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# ORIGINAL ARTICLE

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Trauma

# Contrast-enhanced point of care ultrasound for the evaluation of stable blunt abdominal trauma by the emergency physician: A prospective diagnostic study

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#### Abstract

**Objectives:** Clinical examination alone cannot reliably rule out significant traumatic abdominal injury. Computed tomography (CT) has become the primary method for evaluating blunt abdominal trauma and clinicians rely heavily on it to rule out abdominal injury. Ultrasound examination may miss significant abdominal injury particularly in stable patients. The use of a contrast agent improves ultrasound sensitivity to visceral abdominal injuries. The objective of this diagnostic study is to compare bedside contrast enhanced ultrasound (CEUS) performed by emergency physicians to CT in hemodynamically stable adults for the assessment of blunt abdominal trauma and evaluate CEUS accuracy outcomes.

**Methods:** Hemodynamically stable patients with blunt trauma were prospectively enrolled in the trauma bay. After initial evaluation, we included patients at risk of abdominal injury and for whom an abdominal CT was planned by the trauma leader. Ultrasonography was performed prospectively and at the bedside by the emergency physician followed by abdominal CT used as a reference standard.

**Results:** Thirty-three patients were enrolled in the study; among them, 52% showed positive traumatic findings in abdominal CT scans, and 42% were diagnosed with solid organ lesions. Compared to CT, a focused abdominal sonography (FOCUS) examination, looking for free fluid or perirenal hematoma, showed limited performance for traumatic findings with a sensitivity of 65% (95% confidence interval [CI]: 38%–86%), a specificity of 75% (95% CI: 48%–93%), a negative likelihood ratio (NLR) of 0.47 (95% CI: 0.23–0.95), and a positive likelihood ratio (PLR) of 2.59 (95% CI: 1.03–6.48). When combining FOCUS with CEUS, the sensitivity of the sonography increased to 94% (95% CI: 71%–100%) with a specificity of 75% (95% CI: 48%–93%). The PLR was 3.76 (95%

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CI: 1.6–8.87) and the NLR was 0.08 (95% CI: 0.01–0.54). In our population, abdominal sonography with contrast failed to identify a single positive abdominal CT with a grade 1 kidney injury.

**Conclusions:** A FOCUS examination shows limited sensitivity and specificity to detect positive abdominal CT in stable adults with abdominal trauma. With the addition of contrast and careful inspection of solid organs, abdominal sonography with contrast performed by the emergency physician improves the ability to rule out traumatic findings on abdominal CT. CEUS performed by emergency physicians may miss injuries, especially in the absence of free fluid, in cases of low-grade injuries, simultaneous injuries, or poor-quality examinations.

#### 1 | INTRODUCTION

#### 1.1 | Background

During the last decades, ultrasound (US) for the evaluation of abdominal trauma has evolved from a tool reserved solely for imaging specialists to a tool belonging to the point of care ultrasound (POCUS) armamentarium of the emergency physician (EP). Ultrasound is indeed highly sensitive in detecting free intraperitoneal fluid, and, therefore, protocols such as Focused Assessment with Sonography in Trauma (FAST) examination are widely used for triaging blunt abdominal trauma patients. However, FAST or, even full US studies, may miss significant abdominal injury, particularly in stable patients.<sup>1-3</sup> Contrast enhanced ultrasound (CEUS) has been investigated in adults and children for abdominal trauma and several studies have shown that the use of a contrast agent increases US sensitivity to detect abdominal solid organ lesion (SOL).<sup>4-6</sup> A recent meta-analysis confirms that CEUS has a higher diagnostic value than US for initial abdominal trauma assessment. It shows that CEUS has a pooled positive likelihood ratio (PLR) of 125 and pooled negative likelihood ratio (NLR) of 0.07 for traumatic findings compared to CT and a low heterogeneity. The same work shows that in previous studies CEUS has been performed by experienced radiologists or sonographers or evaluated, retrospectively.7

#### 1.2 | Importance

Blunt abdominal traumas present common challenges for EPs and trauma surgeons, as missed abdominal injuries may cause significant mortality and morbidity. Clinical examination alone cannot reliably rule out significant traumatic abdominal lesions<sup>8,9</sup> and to this day no clinical prediction tool has been externally validated.<sup>10</sup> Therefore, clinicians rely heavily on computed tomography (CT) to reliably rule out abdominal injury. Some authors advocate the use of CT as a screening tool not only among polytraumatized patients<sup>11</sup> but also in patients with low-risk mechanism of injury.<sup>12</sup> Concerns remain regarding costs related to low CT yield when used as a screening tool in low-risk patients, and also

regarding the consequences of high doses of radiation, especially in the younger population.<sup>13,14</sup>

# 1.3 | Goals of this investigation

So far, no previous study has evaluated the ability of EPs to perform CEUS to assess blunt abdominal trauma in the adult population. In this prospective diagnostic study, we assess sensitivity, specificity, and likelihood ratio of bedside abdominal sonography with contrast, performed by the EP, to diagnose abdominal injury in hemodynamically stable blunt abdominal trauma compared to CT as a reference standard. We also explore its role as part of an algorithm to rule out abdominal lesions and reduce the rate of negative abdominal CT.

# 2 | METHODS

# 2.1 | Study design and setting

This prospective investigator-initiated diagnostic study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (Registration number KEK BE 198/14). All patients included gave their witnessed oral consent, followed by a detailed written consent. Patients or the public were not involved in the design, conduct, or reporting of our research. This diagnostic study is compliant with STARD 2015 guidelines. Figure 1 displays the study design.

This study was performed between August 2015 and May 2019 in the Emergency Department of the University Hospital (Inselspital) Bern, Switzerland. This is a level I, university-affiliated tertiary trauma center where 48,000 patients are treated annually. Per year, around 500 patients with major trauma are admitted.

In our institution, patients' assessment and management in the trauma bay takes place under the supervision of a trauma leader, who is a senior EP, and follows the common Advanced Trauma Life Support (ATLS) approach. It includes history, clinical examination, baseline

laboratory tests, and depending on the context, an extended FAST and trauma bay x-ray (LODOX, LODOX Systems).

# 2.2 | Population selection

We included hemodynamically stable adult patients (>18 years) with blunt trauma admitted to the trauma bay. Patients were enrolled if a trained EP sonographer was available on admission and if an abdominal CT was planned as part of the work up—as decided by the trauma leader. We included patients with at least one risk factor for abdominal injury as identified during primary assessment. Risk factors for abdominal injury were defined as suspicion of major thoracic trauma (pneumothorax, rib fractures, hemothorax), pelvic or femoral shaft fracture identified during primary survey, or if an abdominal injury was suspected according to the team leader's clinical impression (history, clinical examination, or trauma bay x-ray).

Exclusion criteria were hemodynamic instability, contraindications to the sonographic contrast agent, or absence of informed consent. Hemodynamic instability was defined as signs of shock (class III and IV hemorrhagic shock, according to ATLS classification) and non-response or transient response to an initial fluid bolus of 1–2 L, suggesting ongoing blood loss. Sonovue is contraindicated in patients with history of hypersensitivity reactions to sulfur hexafluoride lipid microsphere components and during pregnancy and breastfeeding because the safety profile has not been established in this subgroup. However, there are reports that Sonovue has been used off label in this subgroup without adverse event.<sup>15</sup> In our study, pregnancy was ruled out before CEUS in the trauma bay using a rapid POC test ( $\beta$ HCG, i-STAT).

#### 2.3 Sonography (index test) method

All sonographies were performed by one of seven EPs trained in abdominal sonography (certified in POCUS emergency US by the Swiss Society for Ultrasound in Medicine). For the study, each involved physician received basic CEUS training consisting of a 3-h theoretiThis prospective study found that adding contrast to the grey-scale sonography performed by the emergency physician improves sensitivity for the detection of intra-abdominal injuries after blunt abdominal trauma.

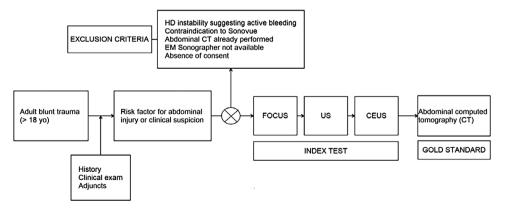
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cal and hands-on-training session. Only one sonographer had previous experience in CEUS.

Sonographies were performed with two US machines (Philips Affinity 70, Phillips Healthcare and Hitachi Noblus; Hitachi Corp) using a 2–6 MHz curved array multifrequency probe. For CEUS, a dual screening technique (CEUS mode/B-mode) was used with a low mechanical index of 0.07.

For abdominal sonography, the sonographer first assessed the presence of intraabdominal free fluid by scanning the perihepatic area, the hepatorenal interface, the perisplenic region, the paracolic gutters, and the pouch of Douglas. The retroperitoneum was also assessed for the presence of fluid or hematoma in the perirenal area (focused abdominal sonography [FOCUS] examination). The solid organs (liver, spleen, and kidneys) were then assessed for injuries in B-mode (US examination). Following US, contrast was injected to further assess the solid organs. As recommended by the manufacturer, 2.4 mL of US contrast agent (Sonovue) was injected through an intravenous access on an antecubital vein by a second operator. One vial (5 mL) was used per patient, which was enough to perform two injections, each followed by a 10 mL flush of normal saline. We usually scanned both kidneys first, followed by the liver and the spleen. The second injection was given once the examiner found the washout to be significant (CEUS examination).

CEUS enables the evaluation of contrast phases which are different for each organ.<sup>16</sup> For the detection of traumatic lesions, parenchymal phase is the most relevant—traumatic lesions usually present as anechogenic areas within the organ. The kidneys enhance first (Video S1) and have a washout time of 2–3 min. The liver has a washout



**FIGURE 1** CEUS, contrast enhanced ultrasound; CT, computed tomography; FOCUS, focused abdominal sonography; HD, hemodynamic;Study design; US, ultrasound.

time between 3 and 5 min. Contrast can be seen in the parenchyma of the spleen as long as 5–7 min after injection.

A positive FOCUS was defined as the presence of intraabdominal free fluid (Video S4) or retroperitoneal fluid or hematoma. A positive US was defined as the presence of a SOL in B-mode. SOL was defined as a distortion of the normal anatomy of the organ or a focal area of hyper- or hypo-echogenicity in the organ parenchyma. A positive CEUS was defined by either a focal anechogenic area of the parenchyma (suggesting laceration) or the total absence of contrast enhancement of the organ (suggesting avulsion) (Pictures S1 and S2, Videos S2 and S3 show examples of organ lesions). The presence of focal contrast enhancement (hyperechogenic zone)—either in the peritoneal cavity or in the parenchyma (suggesting active bleeding)—was also considered to be a positive examination.

The sonographer assessed the quality of each sonographic examination, overall and for each individual organ, as very good, good, moderate, poor, and very poor based on the habitus, their ability to scan the whole organ or region of interest, and the image quality.

After inclusion, sonography was performed and completed within 15 min, followed by abdominal CT. Neither the sonographer nor the radiologist was blinded to clinical information. The study design is depicted in Figure 1.

#### 2.4 Computed tomography (reference standard)

All patients were investigated with abdominal and pelvis CT with contrast. Depending on the patient's history and the first clinical assessment, the scan range included the whole body or just abdomen and pelvis. CT images were acquired on a third-generation Single Source CT (Somatom Definition Edge; Siemens Healthineers). CT was performed with a tube voltage from 100 to 120 kVp and a reference Milliampere-seconds (mAs) of up to 425. On the 128-detector scanner, collimation of  $128 \times 0.6$  mm was used, with a pitch of 0.6. A slice thickness of 0.6 up to 1 mm was reconstructed, with a SAFIRE (Sinogram Affirmed Iterative Reconstruction) level 3 and with appropriate kernels for soft tissue and bones. For the scan, 120 mL of an iodinated contrast agent (Iomeron400; Bracco) was injected using a split bolus protocol.

A positive abdominal CT was defined as any of the following traumatic findings: hemoperitoneum, SOLs, hollow viscus injuries, abdominal vascular injuries, and retroperitoneal or extraperitoneal hematoma. Bony lesions (vertebra or pelvic fracture) were not considered as positive abdominal CT. Severity of SOL was defined using the organ injury scale of the American Association for the Surgery of Trauma (AAST).

#### 2.5 | Data collection and analysis

Clinical data for each patient were collected using the trauma bay protocol form of our institution. The results of the sonography and quality rating were reported by the sonographer in a standard study form which was completed and sealed before the CT examination was performed. The results of CT were collected from the final radiological report. A study assistant transferred these data into REDCap, electronic data capture tools hosted at the Faculty of Medicine of the University of Bern. $^{17}$ 

We performed a sample size calculation based on the following conservative assumptions: (1) 30% prevalence of solid organ laceration detected in CT in all patients who received a CEUS and (2) change in sensitivity of CEUS versus US of 10% using a one-sided test. Therefore, to achieve an 80% power at an alpha level of 5%, 197 participants would have been required and 59 of those with positive CT finding. Patient enrollment was terminated before reaching this prespecified number because of sluggish inclusion.

We used descriptive statistics to present population data. We explored a standard set of performance criteria (sensitivity, specificity, and positive and negative likelihood ratio) for US examinations. The tests' results were considered dichotomous. Sensitivity, specificity, and likelihood ratios were all calculated based on a common  $2 \times 2$  table using the MedCalc software.<sup>18</sup> This software also provides 95% confidence intervals (CI) for all estimates. For sensitivity, specificity, and accuracy, CI is based on Clopper–Pearson confidence intervals, for predictive values on standard logit confidence intervals.<sup>19</sup> and for likelihood ratios on Altmans log method.<sup>20</sup>

First, we assessed the performance of the US in B-mode (US) and US with contrast (CEUS) to detect SOLs. For this analysis, we used the prevalence of SOL among all examined organs in our population (Table 2).

Second, and more relevant for the clinical practice, we looked to see if the sonographic examination can reliably rule out a positive abdominal CT. Using parallel testing, we analyzed the performance of FOCUS examination, as well as FOCUS combined with US and CEUS, respectively, to detect positive abdominal CT. For this analysis, we used the prevalence of positive traumatic abdominal CT in our population (Table 3).

### 3 | RESULTS

#### 3.1 | Participants

Thirty-five patients were enrolled in the study. Two patients were excluded from the analysis (one because no written consent had been obtained and the other one due to a protocol violation). Table 1 summarizes data from the 33 remaining patients. Most patients with a positive abdominal CT were treated conservatively. Four patients required angiography (three for SOL and one for pelvic fracture) and two required surgeries because of hollow viscus injuries. A considerable proportion of patients had associated thoracic, pelvic injuries, or skeletal and soft tissue injuries. Only four patients were discharged home directly from the ED (Table 1).

#### 3.2 | CT findings and outcome

The prevalence of positive abdominal CT was 52% (17/33) and the prevalence of SOLs was 42%. The prevalence of SOLs was 14% among all investigated organs (18/132). Eighteen SOLs were found

**TABLE 1** Demographic data, computed tomography (CT) findings, outcome, and treatment.

|                                 | n (%)        |  |  |  |  |  |
|---------------------------------|--------------|--|--|--|--|--|
| Data                            | Median (IQR) |  |  |  |  |  |
| Demographics                    |              |  |  |  |  |  |
| Age                             | 42 (33-56)   |  |  |  |  |  |
| Gender male                     | 23 (69)      |  |  |  |  |  |
| BMI                             | 24 (22-27)   |  |  |  |  |  |
| Mechanism of injury             |              |  |  |  |  |  |
| Fall                            | 13 (39)      |  |  |  |  |  |
| Traffic accident                | 11 (33)      |  |  |  |  |  |
| Sport                           | 4 (12)       |  |  |  |  |  |
| Associated injury               |              |  |  |  |  |  |
| Spine                           | 5 (15)       |  |  |  |  |  |
| Cerebral                        | 2 (6)        |  |  |  |  |  |
| Pelvic fracture                 | 6 (18)       |  |  |  |  |  |
| Thoracic trauma                 | 9 (27)       |  |  |  |  |  |
| Type of abdominal lesion        |              |  |  |  |  |  |
| Positive abdominal CT           | 17 (52)      |  |  |  |  |  |
| Positive CT for SOL             | 14 (42)      |  |  |  |  |  |
| Hollow viscus injury            | 2 (6)        |  |  |  |  |  |
| Extraperitoneal hematoma        | 2 (6)        |  |  |  |  |  |
| Hemoperitoneum (HP)             | 8 (24)       |  |  |  |  |  |
| Liver                           | 4 (12)       |  |  |  |  |  |
| Spleen                          | 8 (24)       |  |  |  |  |  |
| Kidneys                         | 6 (18)       |  |  |  |  |  |
| SOL without HP                  | 4 (12)       |  |  |  |  |  |
| Destination                     |              |  |  |  |  |  |
| Ward                            | 14 (42)      |  |  |  |  |  |
| IMC/ICU                         | 12 (37)      |  |  |  |  |  |
| Discharge home from ED          | 4 (12)       |  |  |  |  |  |
| Transferred to another hospital | 3 (9)        |  |  |  |  |  |
| Management of SOL               |              |  |  |  |  |  |
| Conservative                    | 13           |  |  |  |  |  |
| Angiography for SOL             | 3            |  |  |  |  |  |
| Abdominal surgery               | 2            |  |  |  |  |  |

Abbreviations: BMI, body mass index; ED, emergency department; HP, hemoperitoneum; ICU, intensive care unit; IMC, intermediate care; IQR, interquartile range; *n*, number; SOL, solid organ lesion.

among 14 patients (four patients had two simultaneous abdominal organ lesions) (Table 1). Free intraabdominal fluid was found in 10 patients, of whom eight were described in the CT report as exhibiting hemoperitoneum and two patients were described as non-hemorrhagic fluid (ascites). Four intraabdominal SOLs were not associated with hemoperitoneum. Hollow viscus injuries were found in two patients and associated with free abdominal air and free fluid on CT. JACEP OPEN

| TABLE 2       | Performance of ultrasound and contrast enhanced             |
|---------------|---|
| ultrasound fo | or solid organ lesions, using a prevalence of 14% (18/132). |

| Index test | US    |                    | CEUS  |                     |
|------------|-------|--------------------|-------|---------------------|
| Se         | 0.39  | 95 CI% 0.17-0.64   | 0.72  | 95 CI% 0.47-0.90    |
| Sp         | 0.99  | 95 CI% 0.95-100    | 0.98  | 95 CI% 0.94-1       |
| NLR        | 0.62  | 95 CI% 0.43-0.89   | 0.28  | 95 CI% 0.13-0.60    |
| PLR        | 44.33 | 95 CI% 5.79-339.42 | 41.17 | 95 CI% 10.12-167.49 |
| NPV        | 0.91  | 95 CI% 0.88-0.94   | 0.96  | 95 CI% 0.91-0.98    |
| PPV        | 0.88  | 95 CI% 0.48-0.98   | 0.87  | 95 CI% 0.61-0.96    |
| Accuracy   | 0.91  | 95 CI% 0.85-0.95   | 0.95  | 95 CI% 0.89-0.98    |

Abbreviations: CI, confidence interval; NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.; Se, sensitivity; Sp, specificity.

#### 3.3 | Sonography results

No adverse event was reported related to Sonovue use. To detect SOL, US showed a low sensitivity (39%, 95% CI: 17%–64%) and high specificity (99%, 95% CI: 95%–100%). Contrast injection increased US sensitivity for SOLs to 72% (95% CI: 47%–90%) with a preserved specificity (98%, 95% CI: 94%–100%) (Table 2). CEUS failed to identify five out of 18 SOLs among 132 solid organs, all of lower grade. A single injury was not associated with a positive FOCUS (details in Table 4).

To identify a positive abdominal CT, the performance of FOCUS was rather low, with a sensitivity of 65% (95% CI: 38%-86%), a specificity of 75% (95% CI: 48%-93%), a PLR of 0.47 (95% CI: 0.23-0.95), and an NLR of 2.59 (95% CI: 1.03-6.48) (Table 3). FOCUS missed one in eight hemoperitoneum, described as localized and nonabundant, but CEUS correctly identified the associated splenic lesion. FOCUS was positive in both cases of hollow viscus injuries and in both cases of ascites. FOCUS failed to identify six out of 17 positive abdominal CT, of which five were SOLs, graded from 1 to 4, not associated with hemoperitoneum. When combining FOCUS with CEUS, the sensitivity of the examination increased to 94% (95% CI: 71%-100%) with a specificity of 75% (95% CI: 48%-93%). The NLR and PLR were 0.08 (95% CI: 0.01-0.54) and 3.76 (95% CI: 1.6-8.87), respectively (Table 3). By combining positive findings of FOCUS and CEUS, we found that only one patient with a grade 1 kidney injury was missed and that none of the five patients requiring intervention for abdominal trauma (angiography or surgery) were missed (Sn 100%, 95% CI: 47.82%-100%). Using this approach, four patients were falsely positive showing positive free fluid scans on the FOCUS without traumatic lesions (two of whom had ascites).

# 3.4 | Limitations

One limitation of the study is obviously its small sample size which resulted from a challenging enrollment due to the emergency setting, a highly selected population at risk of abdominal lesions, time pressure **TABLE 3** Performance of focused abdominal sonography (FOCUS), FOCUS combined with ultrasound (US), and FOCUS combined with US and contrast enhanced ultrasound (CEUS) for the detection of positive traumatic abdominal computed tomography (CT) using a prevalence of 52% (17/33).

| Index test | FOCUS |                  | FOCUS + | US               | FOCUS + U | JS + CEUS        |
|------------|-------|------------------|---------|------------------|-----------|------------------|
| Se         | 0.65  | 95 CI% 0.38-0.86 | 0.76    | 95 CI% 0.50-0.93 | 0.94      | 95 CI% 0.71-1    |
| Sp         | 0.75  | 95 CI% 0.48-0.93 | 0.75    | 95 CI% 0.48-0.93 | 0.75      | 95 CI% 0.48-0.93 |
| NLR        | 0.47  | 95 CI% 0.23-0.95 | 0.31    | 95 CI% 0.13-0.77 | 0.08      | 95 CI% 0.01-0.54 |
| PLR        | 2.59  | 95 CI% 1.03-6.48 | 3.06    | 95 CI% 1.26-7.44 | 3.76      | 95 CI% 1.60-8.87 |
| NPV        | 0.66  | 95 CI% 0.49-0.80 | 0.75    | 95 CI% 0.54-0.88 | 0.92      | 95 CI% 0.63-0.99 |
| PPV        | 0.74  | 95 CI% 0.53-0.88 | 0.77    | 95 CI% 0.58-0.89 | 0.80      | 95 CI% 0.63-0.91 |
| Accuracy   | 0.7   | 95 CI% 0.51-0.84 | 0.76    | 95 CI% 0.58-0.89 | 0.85      | 95 CI% 0.68-0.95 |

Abbreviations: CI, confidence interval; NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value; Se, sensitivity; Sp, specificity.

to perform the CT, and limited availability of a CEUS trained sonographer. Therefore, the large 95% CIs of our results are most likely a direct consequence of the small sample size. On the one hand, given the difficulties in achieving the planned sample size of this study and, on the other hand, considering the favorable findings of this study and previous ones, this limitation strongly suggests conducting a multicenter evaluation of CEUS in blunt trauma.

The prospective design of our study with sealed sonographic examinations guarantees sonographer blinding to CT results. The choice to use an enrichment strategy permitted us to limit costs from Sonovue but also guaranteed that each patient had a clear indication to abdominal CT, the reference standard. The study design achieved to select a population with high prevalence (52%) of abdominal injury but also presenting simultaneous lesions. The prevalence in our study is similar to other published studies,<sup>21</sup> but could positively influence the performance of sonography, especially sensitivity for combined tests,<sup>22</sup> and limit its application to a population with a lower risk of abdominal lesion.

Due to the low number of cases per physician involved, we are not able to evaluate if there is any significant difference in performance between EPs. Our results cannot be transferred to a setting where EPs have a lower level of training in abdominal US.

# 4 DISCUSSION

Our results suggest that CEUS can be safely implemented by EPs who are trained in POCUS abdominal sonography, provided that they have experience in abdominal sonography (200 examinations) and receive at least 3 h of specific training in CEUS to achieve results concordant to those obtained by radiologists in previous studies.<sup>6,7,21,23</sup> In these studies, the sonographers had more than 5 years of experience in abdominal sonography or at least >300 abdominal sonographic examinations.

Compared to standard US, CEUS performed by the EP shows high specificity and an increased sensitivity for the detection of SOLs. Our data are thus consistent with previously published studies showing that CEUS improves the sensitivity for SOL.<sup>6,7,21</sup> The five injuries missed by CEUS were all lower grade (grade 1-2 AAST injuries) and treated conservatively. We would like to emphasize that two lesions reported as "suspicious" on the CT report were clinically insignificant but were still considered as positive CT findings in our analysis, and this lowers the reported CEUS sensitivity (Table 4). Two CEUS examinations were rated as of moderate to very poor quality for the organ involved. Three out of the five patients with missed organ injuries presented with multiple abdominal lesions and sonography correctly identified at least one organ lesion. We suppose that this observation may be due to a search satisfaction bias, a cognitive error in medical image assessment.<sup>24</sup> When performing CEUS, the EP must therefore pay particular attention not to rule out a diagnosis of injury based on a poor-quality examination or to miss simultaneous injuries.

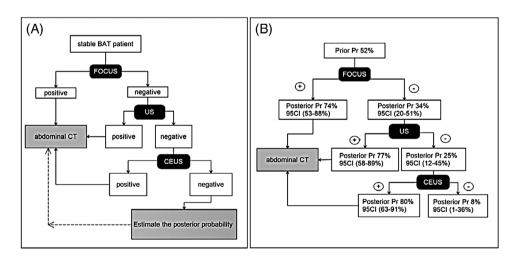
In practice, FOCUS and CEUS follow each other and concentrate on different US findings. FOCUS looks for intrabdominal free fluid or perirenal hematoma, while CEUS concentrates on the organ parenchyma. By combining all positive sonographic findings, the sensitivity of the examination for traumatic CT findings is much higher than CEUS alone but the specificity is limited. In our study, this low specificity is substantially explained by the presence of two patients with ascites, which contribute to the lower positive likelihood ratio compared to previously published studies.<sup>7</sup>

We suggest that in practice abdominal sonography with contrast should be performed in a stepwise fashion (Figure 2B) and that any positive ultrasonographic finding should prompt evaluation by abdominal CT. Moreover, in patients with positive findings on FOCUS or US, we suggest avoiding using US contrast and going straight for CT imaging. In the case of a negative sonographic examination with contrast (FOCUS, US, and CEUS), the posterior probability of a positive abdominal CT will depend on the prior probability of intraabdominal injury. In our population showing a moderate to high prior probability of 52%, the posterior probability of injury is still 25% after a normal bedside noncontrast abdominal sonography (normal FOCUS and US). After a normal bedside contrast sonography (FOCUS, US, and CEUS study), the posterior probability of injury is 8% (Figure 2B). With a population of lower risk, for example, with a prior probability of injury of 15%, we can infer from

TABLE 4 Details of solid organ injuries overlooked by contrast enhanced ultrasound (CEUS).

| Patient | FOCUS<br>abdominal<br>examination | Quality of CEUS                     | CT findings overlooked by<br>CEUS  | Other intra-abdominal<br>traumatic CT findings  | Management   |
|---------|-----------------------------------|-------------------------------------|--|---|--|
| 3       | Positive                          | Good                                | Suspicion of grade 1 splenic<br>injury subdiaphragmatic,<br>no pooling, no<br>hemoperitoneum   | Yes, grade 4 kidney injury,<br>with retroperitoneal<br>hematoma identified in<br>CEUS   | Admission to intermediate<br>care, no angiography,<br>conservative management<br>of both lesions |
| 6       | Negative                          | Good                                | Small hyperdensity of the left<br>lower kidney pole<br>compatible with<br>intraparenchymal<br>hematoma (grade 1 kidney<br>injury). No capsular<br>hematoma, no free fluid.<br>No pooling | None  | Admission to ward, no<br>angiography, conservative<br>management                                 |
| 23      | Positive                          | Moderate                            | Capsular retraction (or<br>suspicion of grade 1<br>splenic injury), no pooling   | Yes, grade 3 liver injury<br>identified in CEUS. Free<br>fluid identified by US   | Admission to intermediate<br>care, no angiography,<br>conservative management<br>of both lesions |
| 27      | Positive                          | Good                                | Grade 2 splenic injury,<br>located on the inferior pole  | No other solid organ injuries<br>but jejunal perforation.<br>Free fluid perihepatic,<br>perisplenic and in pelvis<br>identified by US | Admission to ICU, surgical<br>management (jejunal<br>perforation)                                |
| 31      | Positive                          | Very poor quality<br>over the liver | Subcapsular hypodensity of<br>the segment VII of the liver<br>(grade 2 liver injury)   | Yes, grade 3 right kidney<br>injury with perirenal<br>hematoma, identified in<br>CEUS. Free fluid identified<br>by US                 | Admission to ICU, no<br>angiography, conservative<br>management of both<br>lesions               |

Abbreviations: CEUS, contrast enhanced ultrasound; CT, computed tomography; ICU, intensive care unit; US, ultrasound.



**FIGURE 2** (A) Stepwise approach for ruling out positive traumatic abdominal computed tomography (CT) by sonography. Focused abdominal sonography (FOCUS) looks for intraabdominal free fluid and perirenal hematoma, ultrasound (US) looks at solid organ parenchyma in B-mode, and contrast enhanced ultrasound (CEUS) looks at solid organ parenchyma using contrast enhancement. (B) Posterior probability of positive abdominal CT according to FOCUS, US, and CEUS results in our population. BAT, blunt abdominal trauma; Pr, Probability.

our results that the posterior probability of intrabdominal injury would be 1% after a normal contrast sonographic examination.

We think that further studies should be conducted to evaluate and validate a contrast sonographic strategy in a population with lower prior probability of abdominal injury. The integration of other diagnostic modalities (eg, hematuria screening) could decrease the posterior probability of kidney injury for which contrast sonography shows a higher NLR compared to liver and splenic injuries.<sup>7</sup>

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The EP, seeking to safely discharge his patient home, regularly has to weigh the benefits and risks of an abdominal CT. In the situation of a borderline indication to CT, he may be tempted to overly rely on a normal noncontrast US to rule out intraabdominal injury. Our results illustrate that abdominal sonography without contrast misses some injuries. We show that adding contrast to the POCUS study performed by the trained EP can reduce the risk of a missed intrabdominal injury. Clinical prediction tools for blunt abdominal trauma have not been validated to rule out abdominal injury but can be used to estimate the prior probability of abdominal injury.<sup>9,10</sup> The absence of several variables in stable blunt abdominal trauma have been shown to decrease the prior probability of intrabdominal injury, such as major chest injury, femoral fracture, pelvic injury, and head injury.<sup>10</sup> In these selected patients, a normal contrast abdominal examination, as performed in our study, would virtually rule out an intrabdominal injury. Residual risk management should be discussed with the patient (clinical follow up, ability to return to the ED).

As already implemented in some expert centers,<sup>25</sup> CEUS could be a valuable strategy to minimize radiation exposure and facilitate safe and fast discharge, particularly in situations with a borderline indication to CT. CEUS may also play a role for triaging trauma patients in some special circumstances (ie, centers without CT).

On the launching of the study, Sonovue was the only available US contrast agent in Switzerland. Regarding financial aspects, the cost of Sonovue per patient for an US trauma protocol and those related to the CT contrast agent for abdominal CT are fairly the same. For many US systems, contrast mode is available as an accessory module that costs about 7000 CHF (which corresponds to 8000 USD or 7300 euro). Contrast mode is not yet available for hand-held US systems. We are not aware of any existing cost comparison analysis between CEUS and CT.

In conclusion, we think that bedside abdominal sonography with contrast performed by the trained EP is a promising POCUS tool and should be further explored. In the future, CEUS might gain a broader role, when blended with history, clinical examination, or other parameters such as urine analysis, in ruling out abdominal injury in patients presenting with borderline indication to CT and could be part of a shared decision-making strategy in this setting.

#### AUTHOR CONTRIBUTIONS

Viviane Donner and Beat Lehmann conceived the study. Julian Thaler, Beat Lehmann, Wolf E. Hautz, Thomas Christian Sauter, and Karsten Klingberg conducted the study and supervised data collection. Viviane Donner analyzed the data and drafted the manuscript, and all authors contributed substantially to its revision. Viviane Donner and Beat Lehmann take responsibility for the paper as a whole.

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#### CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare related to the present work. Bracco offered technical support and advice for the use of the contrast agent (Sonovue) and has provided educational grants to the Emergency Department of Inselspital since 2013. However, Bracco was not involved in any part of the study initiation, design, and conductance. No financial or material incentives were perceived by any of the authors. Wolf E. Hautz has received research funding from the European Union, the Swiss National Science foundation, the Zoll foundation, Dräger Medical Germany, Mundipharma Research UK, MDI International Australia, and Roche Diagnostics Germany. These are all outside the submitted work. He has provided paid consultancies to the AO Foundation Switzerland and MDI International Australia, all outside the submitted work. He has received financial support from the EBSCO for a congress he chaired Germany, Isabel Healthcare UK, Mundipharma Medical Switzerland, and VisualDx USA, all outside the submitted work.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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