Intracavitary Applications of Ultrasound Contrast Agents in Hepatogastroenterology

Zeno Sparchez1,2, Pompilia Radu1, Mihaela Sparchez1,3, Tudor Vasile1,4, Ofelia Anton4, Marcel Tantau1,2

INTRODUCTION
Ultrasound (US) examination is the first imaging tool used for diagnosis of digestive tract diseases. The main advantages are: real-time scanning, no radiation, easy performance, and cost-effectiveness. In spite of this, the method has several limits that sometimes decrease the diagnostic performance.

The use of contrast agents has not only improved the diagnostic performance in numerous pathological conditions, but also offered new horizons for US investigation. In 2004, the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) published the first Guidelines on the Use of Contrast-Enhanced Ultrasound (CEUS) [1]. Since then, there has been an exponentially increasing interest in CEUS not only for hepatic but also for non-hepatic lesions. Furthermore, several authors have recently demonstrated that extravascular administration of SonoVue can be another application for CEUS. Therefore, in 2012, EFSUMB released a new update of the Guidelines, which included the recommendation for intracavitary administration of SonoVue [2].

TECHNIQUE OF CONTRAST AGENT INJECTION INTO CAVITIES

The technique for intracavitary administration of SonoVue is similar to the technique used for focal lesions. An ultrasound contrast agent (UCA) (SonoVue, Bracco, Italy) and "Contrast Harmonic Imaging" technique in the presence of a low mechanical index (MI) are used. The differences are represented by the dose and the modality of injection of UCA. According to the EFSUMB Guidelines 2012, for extravascular (intracavitary) CEUS, the dose range recommended is 0.1–1mL SonoVue diluted in 0.9 % saline [2]. The dose of UCA depends on the type of cavity (physiological cavities or non physiological cavities) and on the objective of the study, so that in order to emphasize (or exclude) a connection between two cavities, the anatomy of fistulas or pleuro-peritoneal communication, a higher dose (1–2ml) is necessary, while in order to delineate the cavity of a collection (abscess, pseudocyst), only a few drops of SonoVue are recommended. In this way, artefacts are avoided.

The method of administration is through a drainage tube or needle (18 G Chiba), which is inserted in the cavity or the biliary duct.
Contrast agent injection into physiological cavities and ducts

Bile duct drainage

Percutaneous transhepatic biliary drainage (PTBD) is an alternative method for the palliative treatment of a malignant biliary obstruction.

In order to evaluate the efficiency of PTBD and define the anatomy of biliary ducts, the standard imaging method used to be X-ray percutaneous transhepatic cholangiography (PTC). The accuracy of PTC in detecting biliary obstruction is between 96% and 100% [3, 4]. Despite the relative high rate of accurate diagnosis, this method has several important disadvantages: it is radioactive and inappropriate for patients sensitive to iodine. Drainage tubes can be detected by US, but can hardly be seen in their full length and the peak position is often difficult to locate.

In 2009 and 2010, two studies demonstrated that by adding a drop of SonoVue in 20 ml saline and using the low MI mode, biliary leakage could be evaluated [5, 6]. According to the last reports, intrabiliary–CEUS (IB-CEUS) improves the visualization of the drainage catheters and can determine the biliary obstructive level and degree (Fig.1) [7, 8]. Regarding the accuracy of diagnosis, IB-CEUS is comparable to PTC and may be used as an alternative method to X-ray PTC [7,8].

CEUS-PTC combines the advantages of X-ray-PTC (which allows the detection of the peak position, the anatomy of the bile ducts, the communication between left and right lobe and some complications such as dislocated drainage tubes) (Fig.2), with the advantages of US examination (which can be performed under real-time conditions at bedside, there is no radiation, and most importantly, the method is cost-effective) [9]. Moreover, CEUS PTC may assess the patency of the previously inserted biliary stents.

Peritoneo-pleural communication

Approximately 5% to 10% of the patients with decompensated cirrhosis develop a hydrothorax [10]. This can be due to the passage of ascitic fluid through the diaphragm either via lymphatic channels or via congenital or acquired diaphragmatic defects. The identification of these diaphragmatic defects represents an important step in the management of these patients.

Over the years, many methods have been proposed for diagnosis, including indirect methods (biochemical analysis of pleural and ascitic fluid) and direct methods (injection of dyes and air, radioisotope scintigraphy and instillation of 99mTc sulphur colloid) [11]. All these methods have been reported to be simple, safe, relatively non invasive and able to confirm the passage of ascitic fluid across the diaphragm.

In 2009, Foschi et al showed that administration of 4.8 ml of SonoVue intraperitoneally is a simple and reliable method that can be used for demonstrating the peritoneo-pleural communication [12]. Subsequent reports showed that the required dose is of only a few drops of SonoVue [13]. Compared to scintigraphy, this method offers several advantages, such as: low cost, it is easier to perform, repeatable several times in the short term if needed and able to demonstrate the exact position of the peritoneo-pleural shunt (Fig.3).

Fig. 1. Stenosis of a hepatico-jejunal anastomosis. A) CEUS image shows a 2 cm-long stenosis (<); B) the same aspect is depicted by X-ray cholangiography.

Fig. 2. Partially dislodged catheter. A) IB-CEUS depicting the biliary tree but also a leakage in the peritoneal space (>); B) the same aspect illustrated by X-ray cholangiography.
Other intracavitary applications

Another “off-label” application of UCA is the oral administration of diluted SonoVue. In the literature there are some studies demonstrating that UCA administered in larger volumes of water but with the same concentration, can reveal space-occupying gastric lesions such as tumoral masses (Fig. 4) or gastric balloons, gastroesophageal reflux or gastric emptying [14]. Other conditions, such as cholecysto-duodenal fistulas, spontaneous perforations, constrictions of the gastric outlet tract and patency of endoscopically inserted stents (Fig. 5) can also be revealed with high sensitivity [14, 15].

Contrast injection into non-physiological cavities and fistulas

Abscesses
Abscesses represent a serious health problem. Percutaneous aspiration and/or drainage with appropriate antibiotic administration is an effective approach and an alternative to treat deep abscesses [16]. In order to obtain good results from a percutaneous drainage it is very important to identify anatomical details that can be responsible for the treatment failure. These can be represented by: communication with neighbouring structures (fistulas to the biliary tract, blood vessels or organs) and anatomical details of abscesses (e.g. presence of septa). Injection of saline solution alone offers information with low accuracy on the positioning of the drain, but does not offer accurate details on the anatomy of the collection (size, outline, communication) [13].

According to the last reports, administration of UCA into the drainage catheters increases the accuracy of information on the location characteristics (correct position, mishandled or dislocated) (Fig. 6) and on the complications of drained fluid collections [13, 17]. The communication with the biliary tree is depicted with high sensitivity (Fig. 7) [18]. This is of great importance in patients with perihepatic collections after laparoscopic cholecystectomy.

Fistulas
A fistula is an abnormal connection between an organ or intestine and another anatomical structure. It can be the result of congenital malformations or acquired diseases. The treatment of fistulas is surgical. It had been demonstrated
that an inappropriate evaluation of fistula anatomy (internal openings, type of fistula – simple or complex) is associated with recurrence [19]. Regarding the postoperative complications (e.g. anal incontinence) and the risk of recurrence, an accurate preoperative assessment of the anatomy of the tract is mandatory. The procedures used for fistula assessment include: fistulography, computed tomography (CT), magnetic resonance imaging (MRI) and US. Among all these methods, MRI represents the gold standard for diagnosing anal fistulas and perianal collections. The main limitation of this method is its high cost. Transperineal, transvaginal and endoanal ultrasonography (EAS) are accurate, painless, and cost-effective methods commonly used for a precise diagnosis of perianal fluid collections and fistulas. The sensitivity of EAS lies between 57% and 70% [20]. After surgery, distinguishing a scar tissue from an active tract is very difficult, as both appear as hypoechoic. In these cases, the injection of a contrast agent (hydrogen peroxide or Levovist) via the catheter introduced into the fistula’s tract through the external orifice increases the diagnostic sensitivity up to 95%–96% [21, 22].

The use of SonoVue allows a better visualisation of the fistula tract and of the internal opening (Fig. 8). In evaluating complex fistulas, the diagnostic accuracy of CEUS with SonoVue is significantly higher than of conventional US (92.3% vs. 61.5%) [23]. But there are no significant differences between conventional US and CEUS in characterising simple fistulas [23].

CONCLUSIONS

The main advantages of the described investigations by using CEUS are the lack of radiation and the cost-efficacy (less amount of contrast agent used and significant information obtained). With all of these advantages, the guidelines recommend recourse to extravascular CEUS only if standard diagnostic techniques are inconclusive or when patients are not suitable for these (sensitivity to iodine, or necessity to move the patient out of the intensive care unit).

Conflicts of interest: None to declare.

REFERENCES

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