Review Article

Contrast-enhanced Ultrasound as a Method of Splenic Injury Assessment

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Abstract

Splenic injuries are common in abdominal trauma, as the spleen is one of the most often harmed organs. The treatment of splenic injuries underwent major changes during the past decades, shifting from a surgical approach to nonoperative management. This change of the proceedings results from a constantly growing awareness of the spleen's crucial hematological and immunological function and was possible owing to the advances in radiological techniques. In a setting of high-energy trauma in hemodynamically stable patients, computed tomography (CT) remains the gold standard. Where ultrasonography (US) is of major importance is in cases of unstable patients undergone high-energy trauma or in patients after low-energy trauma. Nevertheless, baseline US's sensitivity is not sufficient to detect splenic traumatic injuries; hence, a new method was developed involving ultrasound contrast agents (UCAs), called contrast-enhanced ultrasound (CEUS). In a low-energy trauma setting, it facilitates the diagnosis of abdominal lesions with a sensitivity close to that of CT, without the disadvantages of the latter. In addition, CEUS can be used in the follow-up of abdominal traumatic injuries. The fact that CEUS preserves CT's sensitivity while not carrying the risk of radiation-induced cancer makes it feasible for children and pregnant women. This review aims to discuss the technical aspects of CEUS, the limitations, and possibilities regarding this modality, present the appearance of both a healthy and injured spleen, and compare CEUS's effectiveness to that of CT through an analysis of retrievable studies.

Keywords: Abdominal trauma, computed tomography, contrast-enhanced ultrasonography, spleen, splenic injury, ultrasonography

Introduction

Splenic injury is a frequent occurrence following blunt abdominal trauma (BAT), and due to the limitations of clinical examinations in assessing the presence and extent of injuries, the employment of imaging techniques has become imperative for precise evaluation of the patient's condition. Within the context of BAT scenarios, the spleen ranks as the second most frequently affected organ, following the liver.[1] Certain anatomical or pathological conditions, such as splenomegaly, can cause an individual to be more susceptible to injuries, even from relatively minor trauma. Moreover, anatomical conditions are different in children and adults, where in case of the former, the spleen tends to protrude below the ribs, while in the latter, the spleen is partially protected by the rib cage.[2] This leads to children being affected by splenic trauma with a frequency of 46,7%, taking into account both multiple and isolated organ lesions.[3]

Historically, splenectomy was considered to be the only treatment for splenic injuries, regardless of their severity. Nevertheless, as professionals acquired more awareness about both the hematological and immunological significance of the spleen, an effort has been made in trying to apply, where feasible, techniques that allowed its preservation. The first attempts of nonoperative management (NOM) were performed by Upadhyaya and Simpson, who back in 1968 suggested sparing surgery involving splenic embolization.[4] Another factor that contributed to the further facilitation of NOM was the rapid advancements in diagnostic imaging.

In a setting of high-energy trauma, if the patient's hematological stability allows to do so, contrast-enhanced computed tomography (CECT) is considered the gold standard for

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assessing thoracic-abdominal, skeletal, and neurological injuries.[2,5,6] However, CECT has its drawbacks, as it is an imaging method performed in a clinically stable scenario. Being based on ionizing radiations and the administration of iodinated contrast mediums (CMs), its use may be limited in case of pregnant women, children, and coexisting chronic kidney disease. Following low-energy trauma or in an instance of hemodynamic instability, Focused Assessment with Sonography for Trauma is a modality of particular usefulness. While being effective in detecting free fluid with a sensitivity ranging from 63% to 99%,[7] it is not viable for parenchymal injuries, where several studies have shown a sensitivity from 41% to 44%.[8-10] The use of ultrasound contrast agents (UCAs) significantly increased the efficaciousness in case of solid organ injuries,[11-13] hence contrast-enhanced ultrasound (CEUS) can achieve a specificity and sensitivity of 99%,[14] avoiding the overuse of CT.

Owing to its superficial location, high vascularity, compact size, uniform parenchyma, and long-lasting enhancement, CEUS is particularly well suited for the spleen.[15] According to the recommendations of the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) updated in 2017, there are several indications for the use of CEUS in the spleen. These comprise characterizing splenic parenchymal inhomogeneity or suspected lesions upon traditional US, confirming suspected splenic infarction, characterizing accessory spleens or splenosis, detecting splenic malignant lesions in oncologist patients when magnetic resonance imaging (MRI), positron emission tomography, and/or CT are inconclusive or contraindicated, diagnosis of splenomegaly, and evaluating the spleen in selected patients who have suffered BAT.[16] This study aims to discuss the current role of CEUS in the assessment of splenic trauma, providing insight into the method, describing the possible findings, and carrying out a comprehensive comparison of CEUS and CT [Figure 1].

Methods

Systematic literature review

We conducted thorough research of literature, including articles and journals published until June 2023. Using keyword variants such as contrast-enhanced ultrasonography, ultrasonography, splenic injury, spleen, abdominal trauma, and CT, we obtained 235 citations from databases such as PubMed, Google Scholar, and Cochrane. After removing duplicate records and those deemed ineligible, we screened 89 citations and excluded 27 of them from further analysis. Finally, we found 49 records that could be used. After meticulous evaluation, we selected 29 articles on the use of CEUS in splenic trauma. We included articles that precisely described the methodology and outcomes of CEUS utilized in splenic trauma assessment, as well as studies that addressed the issue of comparing CEUS to CT. The title and abstract of the citations were screened first, followed by the full text. Citations were excluded for different reasons: intervention, participants, non-Polish, non-English, and result presentation.

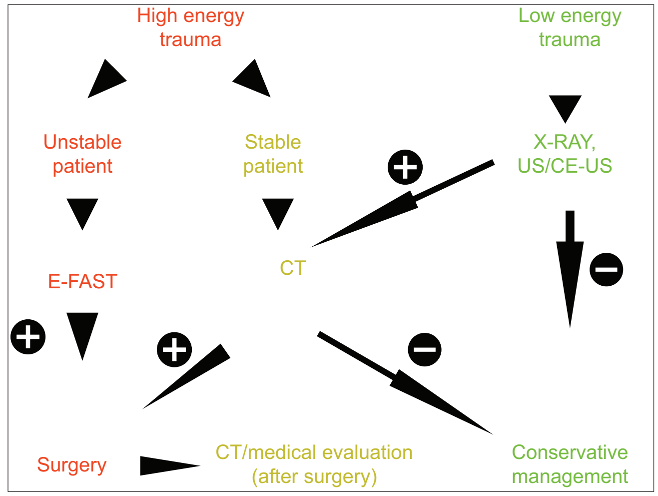

Figure 1: Simplified diagnostic pathways following low-energy and high-energy trauma. Based on the chart published by Zakaria *et al*.[17] and Coccolini *et al*.[18]

Results presentation

We sought to present the underlying mechanism of CEUS concisely, the correct outcome of spleen CEUS, and the manifestation of splenic lesions. In the discussion section, we included a summary of the cited studies comparing CT and CEUS as techniques to diagnose splenic injuries, the limitations of CEUS, and final considerations concerning this novel modality [Figure 2].

Discussion

Contrast-enhanced ultrasound-technical aspects

The initial phase of the examination involves nonenhanced US, comprehensively exploring the parenchymal organs and the peritoneal cavity. Following the administration of the UCA, the window of time available to thoroughly scan each organ becomes constrained, dictated by the specific timing of individual vascular phases.[19] The central principle behind CEUS is to combine standard US imaging with the administration of UCAs, which allows to better visualize the spleen's vasculature and reveals potential parenchymal lesions. UCAs are microbubbles that consist of a protein and/or phospholipid shell filled with gas, of whom there are currently two generations. First-generation agents are air-filled and were found to be particularly fragile, the duration of the contrast effect was rather short, and the signal amplification varied greatly among different individuals.[20] Four transpulmonary UCAs are currently approved by the European Medicines Agency for use in Europe. Levovist® (air with a galactose shell and palmitic acid as a surfactant) (Bayer Schering Pharma AG, introduced in 1996) is no longer produced. Luminity® (perflutren, octafluoropropane with a phospholipid shell) (Lantheus Medical Imaging, Inc., introduced in 2006) is only approved for cardiac use in Europe. Optison® (octafluoropropane – perflutren with an albumin shell) (GE Healthcare Inc., introduced in 1998) is also

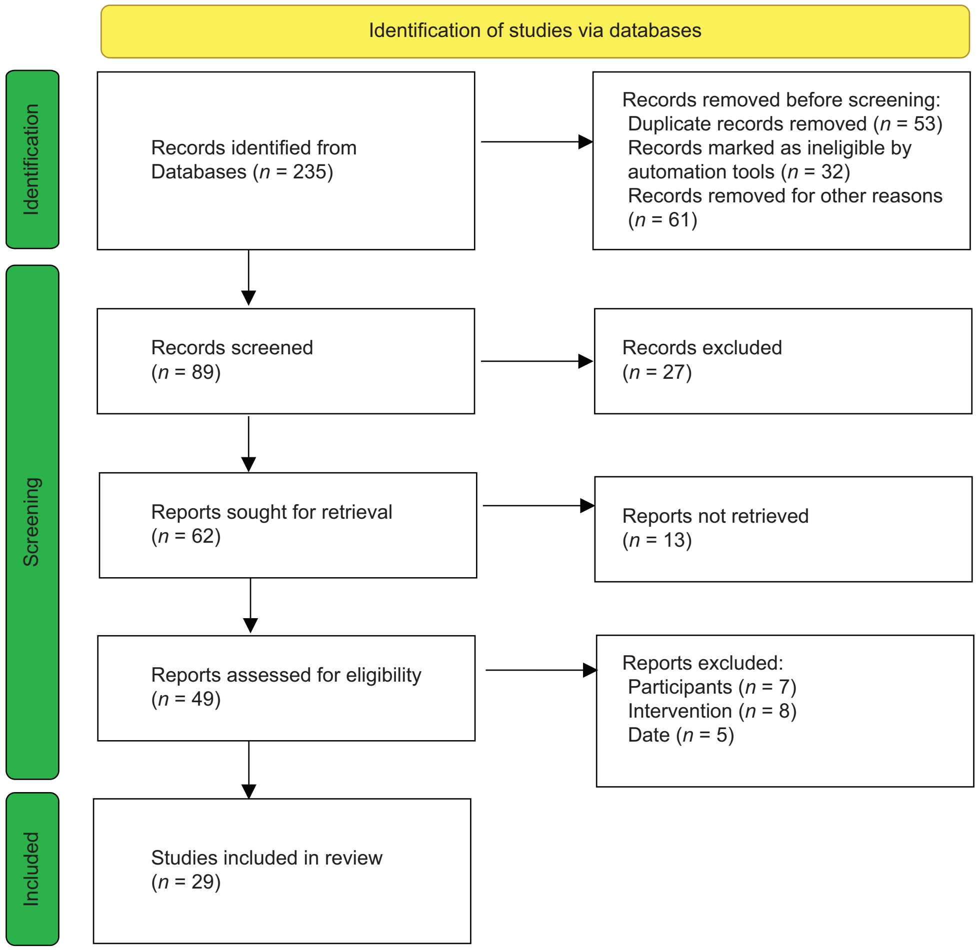

Figure 2: Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of the study selection process

solely approved for cardiac use in Europe. SonoVue® (sulfur hexafluoride with a phospholipid shell) (Bracco Spa, introduced in 2001) is approved in Europe for cardiac, macrovascular, liver, and breast lesions and is the most commonly used agent.[21] Nowadays, the most utilized CM in Europe is SonoVue® (Bracco, Milan, Italy). It belongs to second-generation UCAs, and it is formed by microbubbles filled with sulfur hexafluoride, which provides them much more strength and stability. The membrane phospholipids are metabolized by the liver, while sulfur hexafluoride is eliminated via the respiratory system. These CMs are nonnephrotoxic and do not affect the thyroid gland, so laboratory tests are not required before administering them. They are also well tolerated, with an incidence of anaphylactoid reactions reaching a mere 0.001% and have a short half-life of approximately 12 min.[21] However, caution is advised when administered in patients suffering from cardiac and/or pulmonary diseases.[22] Diagnostic ultrasound (US) and UCAs theoretically could cause bioeffects. Observed *in vitro* cellular effects include sonoporation, hemolysis, and cell death. These effects may be relevant *in vivo* due to interactions between gas bodies and cells. Data from animal models indicate that glomerular capillary hemorrhage and other microvascular ruptures might occur when microbubbles are exposed to ultrasound. Such vascular damage could be harmful in specific situations where it would be clinically significant, such as in the eye and brain.[21] Contrast microbubbles are introduced into the bloodstream through a rapid intravenous bolus, accompanied by a subsequent bolus of 10 mL saline solution, typically delivered via a cannula inserted in an antecubital vein (with a minimum size of 20G).[23] Owing to the strong enhancement of the splenic parenchyma, a lower dosage of contrast agent may be sufficient, with a recommended optimal dosage of SonoVue® (Bracco, Milan, Italy) ranging from 1.2 to 2.4 mL.[16]

Contrast-enhanced ultrasound of the spleen-normal appearance

The spleen is an intraperitoneal organ located in the left upper quadrant of the abdomen. Its size varies depending on the age and typically measures 9–12 cm in the longest dimension. To facilitate the evaluation of the spleen, the patient should suspend respiration and be positioned in the lateral decubitus setting, with the right side down. Normally, splenic parenchyma should be more echogenic than the liver and kidneys.[23]

Although UCAs remain confined to the intravascular space, they are selectively accumulated by the spleen, resulting in persistent enhancement during the later stages.[24] In the arterial phase, the enhancement appears heterogeneous, manifesting itself as a characteristic "zebra striped" pattern, similar to the one observed in CECT and MRI.[2] However, within 60 s, the enhancement becomes uniform and typically endures for over 5 min. The arterial phase (10–35 s) and the late parenchymal phase (3–5 min) hold the greatest diagnostic significance. It is crucial to maintain continuous scanning during the arterial phase while doing it intermittently thereafter to prevent UCA destruction.[16] UCA degradation occurs even at very low acoustic pressures, and it can lead to the development of artifacts appearing as a late-phase contrast washout, especially when the ultrasound beam's focal point corresponds with the analyzed region.[23] Focal lesions are evaluated by comparing their enhancement to that of the surrounding enhanced splenic parenchyma. Deep-seated lesions may be obscured if a substantial volume of UCA is administered.[25,26]

Presentation of splenic trauma in contrast-enhanced ultrasound

Owing to its extensive vasculature, spleen trauma has an extremely high risk of causing life-threatening bleeding and hemorrhagic shock, which most frequently is related to an injury of the hilar region.[2] Consequently, the employment of appropriate modalities is crucial to detect splenic injuries and rapidly assess the patient's condition. Frequently, the most prominent indication of a splenic injury is the presence of hypo-anechoic fluid accumulation in the subcapsular or perisplenic region.[27] Identifying parenchymal lesions can prove exceedingly challenging, particularly when the perisplenic fluid cannot be visualized. Furthermore, the echogenicity of fresh blood closely resembles that of normal parenchyma, which contributes to the potential oversight of even sizable traumatic lesions when relying solely on standard US imaging. However, these limitations can be overcome by employing CEUS.

The evaluation of parenchymal lesions should be conducted during the venous phase, approximately 120–240 s, following the administration of the contrast agent. During this phase, normal parenchyma exhibits heightened and uniform echogenicity, enabling a more accurate assessment of lesions. In CEUS, they appear as branched or linear hypoechoic bands, usually perpendicular to the organ capsule, and can lead, in some cases, to its interruption. The involvement of the splenic capsule is easily recognizable, and the parenchymal contrast enhancements further facilitate the visualization of perisplenic or subcapsular fluid.[1] However, one disconcerting element unrelated to the vascular phases of the spleen is the occurrence of a common, relatively rapid decline in enhancement within the parenchymal splenic veins. Approximately 2–3 min after the injection, these veins assume an anechoic appearance. This phenomenon can likely be attributed to the spleen's effective filtration of microbubbles. Initially, this occurrence may induce some confusion, as the anechoic veins could be mistaken for lacerations. However, with a keen awareness of this issue, it can be effectively addressed. In instances of uncertainty, a re-administration of a small quantity of UCA serves as an efficacious solution.[28]

Lower-severity lesions of the spleen comprise contusive injuries, which are a result of bruising of the parenchyma being caused by direct contact with smaller blood vessels. They occur in cases where fluid is not present and manifest as hypoechoic lesions compared to the normally perfused parenchyma. Other injuries that may occur following splenic trauma are intraparenchymal hematomas and pseudoaneurysms. The former appears as an area of heterogeneous hypoechogenicity, exhibiting indistinct boundaries and limited visualization of vascular structures. Conversely, subcapsular hematomas are typically characterized by a nonenhancing lenticular region surrounding the parenchyma. In certain instances, it may be possible to observe the active extravasation of contrast media within this area.[1]

Finally, pseudoaneurysms are uncommon occurrences that arise as a consequence of arterial wall injury, resulting in the leakage of blood into a confined cavity. While maintaining communication with the arterial lumen, this condition creates a high-pressure cavity that carries the risk of a life-threatening rupture [Table 1].[1]

Conclusion

Limitations of contrast-enhanced ultrasound

In previous literature, CEUS may not only play a role in the early detection of splenic injuries but can also be used to assess the stage of healing.[31] Despite being found extremely useful in many instances, CEUS has its limitations, which have to be taken into account. As mentioned above, a disturbing factor may be the rapid decrease of enhancement in splenic veins, resulting in mild perfusion of splenic vessels. It may complicate the differential diagnosis, as this phenomenon could be interpreted as a laceration. However, as suggested by Valentino *et al*., a re-injection of UCA should be an efficacious means to solve that problem.[28] With respect to the location, CEUS may not be as effective in case of injuries of the upper pole of the spleen and the subphrenic region. Another troublesome area to explore would be the retroperitoneum, owing to the interposition of the intestinal and gastric bloating, and the patient's habitus.[1] Additional limitations of CEUS comprise the lack of three-dimensional scanning and whole-body exploration. Finally, just as in the baseline US, CEUS's effectiveness is limited by the experience of the operator, which may negatively affect the outcomes of this modality.[20] CEUS may replace CT in follow-up studies in expert hand.[32]

Final considerations and future directions

In hemodynamically stable patients undergone high-energy trauma, CECT remains the gold standard imaging method, as stated in Figure 1. However, in case of stable patients after low-energy trauma and patients treated with NOM as a follow-up measure until discharge, CEUS should be considered a feasible modality. In view of the results of the studies presented in Tab. 1, in some instances, CEUS is able

Table 1: Studies comparing the effectiveness of contrast-enhanced ultrasound compared to that of computed tomography in evaluating patients after abdominal trauma

Year	Author	Aim of the study	Methods	Outcome
2023	Zakaria *et al*.[17]	Reporting the experience in the management of pediatric split liver and spleen injuries using CEUS and CECT	246 children who sustained BAT followed a special algorithm for decision-making incorporating FAST, baseline US, CEUS, and CECT	CECT showed the extent of injury in 153 patients' spleen (62%) and 78 patients' liver (32%), while the remaining 15 (6%) patients had both injuries. CEUS detected 142 (57.7%) spleen injuries and 67 (27.2%) liver injuries
2018	Armstrong *et al*.[29]	Determining the sensitivity and specificity of CEUS and comparing it to CT in the evaluation of children with BAT	Children aged 7–18 years with a CT-diagnosed abdominal solid organ injury underwent conventional US and CEUS within 48 h of injury. Two blinded radiologists underwent a brief training in CEUS and then interpreted the CEUS images without patient interaction. Conventional US and CEUS images were compared to CT for the presence of injury and, if present, the injury grade. Patients were monitored for contrast-related adverse reactions	21 injured organs were identified by CT in 18 children. Conventional US identified the injuries with a sensitivity of 45.2%, which increased to 85.7% using CEUS. The specificity of conventional US was 96.4% and increased to 98.6% using CEUS. The positive predictive value increased from 79.2% to 94.7% and the negative predictive value from 85.3% to 95.8%. No adverse reactions to contrast were observed
2015	Sessa *et al*.[14]	Determining the sensitivity and specificity of CEUS in comparison to baseline US and CECT in patients with splenic injuries	256 patients with a history of low-energy BAT were retrospectively evaluated, CEUS and baseline US were performed and compared to CT which was the standard of reference	CEUS identified 34/35 splenic injuries, using CT as the standard of reference. The false negative result was due to a splenic lesion measuring <1 cm, which had no relevant consequences for patient management and prognosis
2011	Lv *et al*.[30]	Evaluating CEUS imaging of active bleeding from splenic and liver trauma	392 patients with liver and/or splenic trauma with concurrent bleeding have undergone CECT and CEUS	CEUS detection rate for active bleeding was not different from that of CECT, with a sensitivity of 72.4%
2006	Valentino *et al*.[12]	Prospectively compare the diagnostic value of US and CEUS with CT for the detection of solid organ injuries in BAT patients	32 patients had 35 abdominal injuries on CT and underwent also CEUS and US	16 lesions were detected on baseline US, and 32 were seen on CEUS. The sensitivity and specificity of baseline US were 45.7% and 91.8%, respectively, and the positive and negative predictive values were 84.2% and 64.1%, respectively. CEUS had a sensitivity of 91.4%, a specificity of 100%, and positive and negative predictive values of 100% and 92.5%, respectively

US: Ultrasonography, CEUS: Contrast-enhanced US, CT: Computed tomography, BAT: Blunt abdominal trauma, FAST: Focused assessment with sonography for trauma

to effectively replace CECT, which can be helpful in reducing unnecessary CT examinations. Conversely, the addition of UCAs elevates substantially the sensitivity of US, especially in what concerns injuries of splenic parenchyma without exposing patients to unnecessary risk, as UCAs are not considered nephrotoxic nor do they carry a significant risk of anaphylactoid reactions. The fact that CEUS can be considered a replacement for CECT in monitoring patients after trauma is beneficial from an ionizing radiation exposition perspective. It is utterly important in case of children and pregnant women who are particularly vulnerable to it and, as a consequence, they necessitate an accurate analysis from a risk–benefit ratio point of view.

Studies addressing CEUS in the assessment of trauma patients have shown very promising results thus far. Nevertheless, the number of investigated patients is still low in comparison to those analyzed in reports concerning CECT. Accordingly, CEUS should be cautiously implemented, and whenever the patient is at risk and doubts about the diagnosis occur, CECT is still to be considered the method of reference.

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Conflicts of interest

There are no conflicts of interest.

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