Contrast-enhanced ultrasound in diagnosis of gallbladder adenoma

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BACKGROUND: **Gallbladder adenoma is a pre-cancerous neoplasm and needs surgical resection. It is difficult to differentiate adenoma from other gallbladder polyps using imaging examinations. The study aimed to illustrate characteristics of contrast-enhanced ultrasound (CEUS) and its diagnostic value in gallbladder adenoma.**

METHODS: **Thirty-seven patients with 39 gallbladder adenomatoid lesions (maximal diameter ≥10 mm and without metastasis) were enrolled in this study. Lesion appearances in conventional ultrasound and CEUS were documented. The imaging features were compared individually among gallbladder cholesterol polyp, gallbladder adenoma and malignant lesion.**

RESULTS: **Adenoma lesions showed iso-echogenicity in ultrasound, and an eccentric enhancement pattern, "fast-in and synchronous-out" contrast enhancement pattern and homogeneous at peak-time enhancement in CEUS. The homogenicity at peak-time enhancement showed the highest diagnostic ability in differentiating gallbladder adenoma from cholesterol polyps. The sensitivity, specificity, positive predictive value, negative predictive value, accuracy and Youden index were 100%, 90.9%, 92.9%, 100%, 95.8% and 0.91, respectively. The characteristic of continuous gallbladder wall shown by CEUS had the highest diagnostic ability in differentiating adenoma from malignant lesion (100%, 86.7%, 86.7%, 100%, 92.9% and 0.87, respectively). The characteristic of the eccentric enhancement pattern had the highest diagnostic ability in differentiating adenoma from cholesterol polyp and malignant lesion, with corresponding indices of 69.2%, 88.5%, 75.0%, 85.2%, 82.1% and 0.58, respectively.**

CONCLUSIONS: **CEUS is valuable in differentiating gallbladder adenoma from other gallbladder polyps (≥10 mm in diameter). Homogeneous echogenicity on peak-time enhancement, a continuous gallbladder wall, and the eccentric enhancement pattern are important indicators of gallbladder adenoma on CEUS.**

(***Hepatobiliary Pancreat Dis Int 2015;14:201-207***)

KEY WORDS: **contrast-enhanced ultrasound; discontinuity; gallbladder wall; eccentric enhancement; gallbladder adenoma; homogeneous echogenicity**

Introduction

Gallbladder adenomas are rare tumors that are incidentally found in approximately 0.5% of cholecystectomy specimens.[1] They are considered pre-cancerous neoplasm requiring surgical resection. At present, it is still difficult to diagnose gallbladder adenomas using imaging means because of their similar features with other benign polyps. It has been reported that diameter ≥10 mm is regarded as the threshold for indicating surgical resection.[2] However, this strategy usually results in a large number of unnecessary gallbladder resections, because pathological diagnosis proved that some of these lesions were cholesterol polyps, adenomatous hyperplasia or inflammatory polyps. Therefore, differentiating adenoma from other benign polyps would greatly improve the management of these patients and reduce unnecessary cholecystectomies.

Contrast-enhanced ultrasound (CEUS) is now widely applied in many fields. CEUS can show the whole process of blood perfusion in the region of interest. It has been investigated in the liver, kidney, breast, thyroid and other organs.[3-8] Numata et al[9] evaluated the value of first-generation CEUS agent (Levovist) in gallbladder neoplasms and found that internal tortuous-type vessels could be useful in diagnosing gallbladder carcinoma. Previous studies[1, 10] investigated the diagnostic value of a

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doi: 10.1016/S1499-3872(15)60351-4
Published online March 13, 2015.

second-generation CEUS agent (SonoVue) in gallbladder diseases. However, these studies usually focus on how to differentiate malignancy from benign polyps. The study on the differentiation between gallbladder adenomas and other neoplasms is paucity. In the present study, we selected patients with unclear gallbladder lesions under conventional ultrasound, and determined the diagnostic value of CEUS for gallbladder adenomas.

Methods

Patients

Between July 2005 and June 2013, 150 patients with suspected gallbladder malignancy who had been diagnosed in community hospitals using ultrasound or computed tomography (CT) visited our department for CEUS examination. Ninety-five of the patients also underwent enhanced CT or magnetic resonance imaging (MRI). Inclusion criteria were as follows: (i) non-mobile, polypoid lesions that protruded into the gallbladder lumen; (ii) for multiple lesions, the lesion larger than 10 mm in diameter; and (iii) absence of the gallbladder wall or adjacent liver parenchyma infiltration.

We excluded 107 patients for the following reasons: (1) infiltration into the adjacent liver parenchyma or discontinuity of the gallbladder wall (n=38); (2) the (largest) lesion was smaller than 10 mm in diameter (n=21); (3) cholesterol polyp was diagnosed and followed up with ultrasound (n=19); (4) surgery was contraindicated because of distant metastasis (n=17); (5) metastatic disease in omental lymph nodes was detected during surgery (n=7); and (6) two or more of the above conditions were met (n=5).

Forty-three patients with 45 lesions were included. Pathological examination revealed cholesterol polyps (11 lesions), inflammatory polyps (1), tubular adenoma (13), adherent biliary sludge (3), adenomatous hyperplasia (2), carcinoma in adenoma (6), and adenocarcinomas (9). Adenomatous hyperplasia, motionless biliary sludge and inflammatory polyps were excluded from analysis because of infrequency in incidence. The remaining 37 patients with 39 lesions were enrolled in the study.

The 39 lesions were divided into 3 groups according to the following pathological results: cholesterol polyps, adenomas and malignancy group. Patients with adenomas associated with canceration were placed into the malignant group. The study was approved by Ethics Committee of Zhongshan Hospital of Fudan University, Shanghai, China. Informed consents were obtained from all study participants. This clinical investigation was conducted according to the principles expressed in the *Declaration of Helsinki*.

Ultrasound and CEUS

All patients fasted for at least 8 hours before examination, and they were scanned in the left lateral decubitus position. The target lesion was investigated using gray-scale and color Doppler ultrasound before CEUS. The lesion was magnified at the best viewing position, ensuring that it was on the ideal plane adjacent to the liver parenchyma for reference and maintained as much as possible in a consistent position. Focus was positioned just below the bottom of the lesion. CEUS was performed by experienced certified technologists using 1.5-7.0 MHz transducers (Philips iU22, Philips Healthcare Solution, Bothell, WA, USA; Technos DU8, Esaote Clinical Solutions, Genoa, Italy; Hivision Preirus, Hitachi, Japan). The transducers were equipped with real-time contrast imaging software. The mechanical index (MI) was set at 0.05-0.10. When CEUS was performed, contrast agent SonoVue (SF6, Bracco, Milan, Italy) was administered as a bolus through the antecubital vein at a dose of 2.4 mL, followed by a flush of 5 mL normal saline. Timer was activated when contrast agent was administered. The target lesion was observed continuously for at least 3 minutes. Another bolus was administered at least 20 minutes later after the first administration if initial enhancement was missed or if the target lesion was changed.

Image analysis

We collected patient demographic data such as age and gender. The following features were documented for each lesion: (i) conventional ultrasound: diameter, echogenicity compared with the gallbladder wall (hyperechoic, isoechoic, and hypoechoic), location (bottom, body, and neck), shape (regular or irregular), and homogenicity (homogeneous or heterogeneous); and (ii) CEUS: lesion contrast arrival time, time to iso-enhancement, and time to hypo-enhancement were recorded (compared with the surrounding liver parenchyma of the same depth). The enhancement pattern was classified as eccentric or diffuse enhancement. Eccentric enhancement refers to that the contrast agent goes into the feeding vessels initially from the bottom, then to the peripheral area and the lesion shows a gradually increasing enhancement (Fig. 1). Diffuse enhancement indicates that the contrast agent goes into the whole lesion synchronously with the enhanced extent gradually increasing (Fig. 2). The peak-time appearance was classified as homogeneous or heterogeneous (Fig. 3). The extent of enhancement during the enhancement phase was classified as hyper-, iso-, or hypo-enhancement, with reference to the adjacent liver parenchyma. The "wash-in and wash-out" pattern was compared with the surrounding liver parenchyma. "Fast-in" and "synchronous-in" indicates that the inflow of the