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● *Original Contribution*

USEFULNESS OF CONTRAST-ENHANCED ULTRASOUND IN DIFFERENTIATING INFLAMMATORY BOWEL DISEASE FROM COLON CANCER

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Abstract—To evaluate the diagnostic performance of contrast-enhanced ultrasound (CEUS) in differential diagnosis of inflammatory bowel disease (IBD) and colon cancer, we enrolled 51 patients with thickened bowel walls (13 with IBD and 38 with colon cancer). Ultrasound and CEUS were performed and both qualitative and quantitative features were analyzed. The intestinal wall stratification was preserved in 63.6% of the IBD group but in only 2.6% of the colon cancer group ($p < 0.01$). On CEUS, disordered enhancement and heterogeneous enhancement were shown in only 9.1% and 0%, respectively, of the IBD group while in 94.7% and 78.9%, respectively, of the colon cancer group ($p < 0.01$). For quantitative analysis, compared to IBD, colon cancer showed later enhancement and slower wash-out with less speed to reach peak intensity ($p < 0.05$). In conclusion, CEUS may prove useful for the differential diagnosis of IBD and colon cancer, but more studies are required. (E-mail: ghyzmw@163.com) **© 2017 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

Key Words: **Inflammatory bowel disease, Colon cancer, Ultrasound, Contrast-enhanced ultrasound, Thickened bowel walls.**

INTRODUCTION

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease, is a type of chronic nonspecific intestinal inflammation of unknown cause. IBD occurs mainly in people aged 20 to 40 with no gender preference and a higher incidence in whites of about 50–150 per million. IBD manifests as abdominal pain, diarrhea, hematochezia and abdominal mass. The diagnosis of IBD should be made after comprehensive consideration of the clinical manifestations and findings of digestive tract radiography, endoscopy and pathology and the exclusion of other diseases. Complications of IBD include intestinal obstruction, perforation and development into cancer, so early diagnosis and treatment may improve the prognosis. Colon cancer is the most common primary malignant tumor of the colon and has an incidence of 40–60 per hundred thousand in developed countries such as Britain and the United States, with an ascending trend in China. This disease usually occurs in those aged 40 to 50 with a male-to-female ratio of 2:1 to 3:1 (Parkin et al. 2005). The clinical manifestations are hematochezia, abdominal pain ande abdominal mass. Pathology is the gold standard for the diagnosis of colon cancer. The 5-y survival rate of colon cancer after radical resection is 60%–80%, so early discovery and treatment are of great significance in improving the prognosis.

The intestinal tract is commonly examined by colonoscopy and digestive tract radiography, which have the advantages of clear visualization of the intestinal cavity and mucosal surface and simultaneous biopsy in colonoscopy. However, these methods face difficulties in revealing the depth of infiltration and scope of lesions and may cause discomfort. Enhanced computed tomography (CT) and magnetic resonance imaging (MRI) are the main methods used to evaluate gastrointestinal blood perfusion, but they also have some limitations. Because of inadequate scanning phases, the enhancement sequence of lesions cannot be observed dynamically and in real time. In addition, high cost, radioactivity and contrast agent allergy, as well as toxicity to the kidney, also limit the application of CT and MRI.

Transabdominal ultrasound (US) has been increasingly used in the diagnosis of intestinal diseases, because it is a non-invasive, convenient method that clearly reveals the thickness and stratification of the intestinal walls, the extent and blood flow distribution of lesions and the shape of the intestinal cavity. However, 2-D ultrasound has

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difficulty in the differential diagnosis of these two common intestinal diseases, IBD and colon cancer, which have similar clinical features and ultrasonic findings such as bowel wall thickening. Previous studies indicated that conventional ultrasound is used mostly in children, with a sensitivity of 48%–75% and a specificity of 92% for diagnosing IBD (Bremner et al. 2006). However, there are few reports on the performance of ultrasound in the diagnosis of intestinal diseases in adults.

Because of different pathophysiological mechanisms, although both inflammation and tumors manifest the characteristic of angiogenesis, they are significantly different in blood perfusion, which is helpful in differential diagnosis between the two diseases. Although color Doppler can detect the increased large arteries feeding the microvascular bed (Rieber et al. 2000), which reflects the characteristics of angiogenesis in intestinal inflammation and tumors, it has a low sensitivity to slow flow and capillaries because of the limits of blood flow velocity and vessel diameter (Migaleddu et al. 2008). In addition, color Doppler signals are also difficult to quantify (Di et al. 2004). Therefore, the value of color Doppler in the differential diagnosis of inflammation and tumors is limited.

Contrast-enhanced ultrasound (CEUS) is a new technology for evaluation of microvessels and tissue perfusion. It has many advantages, including low requirements for kidney function, low risk of allergy, no radioactivity, high resolution (Serra et al. 2007) and dynamic and real-time observation, as well as the accurate and quantitative reflection of blood perfusion of lesions. At present, this technology has been widely used in solid organs such as the liver, pancreas and kidney and proves to be of great clinical significance (Kitano et al. 2004; Park et al. 2001). However, studies on its clinical use in gastrointestinal lesions are still limited.

Based on the differences in pathogenesis and pathologic changes, we hypothesized that there must be hemodynamic differences between IBD and colon cancer. Our study aimed to evaluate the diagnostic performance of CEUS in the differential diagnosis of IBD and colon cancer through real-time observation of the perfusion characteristics by CEUS and quantitative analysis with the time–intensity curve (TIC).

METHODS

Patients

From January 2014 to March 2015, a total of 281 consecutive patients visited Peking University Third Hospital for thickened bowel walls (thickness ≥3 mm) (Girlich et al. 2010) detected by gray-scale ultrasound or CT. We performed conventional US and CEUS on 246 of them, excluding 35 who met the exclusion criteria. Of the 246 patients, 51 received the definite diagnosis of IBD or colon cancer by endoscopy and/or surgery and were enrolled in our study (13 with IBD and 38 with colon cancer). Colon cancer was diagnosed histologically, and the diagnosis of IBD was confirmed by digestive physicians on the basis of comprehensive analysis of the clinical symptoms, colonoscopy findings and pathologic results. This study was approved by the institutional review board, with written informed consent obtained from each patient. The exclusion criteria were similar to the ultrasound contrast agent contraindications, including acute coronary syndrome, severe arrhythmia, age <18 y, pregnancy and refusal to take the CEUS examination.

The IBD group comprised 13 patients (10 women, 3 men, age range: 18–75 y, mean: 36.2 ± 6.5 y), of whom 8 had ulcerative colitis and 5 had Crohn's disease. All had symptoms of abdominal pain and diarrhea, and 5 had hematochezia. The tumor group comprised 25 men and 13 women with an average age of 64.5 ± 10.3 y (range: 27–77 y). In this group, 23 had symptoms of abdominal pain, 13 had hematochezia and 15 had changes in bowel habits.

Ultrasound and CEUS protocol

All patients underwent ultrasound and CEUS examinations performed with a Philips IU22 (Philips Healthcare, Bothell, WA, USA) with C5-2 convex array probes and C9-3 linear array probes. All examinations were performed by one of two experienced radiologists with more than 10 y of experience in CEUS imaging (B.Z. and S.T.). Medical records and US and CEUS images/videos were retrospectively reviewed and analyzed by two authors (F.Z. and H.Y.G.), respectively, to reach a consensus on the features of US and CEUS parameters. In cases of discrepancy, a third investigator (L.Y.M.) reviewed the images independently to make a final decision. All were blinded to the results of any other examinations when performing the US and CEUS examinations or analyzing the results.

The US examinations were performed in a supine position to search the entire abdomen for thickened bowel walls (whole wall thickness >0.3 cm) using a "mowing the lawn" scanning method (Puylaert 2003). During scanning, the probe was appropriately pressed to eliminate the disturbance of bowel gas. When color Doppler flow imaging (CDFI) was performed, to optimize the color Doppler signals, minimal pressure was applied to the abdominal wall, and the appropriate scale and gain were obtained. The features of the thickened bowel walls were as follows:

1. Thickness: Thickness of the whole intestinal wall from the serosa to the mucosa.
2. Stratification: Starting from inside, the five layers of the intestinal wall are the interface between the intestinal lumen and mucosa, muscularis mucosa, submucosa, muscularis propria and serosa, with high-,