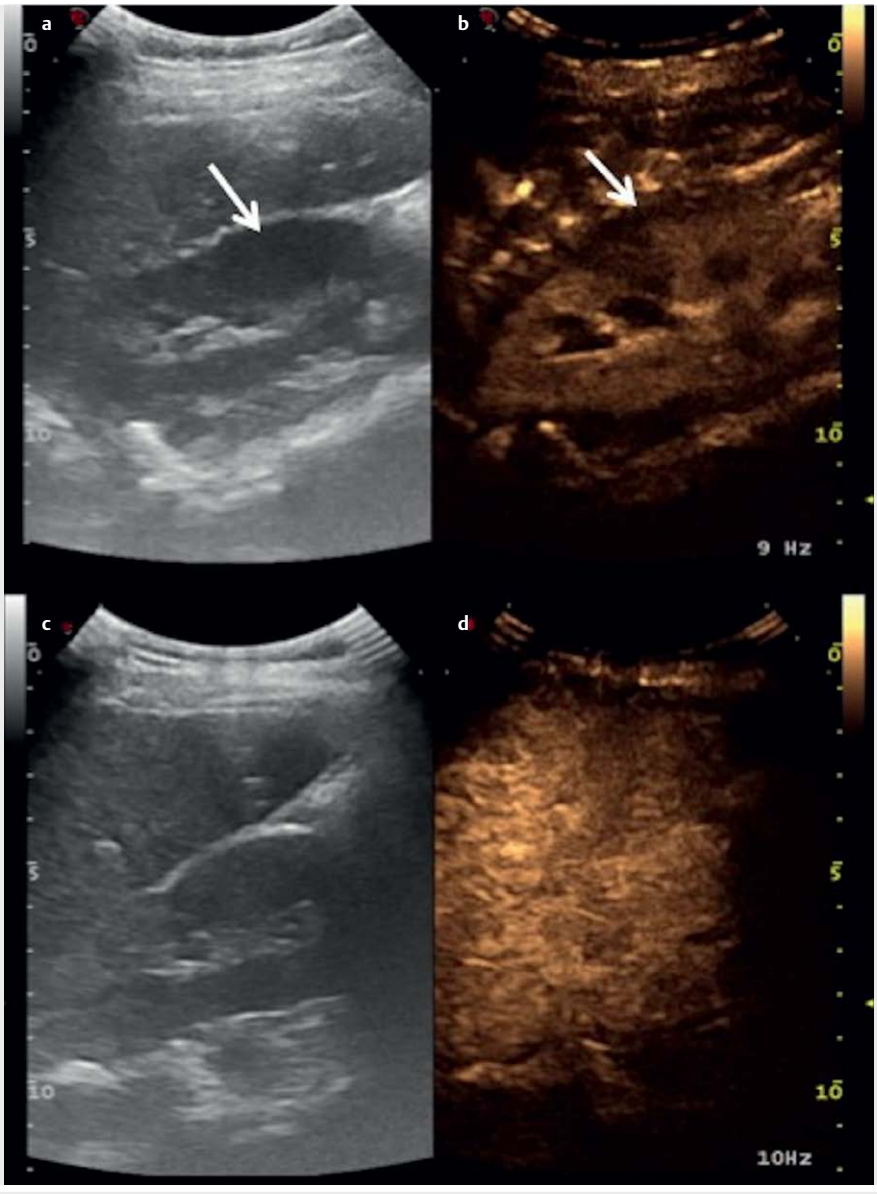
▶ **Fig. 10** Abscess in Crohn's disease. Similarly to ▶ **Fig. 9**, this is a case of a 37-year-old male patient with Crohn's disease with an intestinal abscess tightly attached to the abdominal wall (arrow).

atitis have pain and it is not easy to examine the whole pancreas on US [10, 51]. In this case, CT exam performed in the emergency department is the gold standard and helps to grade the process [52].

In the case of acute gastrointestinal inflammation caused by diverticulitis, appendicitis, or inflammatory bowel disease (IBD – like Crohn disease), CEUS can improve the detection of their complications, such as abscess and phlegmon (▶ **Fig. 8, 9**) [53–55]. Abscess appears as a non-enhancing rounded lesion with hyperemic borders, while phlegmons are mass-like with a non-homogeneous pattern of enhancement (▶ **Fig. 10**) [53, 56]. IBD is a lifelong chronic disease and patients are often young. Currently, US and CEUS are similar to CT and magnetic resonance imaging (MRI) in detecting active disease and follow-up of intestinal lesions [57, 58]. Detection and evaluation of vascular flow in the bowel wall is an important factor in the diagnosis and management of IBD. On baseline US, it may de difficult to distinguish the necrotic liquefied center of an abscess, but after contrast injection, the presence of non-enhanced necrotic central nucleus and a peripheral enhanced wall



▶ **Fig. 11** Renal abscess. CT **a** and US (**b–c**) signs of a renal abscess in the upper right pole in an elderly patient (arrow). The CEUS study (**c**) confirms the presence of an abscess with an anechoic necrotic center and peripheral enhancement, as demonstrated by the CT examination. The basic US scan **b** does not allow complete visualization of the pathology.



▶ **Fig. 12** Acute pyelonephritis. The basic US image in **a** highlights a blurred hypoechoic area in the right kidney. After the administration of contrast medium, the CEUS examination **b** confirms the presence of a triangular area with reduced enhancement compared to the remaining parenchyma: the finding refers to an area of pyelonephritis (arrows). It is also associated with perirenal free fluid collection. The images in **c** and **d** are images from a follow up CEUS study after twenty days of antibiotic therapy.

occasionally with internal septa with perifocal hyperemia can be easily demonstrated, especially during the arterial phase (▶ **Fig. 11**).

Similarly, in patients with acute pyelonephritis, the inflammatory areas within the cortical renal spaces are better depicted with CEUS than baseline US. These areas appear as rounded or wedge-shaped hypoenhancing foci within the normally enhancing renal parenchyma, with marginal hyperemia (▶ **Fig. 12**) [62]. The presence of some perfusion can differentiate acute renal infection from infarction. In the latter scenario, the sonographic contrast signal is absent [63, 64].

Limits of CEUS

In an emergency setting, CEUS exam has several limitations, primarily related to the intrinsic limitations of US, i. e., intestinal movement, obesity, presence of free intraperitoneal air, and the inability of the patient to maintain breath-hold. Moreover, it does not have panoramic view, unlike CT which allows the complete visualization of the whole abdomen. CEUS may not diagnose deep or localized bleeding in a poorly studied abdominal parenchyma, such as the lower pole of the spleen or in the case of retroperitoneal collections. In these cases, an abdominal CT scan should be performed urgently. Despite these limitations, CEUS also has several advantages as explained in this review, including its rapid availability in an emergency context, patients who are bedridden, in intensive care units, or who are difficult to transport to the radiology department for a CT scan.

In conclusion, use of CEUS in the acute non-traumatic setting is not yet widespread, but it should be, especially because it is a simple and safe imaging modality in the study of inflammatory, ischemic, and hemorrhagic pathologies of the abdomen. Furthermore, CEUS improves the accuracy of baseline US imaging, while limiting the use of CT and related radiation exposure, especially in younger patients.

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Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Formal consent is not required for this type of study.

This article does not contain any studies with animals by any of the authors.

Conflict of Interest

The authors declare that they have no conflict of interest related to the publication of this article.

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