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Contrast-enhanced ultrasound imaging of active bleeding associated with hepatic and splenic trauma

Ecografia con mezzo di contrasto nel sanguinamento attivo associato a trauma epatico e splenico

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Abstract
Purpose. The aim of this study was to evaluate contrast-enhanced ultrasound (CEUS) imaging of active bleeding from hepatic and splenic trauma.
Materials and methods. Three hundred and ninety-two patients with liver or/and spleen trauma (179 liver and 217 spleen injuries), who underwent CEUS examinations following contrast-enhanced computed tomography (CT), were enrolled in this retrospective study over a period of >4 years. CEUS detected contrast medium extravasation or pooling in 16% (63/396) of liver or spleen lesions in 61 patients, which was confirmed by contrast-enhanced CT. Special attention was paid to observing the presence, location, and characteristics of the extravasated or pooled contrast medium.
Results. The CEUS detection rate for active bleeding was not different from that of contrast-enhanced CT (p=0.333). Information from surgery, minimally invasive treatment and conservative treatment was used as reference standard, and the sensitivities of the two techniques were not different (p=0.122). Of 63 lesions in 61 patients, CEUS showed that 74.6% (47/63) (21 liver lesions and 26 spleen lesions) presented contrast medium extravasation or pooling, both in the organ and out the capsule, in 14.3% (9/63) and only outside the capsule in 11.1% (7/63). CEUS imaging of active bleeding from hepatic and splenic trauma presented various characteristics, and the sizes and shapes of the active bleeding due to contrast medium extravasation or pooling were variable.
Conclusions. CEUS can show the active bleeding associated with hepatic and splenic trauma with various imaging characteristics, thus making it possible to diagnose

Riassunto
Obiettivo. *Scopo di questo lavoro è stato valutare l'imaging con ecografia con mezzo di contrasto (CEUS) nel sanguinamento attivo nei traumi epatici e splenici.*
Materiali e metodi. *Trecentonovantadue pazienti con trauma epatico e/o splenico (179 traumi epatici e 217 splenici), sottoposti ad esame CEUS seguito da tomografia computerizzata (CT) con mezzo di contrasto, sono stati arruolati in questo studio retrospettivo per un periodo di più di 4 anni. La CEUS ha rilevato lo stravaso o l'accumulo di mdc nel 16% (63/396) delle lesioni epatiche o spleniche in 61 pazienti, confermato poi dalla TC con mezzo di contrasto. È stata prestata particolare attenzione nell'osservare la presenza, la localizzazione e il carattere dello stravaso o dell'accumulo del mezzo di contrasto.*
Risultati. *La capacità della CEUS di individuare un sanguinamento attivo non si è dimostrata differente da quella della TC con mezzo di contrasto (p=0,333). Le informazioni ottenute dalla chirurgia, sia dal trattamento minimamente invasivo sia da quello conservativo, presi come riferimento standard, e la sensibilità delle due tecniche non si sono dimostrate differenti (p=0,122). Nelle 63 lesioni in 61 pazienti, la CEUS ha mostrato che il 74,6% (47/63) delle lesioni (21 lesioni epatiche e 26 spleniche) ha presentato stravaso o accumulo di mdc, entrambi all'interno dell'organo o fuori dalla capsula nel 14,3% (9/63) e solo fuori dalla capsula nell'11,1% (7/63). L'imaging CEUS del sanguinamento attivo da traumi epatici e splenici presenta differenti caratteristiche, e le dimensioni e le forme del sanguinamento attivo dovuto allo stravaso o all'accumulo del mezzo di contrasto sono variabili.*

active bleeding using CEUS.

Keywords Liver · Spleen · Trauma · Active bleeding · Contrast media · Ultrasonography · Microbubbles

Conclusioni. *La CEUS può mostrare il sanguinamento attivo associato a trauma epatico e splenico con diverse caratteristiche di imaging, rendendo quindi possibile diagnosticare il sanguinamento attivo.*

Parole chiave *Fegato · Milza · Trauma · Sanguinamento attivo · Mezzo di contrasto · Ecografia · Microbolle*

Introduction

Active bleeding from hepatic and splenic trauma is a major cause of death and disability. It is very important to diagnose active bleeding immediately after trauma. Computed tomography (CT) has played an important role in identifying active bleeding [1–4]. Digital subtraction angiography (DSA) cannot only be used to identify active bleeding but also to arrest bleeding after penetrating trauma to the abdomen [5, 6]. CT findings have been shown to have significant clinical implications and can help the trauma surgeon determine nonoperative or surgical treatment [7]. However, CT and DSA are slow and often not available in the Emergency Department, creating a possible risk for critically ill patients. Additional drawbacks include: (a) high expense, (b) need for highly trained staff and (c) need for patient transfer from the Emergency Department.

There is good evidence that rapid detection and early intervention in the critically ill patient improves outcome [8, 9]. With the development of contrast media, contrast-enhanced ultrasound (CEUS) has improved the sensitivity of conventional US for detecting and characterising focal liver lesions [10]. Previous studies by Tang et al. also demonstrated the value of CEUS in diagnosing abdominal parenchymal organ trauma [11, 12]. CEUS has also been used to diagnose active bleeding from parenchymal organ trauma. Catalano et al. performed CEUS examinations in 83 traumatic emergencies, and their clinical study showed for the first time how US can detect contrast medium extravasation, a significant indicator of active haemorrhage. They concluded that their preliminary work showed that CEUS may be a new tool for detecting active bleeding [13]. However, whether CEUS can evaluate active bleeding from abdominal parenchymal organ trauma is still a matter of debate. Clevert et al. [14] found that active bleeding could be identified by CEUS in one out of 18 patients. Thus, the purpose of our study was to observe the CEUS imaging features of active bleeding from hepatic and splenic trauma.

Materials and methods

The study was approved by the ethics committee of the Chinese People's Liberation Army General Hospital and was designed according to the Health Insurance Portability and Accountability Act. Informed consent for both CEUS and the use of related data for future research was obtained from each patient before and after the procedure.

Patients

A total of 392 patients with liver and/or spleen trauma (179 liver and 217 spleen injuries) were enrolled in this retrospective study covering a period of >4 years (September 2004 to December 2008). The mechanisms of injury included accidental fall, motorcycle crash, motor vehicle crash, and automobile–pedestrian collision. Initial haemodynamic stability was achieved with controlled fluid resuscitation with ≤2,000 ml of fluid (balanced salt solution, BBS). During this time, all patients were examined by CEUS following contrast-enhanced CT.

Ultrasound imaging

US contrast agent used in this study was SonoVue (Bracco, Milan, Italy), a second-generation contrast medium for diagnostic imaging approved in China in 2003, which consists of stabilised microbubbles containing an inert gas (sulfur hexafluoride, 8 μl/ml of solution) and covered by a phospholipid membrane [15]. SonoVue is reconstituted with 5 ml of normal saline in a few seconds and is immediately administrable. There is no need for fasting or preliminary laboratory tests. Intravenous injection of the contrast medium can be repeated [16]. A Sequoia 512 scanner (Siemens Medical Solutions, Mountain View, CA, USA) with 4V1 transducers with 3.0–5.0 MHz was employed for patient imaging. CEUS examination was performed at the patient's bedside in the Emergency Department following contrast-enhanced CT and conventional US. CEUS was performed with contrast pulse sequencing (CPS) at a mechanical index of 0.15–0.17. The scan settings during the examination (including gain, scanning depth, and time gain control) were optimised for each region independently. The focus was set to the deepest level of the organ examined. SonoVue, a dose of 0.025 ml/kg, was administered as a quick bolus through an antecubital vein.

Ultrasound image interpretation

Two US specialists, each with 5 years' experience in diagnosing abdominal parenchymal organ trauma, performed the examinations. CEUS was performed to confirm liver or spleen injuries on the basis of echoic/hypoechoic perfusion defects in the organ parenchyma and/or capsule. CEUS images and animations of the injury region and surrounding area were carefully assessed to confirm the existence of contrast medium extravasation and pooling indicating active bleeding.

Clinical follow-up

Information from surgery, minimally invasive treatment and conservative treatment was used as the reference standard. The clinical outcome of each patient was determined from a chart review by one of the investigators. For patients undergoing surgery or minimally invasive treatment after CEUS and CT, the findings of surgery or the minimally invasiveness procedure (i.e. the official description as mentioned in the report of the trauma surgeon and angiographer or US specialist) were used for comparison with CEUS and contrast-enhanced CT. For patients not undergoing further diagnostic procedures or surgery, follow-up information was obtained from either the patient's chart or the trauma surgeon in charge of the patient. This clinical follow-up was used for comparison with CEUS and contrast-enhanced CT in these patients.

Statistical analysis

All data are presented as descriptive variables. Differences between group means were determined by analysis of variance (ANOVA) (SyStat Ver 13.0, SPSS, Inc, Chicago, IL, USA), with the chi-square test for 2×2 tables, where applicable. The level of statistical significance was set at $p<0.05$.

Results

General characteristics

CEUS results were compared with those of contrast-enhanced CT for 392 patients with 396 liver or/and spleen lesions (Table 1). The detection rate of CEUS was not different from that of contrast-enhanced CT (p=0.333). The information from surgery, minimally invasive treatment and conservative treatment was used as a reference standard, and the sensitivities of the two techniques were not different (p=0.122).

Table 1 Contrast-enhanced ultrasonography (CEUS) showed active bleeding in 392 patients with 396 liver or/and spleen lesions compared with contrast-enhanced computed tomography (CECT)

Methods	Detection rate, % (n)	Sensitivity, % (n)
CEUS	16.0 (63/396)*	72.4 (63/87)**
CECT	17.2 (68/396)	81.2 (68/83)

*p=0.333, **p= 0.122

Tabella 1 *La CEUS ha mostrato la presenza di sanguinamento attivo in 392 pazienti con 396 lesioni epatiche e/o spleniche, a confronto con la TC con mezzo di contrasto (CECT)*

Metodica	*Identificazione, % (n)*	*Sensibilità, % (n)*
CEUS	*16,0 (63/396)**	*72,4 (63/87)***
CECT	*17,2 (68/396)*	*81,2 (68/83)*

**p=0,333, **p= 0,122*

CEUS identified contrast medium extravasation or pooling in 16% (63/396) of livers or spleens in 61 patients (47 men, 14 women; mean age 27.8 years). The 63 liver or spleen lesions with contrast-medium extravasation or pooling indicating active bleeding consisted of 29 liver and 34 spleen lesions.

Imaging

Of 63 lesions in 61 patients, CEUS identified contrast medium extravasation or pooling in 74.6% (47/63) lesions (21 liver and 26 spleen), both in the lesion and out of the capsule in 14.3% (9/63) and only outside of the capsule in 11.1% (7/63). CEUS represented active bleeding as a region of hyperechoic or isoechoic perfusion associated with contrast medium extravasation or pooling during the different CEUS phases. In particular, it often appeared hyperechoic in the arterial and late parenchymal phases and isoechoic in the early parenchymal phases. CEUS imaging of active bleeding from hepatic and splenic trauma presented different features: (a) active bleeding from a liver or spleen trauma involving the organ capsule appeared as a spring or fountain with a high velocity, or as a drip with a low velocity when there was effusion around the injured organ (Fig.1a,b); (b) active bleeding inside the lesion of liver or spleen parenchyma appeared as an isolated, hyperechoic or isoechoic region or spot with variable size and shape, such as round, oval, plum flower and band (Fig. 2a,b); (c) active bleeding from liver or spleen trauma involving the organ capsule appeared as a contrast band along the capsule due to contrast medium extravasation when there was no effusion around the injured liver or spleen. With blood flowing, some extravasated contrast medium moved as a

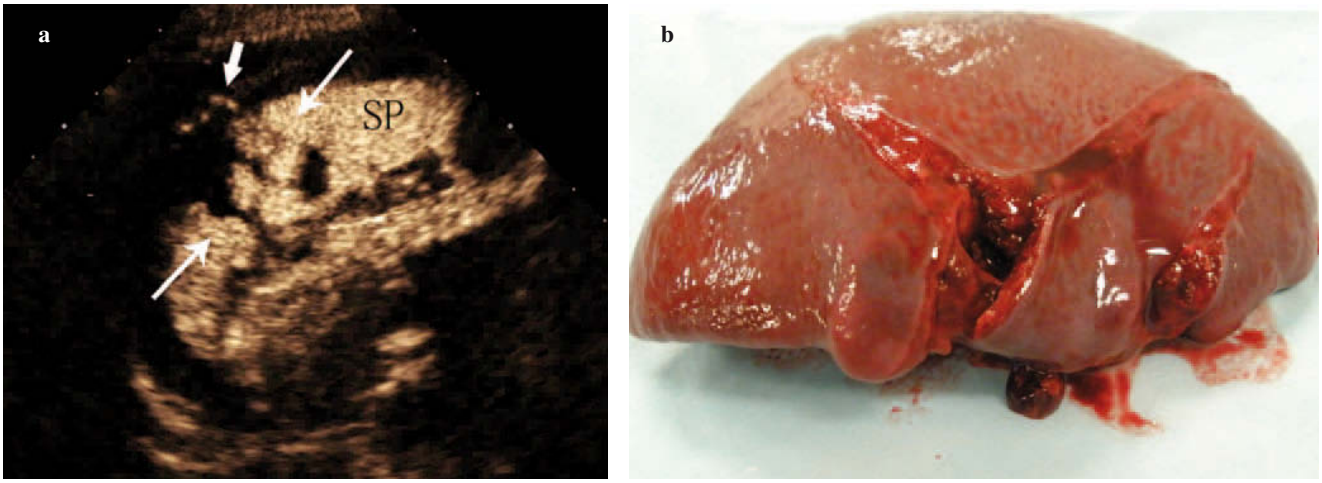


Fig. 1a Contrast-enhanced transverse oblique ultrasound image in a 32-year-old man involved in a traffic accident. The splenic lesion appeared as an anechoic and hypoechoic perfusion defect area with a clear irregular border (*long arrows*) and involved the splenic capsule. The active haemorrhage appeared as an isolated, fountain-like, hyperechoic stripe (*short arrow*). *SP* spleen. **b** Gross specimen obtained in the same patient as in **a**. Surgery confirmed completely the origin of the haemorrhage, as shown by contrast-enhanced ultrasound.

Fig. 1a *Scansione trasversale obliqua di ecografia con mezzo di contrasto in un uomo di 32 anni coinvolto in un incidente stradale. La lesione splenica appare come area anecogena ed ipoecogena con difetto di perfusione con bordi netti irregolari (frecce lunghe), e coinvolge la capsula splenica. L'emorragia attiva appare come una striatura iperecogena isolata "a getto" (freccia corta). SP: milza.* ***b*** *Pezzo operatorio ottenuto dallo stesso paziente della Figura 1a. La chirurgia ha confermato completamente l'origine dell'emorragia che era stata evidenziata con la CEUS.*

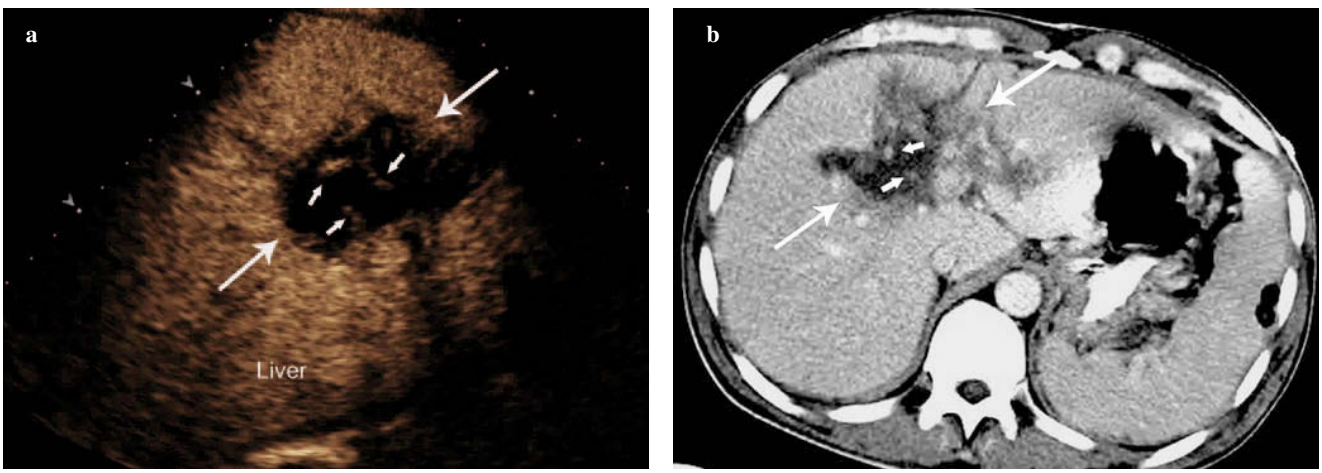


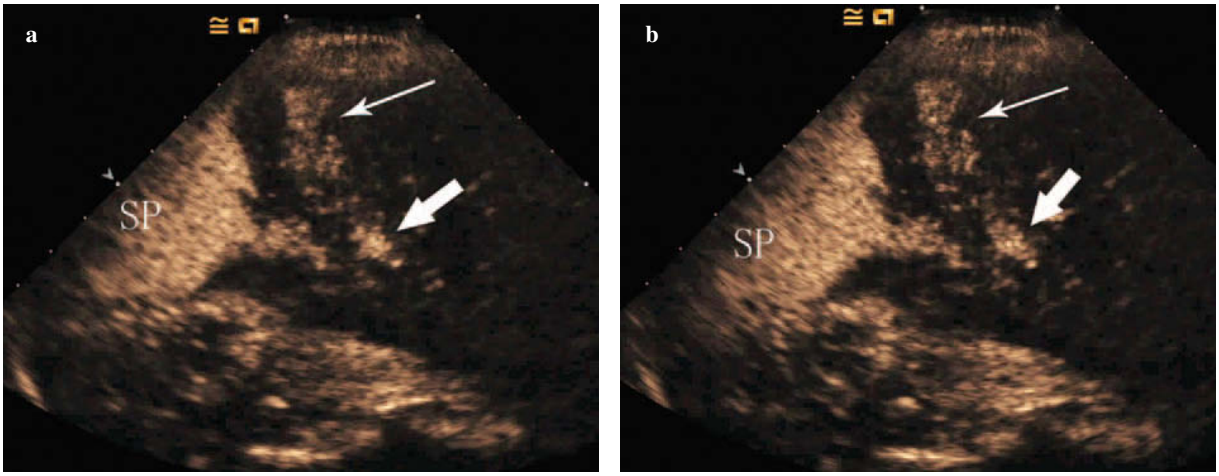
Fig. 2a Contrast-enhanced ultrasound (CEUS) image in a 44-year-old man involved in a serious traffic accident. The hepatic lesion appeared as an anechoic and hypoechoic perfusion defect area with a clear irregular border (*long arrows*). The sites of active haemorrhage appeared as isolated, hyperechoic and isoechoic band-like spots with variable size and shape (*arrows*) **b** Computed tomography (CT) image shows the liver lesion as an area of low attenuation (*long arrows*) and demonstrates active bleeding as high attenuation (*short arrows*) because of contrast blush.

Fig. 2a *Immagine CEUS in un uomo di 44 anni coinvolto in un grave incidente stradale. La lesione epatica appare come un'area anecogena ed ipoecogena con difetto di perfusione con margini netti irregolari (frecce lunghe). I siti di emorragia attiva appaiono come spot a banda isolati, iperecogeni ed isoecogeni con dimensioni e forma variabili (frecce)* ***b*** *L'immagine TC mostra la lesione epatica come un'area di bassa attenuazione (frecce lunghe) e dimostra il sanguinamento attivo come area di elevata attenuazione (frecce corte) a causa dello stravaso di mezzo di contrasto.*

brooklet or in a serpentine pattern. The sizes and shapes of the enhanced regions due to contrast medium extravasation or pooling were variable. At the site of injury, the remaining normal parenchyma often presented regions of similar enhancement to that of the contrast medium extravasation and pooling area. The way to distinguish them was that the remaining normal parenchyma showed unchanged shape (Fig. 3a–c).

Clinical follow-up

Of the 63 traumatic organs with active bleeding, 28.5%



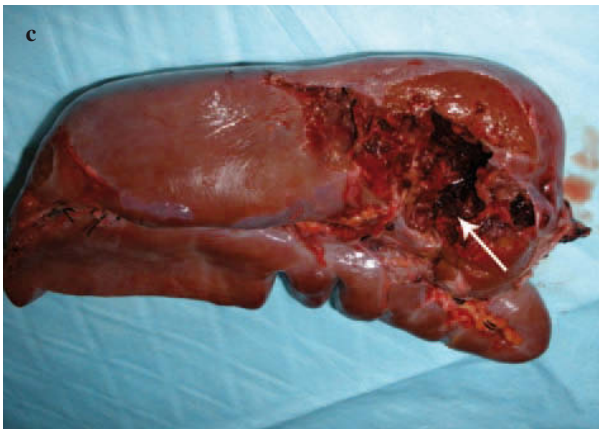


Fig. 3a-c Contrast-enhanced ultrasound (CEUS) images in a 23-year-old woman involved in an fall. **a** Transverse oblique US image of the spleen depicts the injury region as an anechoic and hypoechoic perfusion defect area with an irregular border in middle–lower spleen. **b** Within the lesion, there were enhanced perfusion regions, including the remaining normal parenchyma (*fine arrow*) and contrast medium extravasation and pooling (*thick arrow*). The remaining normal parenchyma appeared with unchanged shape, whereas contrast medium extravasation and pooling changed shape continuously (*thick arrows* in **a** and **b**). *SP* spleen. **c** Gross specimen after splenectomy confirmed the CEUS finding. The *arrow* indicates the location where the active bleeding was found during the operation.

Fig. 3a-c *Immagini CEUS in una donna di 23 anni coinvolta in una caduta accidentale.* ***a*** *Scansione ecografica trasversale obliqua della milza che mostra l'area lesionata con aspetto anecogeno ed ipoecogeno con difetto di perfusione con margini irregolari nella regione medio-inferiore della milza.* ***b*** *All'interno della lesione ci sono regioni che presentano enhancement perfusionale e rappresentano parenchima residuo normale (freccia sottile) e stravaso e accumulo di mezzo di contrasto (frecce spesse in* ***a*** *and* ***b****). SP, milza.* ***c*** *Il pezzo operatorio dopo splenectomia conferma i rilievi della CEUS. La freccia indica la localizzazione del sanguinamento attivo rilevato durante l'operazione.*

(18/63) underwent immediate surgery after CEUS. The surgical findings confirmed the origin of the haemorrhage as shown by CEUS in 94.4% (17/18) instances. One of two sites of haemorrhage was missed by CEUS in 5.6% (1/18). A total of 68.3% (43/63) patients received percutaneous minimally invasive treatments, including 41 under CEUS guidance and two under DSA guidance. The active haemorrhage detected by CEUS was confirmed, and the appropriate control measures implemented. The remaining 3.2% (2/63) were selected for conservative treatment, with physical examination and monitoring of vital signs at short intervals. The active bleeding disappeared in both patients 20 and 40 min, respectively, after CEUS.

Discussion

SonoVue, the second-generation contrast medium used in this study, allows boosting of the lesion-to-parenchyma conspicuity, which increases US sensitivity. CEUS has been largely employed in the evaluation of focal lesions [17, 18] but also to improve US accuracy in detecting parenchymal organ injury after blunt abdominal trauma [19–23]. CEUS can help depict findings that are not accessible on conventional US, such as tissue hypoperfusion, nonperfusion, hyperaemia and contrast extravasation. Although recent papers have reported that CEUS can detect active bleeding in some abdominal emergencies [24], the imaging characteristics have not been determined with double-blind comparisons of CEUS and reference standards (surgery, angiography, interventional US, etc.). Our study describes CEUS imaging of active bleeding from hepatic and splenic trauma.

CEUS identified sites of active bleeding by comparing variations in perfusion with surrounding tissues. The variability of perfusion was caused by extravasation and/or pooling of the intravascular contrast agent. However, active bleeding not only presented as a hyperechoic area but also as a hyperechoic or isoechoic area, in contrast to the findings of some recent studies [11, 22]. All active bleeding sites were characterised by activity, which enabled ready detection by real-time CEUS. In addition, the active bleeding sites presented various shapes depending on the different locations, velocities and quantities.

This study showed that the sensitivity of CEUS was 72.4%. Compared with CEUS, contrast-enhanced CT can provide valuable information to direct the initial clinical management of patients with hepatic or splenic trauma by demonstrating active bleeding. Marmery et al. [25] reported that CT for active haemorrhage had a sensitivity of 76% (76/100) in 392 haemodynamically stable blunt-trauma patients. Our study showed that the sensitivity of contrast-enhanced CT was 81.2%. In the diagnosis of active haemorrhage from hepatic or splenic trauma, contrast-enhanced CT has several advantages over CEUS, such as screening the entire abdomen and no limitations due to obesity, meteorism or subcutaneous emphysema. As a result, it has been popular among radiologists and surgeons. CT has also been an important imaging modality in predicting the necessity for surgical or nonsurgical treatment [26–29]. CT is safe for haemodynamically stable patients with blunt trauma [30]. However, some patients with haemodynamic instability are difficult to diagnose. Our study demonstrated that CEUS enabled a bedside diagnosis and avoided patient transfer. Moreover, CEUS could predict the need for surgical or nonoperative treatment. The rapid diagnostic capabilities of CEUS could contribute to a decrease in morbidity and mortality from traumatic abdominal injuries.

In the diagnosis of active bleeding, CEUS has several advantages: (1) it can detect active bleeding from hepatic and splenic trauma with excellent imaging characteristics; (2) real-time imaging allows CEUS to accurately evaluate active bleeding because active bleeding is characterised by activity. (3) the examination is rapid, with a room time <10 min. The use of CEUS saves time and is safe.

Our study has several limitations: (1) CEUS shares with conventional US several limitations, such as patient obesity, meteorism, subcutaneous emphysema etc. Moreover, CEUS lacks the panoramic quality of CT. (2) CEUS requires rapid and skilful diagnosis because the duration of a single CEUS examination is only 6–8 min. (3) In theory, CEUS can show active haemorrhage with any velocity. However, when there is no effusion around the injured liver or spleen, it may miss some active bleeding. (4) The real correlation between bleeding velocity and CEUS imaging – whether active bleeding from an artery, vein or capillary can be accurately detected or not – needs to be investigated by further studies.

In our opinion, CEUS should be considered for the initial detection of active bleeding from hepatic or splenic trauma. It should not be intended as a substitute for CT but as a selective possibility to boost the role of US in the initial screening of patients with abdominal trauma.

In conclusion, our study has shown that active haemorrhage from liver and spleen trauma appeared with various imaging features on CEUS, according to which the diagnosis can be established. CEUS could exactly predict the need for surgery and nonoperative management. When active bleeding was detected, immediate surgical or minimally invasive therapy was required.

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Conflict of interest None

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