The diagnostic value of three detection techniques of ultrasound in the active stage of Crohn's disease

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Abstract. – OBJECTIVE: The widespread availability of Ultrasound machines and their relatively low cost and functionality make them an attractive tool to use during the treatment of ongoing Crohn's Disease (CD). This study aims at exploring the value of conventional, power Doppler and contrast-enhanced ultrasound during the active stages of CD.

PATIENTS AND METHODS: 24 patients in the active stages of Crohn's disease were enrolled in the study. The full, medial and lateral intestinal wall thicknesses and the thickness ratio of medial to lateral intestinal wall of the segmental lesions were measured by conventional ultrasound. The diseased intestinal wall was also examined by power Doppler ultrasound to assign Limberg classification types: 3 cases were Limberg II, 9 cases were Limberg III and 12 cases were Limberg IV type. Importantly, the full and medial thicknesses of the intestinal walls with different Limberg types were compared, and statistically significant differences were found ($p<0.05$). Finally, images of the diseased segments were taken by contrast-enhanced ultrasound, and the contrast agent bolus arrival, the inflow and the peak enhancement times were calculated in order to be able to distinguish intestinal wall thickness differences according to different Limberg types.

RESULTS: Cases with Limberg types III and IV mostly showed total intestinal enhancement, while Limberg II type cases showed mostly medial intestinal enhancement. When comparing the inflow and peak times of contrast-enhanced ultrasound of patients with different Limberg types, the differences found were statistically significant ($p<0.05$).

CONCLUSIONS: This study confirms incrassation of the intestinal wall being the main ultrasonic appearance of active CD. Both power and contrast-enhanced ultrasound are effective tools in the management of active CD: while power ultrasound can be used to carry out Limberg typing, contrast-enhanced ultrasound can analyze and diagnose incrassation segments of the intestinal wall with different disease stages.

Key Words
    Contrast-enhanced ultrasound, Power Doppler ultrasound, Crohn's disease, Limberg types.

Introduction

Crohn's disease (CD) is a common inflammatory bowel disease, which can occur in any portion of the intestinal tract, however the terminal ileum and proximal colon are the most common sites affected. In recent years, the occurrence of Crohn's disease in China has been increasing year after year[1]. A characteristic of Crohn's disease is the alternation of active and remission stages. During the active stage serious complications can ensue, such as toxic enteritis, abscess formation, perforations or fistulae. Recurrent disease can seriously reduce the quality of living of patients often resulting in severe anxiety and depression, leading to abandoning the treatment and even committing suicide[2]. Being able to accurately diagnose every episode of the active disease is important for providing the best treatment, and ultrasound is a simple and very effective means of assessing the activity of Crohn's disease[3]. For this study, 24 active stage patients were chosen to compare the use of conventional, power Doppler and contrast-enhanced ultrasound for the patients' follow-up after Crohn's disease diagnosis.

Patients and Methods

Patients

24 patients with symptomatic Crohn's Disease (CD) admitted in our hospital from the period of June 2012 to May 2014 were selected for the study. All cases met the diagnostic criteria for CD specified in the "Chinese consensus norms of diagnosis and treatment of inflammatory bowel disease" (2008); all cases were confirmed by colonoscopy and pathological examination to exclude patients whose lesion segments were at the rectum or perianal. There were a total of 24 patients, 14 male and 10 female; ages ranged

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from 19 to 64 years old, average age of 33.1±3.9 years; for 17 cases this was the first time they had been diagnosed with CD; the score of the Crohn's disease activity index (CDAI) ranged from 150 to 450, with an average of 342.5±83.7. The Ethics Committee of our hospital approved the study and all patients signed an informed consent.

Methods
Instruments

For color Doppler ultrasonography the American GE Logiq E9 type machine was used, with the following probe frequencies: a probe frequency of 2-5 MHz (Alpharetta, GA, USA) a high-frequency linear array probe at 4-9 MHz; and a probe for ultrasonic imaging at 4-9 MHz. Images were processed by a low mechanical index using Real-time imaging technology.

Detection Methods

After 4 h water deprivation and fasting for 12 h, patients received cathartic (constant Kangzheng Qing) of 2000-3000 ml, 2.5% isotonic and 1000 ml mannitol 1 h before examination. Patients were firstly treated with conventional ultrasonic check. Through low frequency probe, ileocecal, ascending colon, transverse colon, descending colon and sigmoid, were sequentially scanned. Then we changed into high frequency probe until suspicious lesions segment was found, and we selected the maximum longitudinal to sting the instrument at a low mechanical index Real-time imaging mode with bolus injection of ultrasonic contrast agent. SonoVue (injected through peripheral intravenous) at a dose of 2.4 ml was used with 5 ml 0.9% normal saline to wash the vessel. We started collecting images at the same time and recording the situation of intestinal perfusion injected with contrast agent within 180 s. Then, we saved the static section of the lesion segment of intestinal wall to scan and measure the thickness.

Observation Index
Conventional Ultrasonic Appearance

The lateral (muscularis propria and serosa) and medial thicknesses (muscularis mucosae and submucosa) of the intestinal wall were measured. An increase of ≥ 4 mm in thickness of the intestinal wall was considered significant.

Ultrasound Appearance

A semi-quantitative approach was adopted in order to assign a Limberg grading to the ultrasonographic images. Possible Limberg scores included 5 grades, as follows: Grade O: normal intestinal wall. Grade I: thickened intestinal wall. Grade II: thickened intestinal wall with occurrence of short vessels. Grade III: thickened intestinal wall with occurrence of long vessels. And grade IV: thickened intestinal wall with occurrence of long vessels connected to the mesentery.

Contrast-enhanced Ultrasound Appearance

The times of contrast agent bolus arrival and peak enhancement were measured, and the inflow time (peak time minus arrival time) was calculated. The arterial phase spanned a time from 30 to 40 s after injecting the contrast agent, the venous phase from 40 to 120 s after the injection, and the lag phase from 120 to 180 s after that.

Statistical Analysis

SPSS17.0 (SPSS Inc., Chicago, IL, USA) was used to make the statistical analyses. The t-test was used for measurement data, indicated by x±SD. The X^2-test was used to compare the rates. A $p<0.05$ was considered statistically significant.

Results

Conventional Ultrasonic Appearanceof Crohn's Disease in Active Stages

The main sign of conventional ultrasonic examination was an increase in the full thickness of the diseased intestinal wall (Figure 1), with the thickness of the medial intestinal wall clearly increased (Figure 2) and the thickness of lateral intestinal wall appearing normal. The incrassation of the wall in 24 patients was from 5.5 to 12.1 mm, and the average was 8.7±0.5 mm; the incrassation of the lateral intestinal wall from 1.4 to 4.1 mm, and the average was 2.9±0.5 mm; the incrassation of medial intestinal wall was 3.3 to 8.7 mm, and the average was 6.1±0.4 mm. The thickness ratio of medial to lateral intestinal wall was 1.1 to 3.0 mm, all were more than 1, with an average of 2.4±0.7 mm.

Diagnostic Appearance of Crohn's Disease in the Active Stage with a Power Doppler Ultrasound

Among 24 patients with Crohn's disease, 3 cases were Limberg II type (12.5%), 9 cases were Limberg III type (37.5%) and 12 cases were Limberg IV type (50.0%).
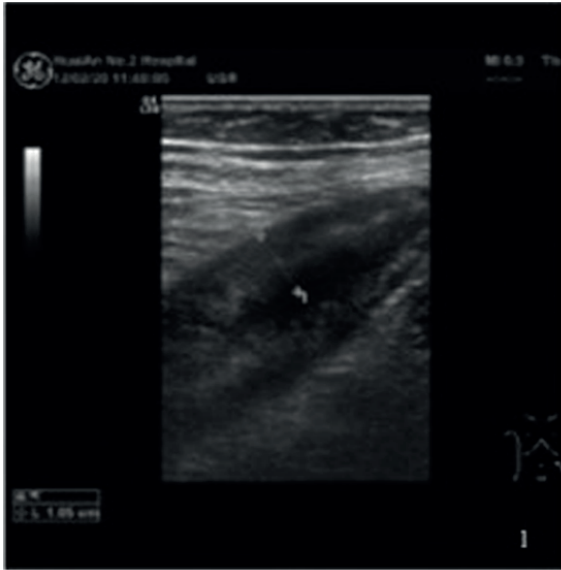
Figure 1. Conventional ultrasound showing the increased full thickness of the intestinal wall in Crohn's disease during the active stage.

Figure 2. Conventional ultrasound showing the increased thickness of medial intestinal wall in Crohn's disease during the active stage.

Appearance of Crohn's Disease i n the Active Stage using Contrast-enhanced Ultrasound

Comparisons of Ultrasonic Appearance in Patients with Different Limberg Types

The full and medial thickness of the intestinal walls with different Limberg types were compared, and the differences found had statistical significance ($p<0.05$). On the other hand, when comparing the lateral and medial thicknesses of intestinal walls with different Limberg types, the differences found were not statistically significant ($p>0.05$). The results are shown in Table I.

Comparisons of Contrast-enhanced Ultrasound Patterns of Patients with Different Limberg Types

Limberg types III and IV cases mostly showed total intestinal contrast-enhanced ultrasound, while Limberg II type cases showed mostly medial intestinal enhancement (Table II).

Comparisons of contrast-enhanced ultrasound enhanced-times in patients with different limberg types

Among 24 patients, the arrival time of acoustic contrast agent was in the range from 9 to 25 s, and the average was 14.0±0.9 s; the peak time to contrast-enhancement was from 14 to 36 s, and the average was 24.4±1.6 s; inflow time was from 5 to 23 s, and the average was 10.5±1.4 s. When comparing the inflow and peak times of contrast-enhanced ultrasound in patients with different Limberg typing, the differences found were statistically significant ($p<0.05$). However, when comparing the arrival times of contrast-enhanced ultrasound, the differences found did not have statistical significance ($p>0.05$). The results are shown in Table III.

Table I. Comparison of ultrasonic appearance of patient's colons with different Limberg types (x±s).

Limberg typing	Number of cases	Full thickness of intestinal wall (mm)	Thickness of medial intestinal wall (mm)	Thickness of lateral intestinal wall (mm)	Thickness ratio of medial and lateral intestinal wall
II type	3	6.4 ± 0.4#	3.6 ± 0.7#	3.1 ± 0.4	2.1 ± 0.3
III type	9	7.8 ± 0.7*	5.3 ± 0.6*	2.8 ± 0.6	2.2 ± 0.4
IV type	12	10.3 ± 0.8	7.3 ± 0.4	2.9 ± 0.3	2.3 ± 0.3

Note: #Comparison to Limberg III type and IV type, $p<0.05$; *Comparison to Limberg IV type, $p<0.05$.

Table II. Comparisons of contrast-enhanced ultrasound patterns in colons of patients with different Limberg types [n (%)].

Limberg typing	Number of cases	Total intestinal enhancement	Mainly medial intestinal enhancement
II type	3	0 (0)	2 (66.7)
III type	9	7 (77.8)	2 (22.2)
IV type	12	8 (66.7)	3 (25.0)

Table III. Comparisons of contrast-enhanced ultrasound enhanced-time in patients with different Limberg types (x± SD, s).

Limberg typing	The number of cases	Arrival time	Peak time	Inflow time
II type	3	12.6 ± 1.7	$30.7 \pm 3.7\#$	$18.1 \pm 4.1\#$
III type	9	12.4 ± 1.8	$27.1 \pm 2.5*$	$10.7 \pm 1.2*$
IV type	12	12.2 ± 1.5	21.1 ± 1.7	8.9 ± 1.3

Note: #Comparison to Limberg III and IV types, $p<0.05$; *comparison to Limberg IV type, $p<0.05$.

Discussion

Crohn's disease is a chronic disease with characteristic recurrent attacks, thus it needs repeated check-ups and treatments. Studies show that radio-active CT is unsuitable for checking Crohn's disease repeatedly[4]. Furthermore, endoscopy has important value in the diagnosis of activity of Crohn's disease, but it frequently causes severe pain and is not recommended for all patients[5]. Finally, capsular endoscopy is considered a method of significant progress in the diagnosis of inflammatory bowel diseases, but it cannot show the state of the intestinal wall, thus it should be used cautiously in patients suspected of having intestinal wall narrowing[6]. Consequently, advantages such as its low price, non-invasiveness, non-radiation, and good repeatability, have made ultrasonic examination a major technique for checking the evolution of CD[7].

Crohn's disease in the active stages causes intestinal damages that range from damage to the mucous layer to damage throughout the entire intestinal wall. The patients at a severe stage of the disease will suffer from intestinal fistulas[8]. With continuous infiltration of inflammatory cell throughout the intestinal wall, blood supply increases, and vessels expand; and after continual infiltration, connective tissue proliferation and edema calidum appear, and fibrosis begins[9]. The main manifestations in the whole progress are incrassation of the intestinal wall and increase in blood supply, with influences of CD on every layer of the intestinal wall being different. Ultrasonic examination is not sensitive to the changes of the mucous layer in the early stages, but it can detect changes in the intestinal wall effectively, especially changes in its thickness[10]. The appearance of ultrasonic examination of CD in the active stages shows the thickness of segments of the intestinal wall being increased. With this research, the thicknesses of the medial and lateral intestinal walls are further identified, and it is shown that differences in the thickness of the two layers are related to different inflammatory and pathological stages of disease, which allow for better judgement of the disease activity status. Other studies have shown that power ultrasound can assess the inflammation status of the intestinal wall effectively and can identify medium and small vessels in the intestinal wall[11]. With more severe inflammation of the intestinal wall, the blood vessels are increased, and the degree of Limberg typing also increases accordingly[12,13]. In this study, we show that focusing mainly on the thickness of the medial intestinal wall during ultrasound investigations can help determine the status of the disease by showing a thicker medial intestinal wall at higher Limberg types. Contrast-enhanced ultrasound enhances sensitivity to minor blood vessels, lowers the velocity of the blood flow, and is widely used in the diagnosis and assessment of inflammatory bowel diseases[14,15]. A contrast-enhanced ultrasound of CD distinguishes mainly 4 patterns: high enhancement of the full thickness of the intestinal wall, high enhancement of the medial intestinal wall, high enhancement of the submucosa, and no enhancement of the intestinal wall. The latter two are mainly characteristic of patients with CD in the remission stage, and the first two are common in patients with active CD. In this research, Limberg III and IV types showed mainly total intestinal enhancement, suggesting that the inflammation of the lateral intestinal wall was severe in those cases. Limberg II type showed mainly enhancement of the

medial intestinal wall, suggesting that inflammation had only mildly progressed to the lateral intestinal wall, and the increase in thickness was mainly due to the thickened medial intestinal wall. Our results also suggest that Limberg typing does not relate well to the arrival time of the acoustic contrast agent, but instead the Limberg type is closely related to the inflow and peak times in a contrast-enhanced ultrasound, showing a negative correlation: with increasing Limberg typing, peak time and inflow time of contrast-enhanced ultrasound decrease. This allows one to assess the activity of CD to some extent.

Conclusions

Incrassation of intestinal wall is the main ultrasonic appearance in active CD. Using power ultrasound it is possible to accurately carry out Limberg typing, and applying contrast-enhanced ultrasound can diagnose incrassation of the intestinal wall in different types. Ultrasonographic techniques are not only simple and effective means for initial diagnostic screening of suspected CD, but are very valuable for evaluating management of active CD.

Conflict of Interests:

The authors declare no Conflict of interest.

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