The role of CEUS in the diagnosis of gallbladder disease

Conventional ultrasound (US) is the imaging modality of choice for the diagnosis of pathologies of the gallbladder. However, US has a significant limit in its ability to show the microcirculation of some biliary lesions which can lead to diagnostic failures. The use of contrast-enhanced US (CEUS) has the potential to overcome these limitations and allow a more confident diagnosis.

This review summarizes the methodology, image interpretation, enhancement pattern, clinical usefulness, and indications for CEUS in gallbladder lesions.

CEUS may be indicated under the following circumstances: 1) For differential diagnosis between a malign or benign tumor of the gallbladder. 2) to distinguish between motionless sludge and gallbladder carcinoma. 3) to assess the extension of gallbladder carcinoma in adjacent hepatic parenchyma. 4) in patients with impaired renal function.

INTRODUCTION

B mode ultrasound (US) is the first imaging investigation carried out for the diagnosis of biliary pathologies. The technique has a high sensitivity for the detection of gallbladder stones and intra-hepatic or extra-hepatic bile duct dilatation. The main limitation of ultrasound is its low ability to assess vascularity and therefore to establish the nature of gallbladder and biliary duct tumors [1]. Color and power Doppler US techniques have been developed to overcome these drawbacks but several limits still remain, e.g. in cases of slow flow or deep blood vessels [1,2].

Microbubble contrast agents (CA) can give an accurate assessment of the blood flow within a lesion and so permit the diagnosis of the nature of that lesion. Another important feature of the technique is that micro-bubble agents are not radioactive, being composed of a sulphur hexafluoride gas with a phospholipid shell. Such contrast agents are metabolized by the liver and the sulphur hexafluoride gas is exhaled via the lungs.

After several studies showed that the use of contrast-enhanced ultrasound (CEUS) substantially improved the detection and characterization of gallbladder lesions, CEUS was accepted in 2011 in the Guidelines and Good Clinical Practice recommendations for CEUS - update 2011, for clinical practice [2,4,5].

The vascular phases of the gallbladder are different from those of the liver because the blood supply is provided entirely by the cystic artery and not by portal.
vein branches. Therefore only 2 phases can be followed: arterial phase (10–20 s after bolus injection) and late phase (31–180 s after contrast injection). The late phase persists for a short time as compared to that of the liver [6, 7]. Enhancement is assessed by comparing the echogenicity of a lesion with the echogenicity of the liver parenchyma.

**PATHOLOGY.**

**Polypoid lesions of the gallbladder.**

US has a sensitivity of 90% for the detection of polypoid lesions but distinguishing a potentially pre-malignant adenoma from a benign cholesterol polyp is not always possible. There are several features that can suggest the benign nature of polypoid lesions. For example size less than 10 mm, multiplicity and an increased echogenicity.

The US appearance of cholesterol polyps is that of multiple, non-shadowing, oval lesions attached to the gallbladder wall. The size is usually 2-5 mm and the diagnosis is made easily with US. Larger lesions (up to 20 mm) should be differentiated from adenomas or gallbladder carcinomas. On CEUS, the majority (93%) of the lesions are hyper-enhanced in arterial phase with dotted- or branched-type tumor vessels and hypo-enhanced in late phase [2,6].

**Gallbladder adenomas.**

These appear on US as a sessile polypoid mass, with an echogenicity slightly greater or similar to the liver, with a smooth or lobulated surface and a relatively homogeneous internal texture. On CEUS examination adenomas can appear during the early phase as mostly homogeneous hyper-enhanced whereas in the late phase they appear equally iso- and hypo-enhanced [2] [Figure 1].

**Gallbladder sludge.**

This is a mixture of particulate matter and bile that occurs when the solutes in bile precipitate. In the differentiation between gallbladder cancer and motionless biliary sludge CEUS has a sensitivity of 100% [2]. Because of the lack of vessels the mass will appear non-enhanced in both vascular phases.

**Adenomyomatosis.**

This is a hyperplastic cholecystosis that may involve the gallbladder in a focal, segmental or diffuse form. It is characterized pathologically by hyperplasia of the wall with formation of intramural mucosal diverticula (the so-called Rokitansky-Aschoff sinuses) penetrating into the muscular wall of the gallbladder. US examination depicts ”comet tail” artifact echogenic intramural foci but is less sensitive in visualizing the diverticular wall which has a characteristic ”moth-eaten” enhancement on CEUS examination in the arterial phase [1,6,7].

**Acute cholecystitis.**

This is an inflammation of the gallbladder wall typically caused by a calculus obstructing the cystic duct. On CEUS examination the gallbladder wall enhances earlier and stronger than the adjacent liver parenchyma during the arterial phase and has an obvious “wash-out” in the late phase [Figure 2]. CEUS examination has an important role in detecting abscess formation in the surrounding liver parenchyma and a focal interruption of enhancement in the gallbladder wall, suggesting perforation [2,3,5,7].

**Gallbladder malignant tumors.**

On US examination gallbladder carcinoma can appear like a polypoid intraluminal lesion, a tissue mass infiltrating the gallbladder wall and the surrounding hepatic parenchyma or a diffuse mural thickening [1]. On CEUS examination, the arterial branches that supply the gallbladder carcinoma tend to show irregularly tortuous extension. The late phase washout of the CA agent within 35-60 seconds after administration may be a key for differential diagnosis [2] [Figure 3]. Improved gallbladder wall visualization following CA administration and the malignant feature of late-phase hypovascularity compared to the hepatic parenchyma may provide sharp demarcation of tumor outline. The possible disruption of the gallbladder wall integrity is better visualized on CEUS examination [7].

Metastases to the gallbladder are very rare. The most common condition leading to a metastatic tumor of the gallbladder is malignant melanoma. The lesions are usually multiple, hyperechoic broad base polypoid lesions larger than 10 mm. The lesions are hyperenhancing in arterial phase with a rapid wash out.

**DIFFERENCE BETWEEN BENIGN AND MALIGNANT LESIONS.**

All gallbladder tumors, whether benign or malign, are supplied by arterial vessels from branches of the cystic artery. Thus in the arterial phase most of the lesions are hyper-enhanced in the early phase of CEUS so this feature can not differentiate between malignant and benign lesions [2,4,6]. The type of enhancement (dotted vessel enhancement in benign lesions and tortuous vessel enhancement in malignant lesions) and a quick wash out of the contrast agent (within 35-60 s) are solid clues for the diagnosis [6,7].

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**FIGURE 2.** Acute cholecystitis a) B mode US shows a thickened, double layer gallbladder wall and a gallbladder stone; b) in arterial phase both the wall and the surrounding parenchyma are hyperenhanced.
In the diagnosis of gallbladder lesions CEUS overcomes the limitations of conventional US and has a high accuracy in the diagnosis of certain gallbladder lesions and in assessing malignancy. In clinical practice CEUS may be used in the following settings: 1) For patients with renal impairment for whom the use of contrast agents in CT imaging is not allowed. 2) To make a differential diagnosis between a malign and a benign tumor of the gallbladder. 3) To make a differential diagnostic between motionless sludge and gallbladder carcinoma. 4) To assess the extension of gallbladder carcinoma in adjacent hepatic parenchyma.

REFERENCES