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● *Original Contribution*

PRELIMINARY ANALYSIS OF CLINICAL SITUATIONS INVOLVED IN QUANTIFICATION OF CONTRAST-ENHANCED ULTRASOUND IN CROHN'S DISEASE

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Abstract—To assess influencing factors for quantitative analysis of contrast-enhanced ultrasound (CEUS) in Crohn's disease (CD), dynamic CEUS examinations from 77 consecutive CD patients were recorded. Peak intensity (PI) values were calculated using the pre-installed quantification software of the ultrasound scanner. The influence of depth, pressure from the ultrasound probe and intraluminal gas was analyzed. The PI value of the anterior wall was lower than that of the posterior wall when the depth was ≤3.4 cm (17.9 dB vs. 21.3 dB; $p < 0.05$) or evident pressure was exerted (19.1 dB vs. 22.5 dB; $p < 0.01$). In the presence of intraluminal gas, the PI of the anterior wall was higher than that of the posterior wall (20.7 dB vs. 18.8 dB; $p < 0.05$). Nevertheless, no significant difference was found between the PI value of anterior and posterior walls when the depth was >3.4 cm (19.8 dB vs. 20.3 dB), moderate pressure was exerted (20.5 dB vs. 21.1 dB) or luminal gas was excluded between the two bowel walls (18.9 dB vs. 21.2 dB; $p \geq 0.05$). The factors of depth, pressure from the ultrasound probe and intraluminal gas can affect the quantification results of CEUS. It is preferable to place the region of interest in the posterior wall when luminal gas is absent and in the anterior wall when luminal gas is present. In the latter case, more attention should be paid to reducing pressure by the ultrasound probe. (E-mail: liugj@mail.sysu.edu.cn) **© 2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Contrast-enhanced ultrasound, Quantification, Time intensity curves, Peak intensity, Influencing factors, Crohn's disease.**

INTRODUCTION

Crohn's disease (CD) is a type of inflammatory bowel disease, characterized by relapsing episodes, varying degrees of severity and unexpected complications. Patients with CD often undergo multiple imaging examinations, including endoscopy, computed tomography (CT), magnetic resonance imaging (MRI) and ultrasound (US), for initial diagnosis and evaluation of disease activity, treatment response and follow up (Gatta et al. 2012). Conventional endoscopy does not allow transmural evaluation and fails to visualize the area distal to the presence of a suspected stenosis (Benitez et al. 2013). Currently, CT enteroclysis (CTE) and MRI enteroclysis are increasingly accepted as first-line modalities for the evaluation of CD because they can provide a panoramic view of the entire abdomen. However, compared with US, CTE subjects patients to ionizing radiation, and MRI enteroclysis is very sensitive to pulsation and movement artifacts (Horsthuis et al. 2008; Ordás et al. 2014).

US is a non-invasive and real-time imaging modality and has become an increasingly important technique in the diagnosis and follow-up of CD. A number of studies have reported a positive correlation between bowel wall thickness and clinical disease activity (Arienti et al. 2000; Fraquelli et al. 2005). Nevertheless, such evaluation fails to assess bowel wall vascularization. The neovascularization of the bowel wall, characterized by the development of new capillary vessels, is an early pathologic change occurring in patients with active CD (Hatoum and Binion, 2005).

Although power Doppler imaging made the evaluation of the intestinal and extra-visceral vessels possible,

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its stability varies significantly with US equipment, operators and patients (Robotti et al. 2004). However, the application of contrast-enhanced ultrasound (CEUS), using a second-generation ultrasound contrast agent (UCA) and a low mechanical index, real-time, contrast-specific imaging technique, may provide excellent spatial and temporal resolution in displaying microcirculation perfusion of tissue. Because the UCA microbubble could act as a pure blood pool tracer with no leakage into the interstitial space, CEUS is quite suitable for the quantitative assessment of tissue perfusion (Blomley et al. 2001; Greis 2009). Specific perfusion parameters of tissue can be achieved by selecting a region of interest (ROI) in the target tissue using quantification software (Greis 2011). Many factors may affect the value of perfusion parameters computed from the time intensity curve (TIC), such as scanner setting, patient body habitus, and even methods of contrast injection (Tang et al. 2011).

Despite some reports of quantitative assessment of perfusion with CEUS in liver (Dietrich et al. 2011; Dietrich et al. 2012; Ignee et al. 2010), there is no consensus on assessing perfusion of the intestinal wall in CD with CEUS in a quantitative manner. Taking the fixed imaging settings, the injection method and scanning technique as preconditions, the depth of an ROI, the pressure from probe exerted on inflamed bowel wall and the gas in gut cavity may affect the perfusion parameters from TIC.

In the present study, we retrospectively analyzed how these factors affect the quantitative parameters for CEUS to reduce interference and obtain more objective results in the evaluation of CEUS in CD.

METHODS

Patients

We retrospectively analyzed 77 consecutive patients with confirmed CD who were examined in our hospital from November 2013 to May 2014 (55 men and 22 women; age range 18–69 y, mean 35 ± 15 y). Exclusion criteria were poor bowel preparation, age <18 y or >80 y, allergy to contrast agent, severe cardiopulmonary diseases and pregnancy or lactation in women. Informed written consent was signed by each patient who receives CEUS examinations.

US and CEUS methods

Both US and CEUS examinations were performed using the same equipment (LOGIQ E9; GE Healthcare, Milwaukee, WI, USA), equipped with a high-frequency linear probe (9 L, frequency range 6.0–9.0 MHz). All examinations were performed by the same radiologist, who had more than 15 y of experience in abdominal US and 10 y of experience in CEUS.

Patients fasted overnight before the examination. Each patient was required to drink 2000 mL of a warm-water solution of mannitol (containing approximately 250 mL of mannitol) in 45 min (consuming 500 mL every 15 min).

The examinations were performed in the supine position, starting from jejunum to the ileum, emphasizing the distal segment of ileum, which was involved mostly in CD, and then scanning clockwise along the ascending colon and ending in the sigmoid colon. The following information was obtained in gray-scale baseline US examinations: location of the thickened bowel wall; thickness of the wall; depth of the bowel (distance from the abdominal surface to the bottom line of the posterior wall of bowel); presence or absence of intraluminal gas; and the level of pressure exerted on the abdominal wall (moderate or evident; reference criteria are stated below). Power Doppler imaging at optimized settings was used to evaluate the blood supply of thickened bowel walls according to the scoring system of Limberg (Limberg 1999).

A bolus of 2.0 mL of UCA (SonoVue, Bracco, Italy) was injected into the antecubital vein, followed by 5 mL of 0.9% normal saline solution. The target bowel was scanned continuously for 60 s under fixed CEUS settings and imaging section. Resolution mode (transmit frequency = 5 MHZ) of the CEUS presetting was used, with mechanical index ranging 0.14–0.19, and focus positioned at the posterior wall of the target bowel (Table 1). Dynamic videos were stored as raw data. Videos were retrospectively analyzed off-line in consensus of two investigators, who had approximately 3 y of experience in CEUS of the bowel. They were not involved in the sonographic examination and were blinded to each patient's identification, clinical history, histopathological results and other imaging results.

Data analysis

To assess the influence of depth to peak intensity (PI), ROIs were divided into two groups (>3.4 cm and ≤ 3.4 cm) according to their depth measured from skin

Table 1. Imaging settings of CEUS

Methods of CEUS	Parameters
Probe	9 L
Contrast agent dose	2 mL
CEUS mode	Resolution
Transmit frequency	5.0 MHz
MI	0.14–0.19
Gain	16 dB
Number of focus	1
Position of focus	Posterior wall of target bowel
Frame frequency	11 f/s

CEUS = contrast-enhanced ultrasound; MI = mechanical index.