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● *Original Contribution*

CORRELATION BETWEEN DISEASE ACTIVITY AND ENDORECTAL ULTRASOUND FINDINGS OF CHRONIC RADIATION PROCTITIS

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Abstract—The aim of this study was to summarize the imaging features of chronic radiation proctitis (CRP) on endorectal ultrasound (ERUS) and investigate the value of ERUS in the evaluation of disease activity. 40 CRP patients and 30 control patients were investigated by ERUS. Rectal wall thickness and layers, ulcers and rectovaginal fistulas were evaluated by B-mode ultrasound. Power Doppler imaging was used to evaluate the vascularity of the rectal wall using a semiquantitative score. Disease activity was calculated according to the National Cancer Institute Common Terminology Criteria for Adverse Events 4.0 (CTCAE 4.0). Imaging findings for patients with mild and severe CRP were compared. For 30 patients in the control group, the average maximum thickness of the rectal wall was 3.07 ± 0.73 mm, with all exhibiting typical wall stratification and level 0 vascularity. For the 40 CRP patients, there was marked thickening of the rectal wall (average thickness = 9.42 ± 1.94 mm), which was significantly thicker than in the control group ($p < 0.05$). The rectal walls of the mild group were significantly thinner than those of the severe group (8.71 ± 1.67 mm vs. 10.00 ± 2.00 mm, $p < 0.05$). Among the 22 severe cases, 19 cases (19/22, 86.4%) exhibited hyper-vascularity (level IV) or blurred wall stratification (including hypo-echoic submucosa, ulcer and fistula); 12 of the 18 mild cases (166.7%) exhibited a vascularity of level III and typical wall stratification. A significant association ($p < 0.05$) was observed between stratification and vascularity of the rectal wall and CRP activity. When ERUS findings of blurred rectal wall stratification or increasing vascularity (level IV) were used to evaluate CRP activity, the sensitivity was 86.4% (95% confidence interval: 64.0–96.4) and the specificity was 66.7% (95% confidence interval: 41.2–85.6). Thickening of the rectal wall, blurred wall stratification and increased vascularity are characteristic ERUS findings of CRP. ERUS is helpful in the comprehensive evaluation of disease activity and may provide objective evidence during treatment planning and follow-up. (E-mail: wangl9@mail.sysu.edu.cn) **© 2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Chronic radiation proctitis, Endorectal ultrasound, Ultrasonographic features, Power Doppler imaging, Disease activity.**

INTRODUCTION

Radiotherapy (RT) has been widely used effectively in the treatment of pelvic malignancies such as cervical cancer (Ma et al. 2015; Perez et al. 1999). Chronic radiation proctitis (CRP) is a late side effect that affects 5%–20% of pelvic cancer patients beginning 3 to 6 mo after the end of RT and may present for months or years. For patients with CRP, rectal bleeding is the most common symptom, and diarrhea, urgency, tenesmus incontinence and pain can also occur (Leiper and Morris 2007; Vanneste et al. 2015; Williams and Yan 2010). To evaluate and report the severity of CRP in a reliable manner, many scoring systems such as endoscopic scores, symptom scores and quality-of-life scores have been created (Wachter et al. 2000). However, no systematic and objective scoring system has been published so far. Endoscopy is widely used for the diagnosis and evaluation of CRP, as it is used effectively not only to evaluate rectal mucosal damage and rule out other causes of proctitis such as infectious colitis, but also to determine preliminarily the extent and severity of CRP (Wu et al. 2015). Neovascularization and submucosal fibrosis are the main pathologic changes in CRP. Endoscopy, however, can only detect neovascularization of the

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mucosa; neovascularization and fibrosis of the submucosa are out of the range of view of endoscopy. Moreover, rectal ulcers are also commonly observed in CRP patients. For those rectal ulcers may be observed in approximately 26% of patients who have been treated with argon plasma coagulation (APC) (Vanneste et al. 2015). Detection of deep ulcers must be done carefully because of the risk of perforation. Necrotic material and contents on the ulcer surface sometimes cause endoscopy to miss the ulcers. Therefore, a new method that can detect the submucosal and muscularis propria layers is needed in the evaluation of CRP.

Endorectal ultrasound (ERUS) has played an important role in the assessment of anorectal diseases in past decades. ERUS can clearly visualize the five layers of the rectal wall: three hyper-echoic and two hypo-echoic layers (Cao et al. 2016; Sudakoff et al. 2002). Therefore, ERUS may effectively detect the morphologic changes of CRP in submucosal, muscularis propria and perirectal tissues. Furthermore, ERUS could evaluate the vascularity of the rectal wall with the use of power Doppler imaging, as it has been applied in the evaluation of inflammatory bowel diseases.

To our knowledge, the ERUS features of CRP have been reported in only one case report (Williams and Yan 2010) and have not been systematically reported previously. The aim of this study was to describe the ERUS features of CRP in patients with different clinical presentations, and investigate its value in the clinical evaluation of disease activity.

METHODS

Study design

This prospective study was approved by the institutional review board of the Sixth Affiliated hospital of Sun Yat-Sen University, and informed consent was obtained from all patients. Between July 2015 and May 2016, 65 consecutive patients treated with RT for cervical cancer more than 3 mo earlier and diagnosed with CRP on the basis of clinical symptoms were enrolled in this study. Finally, 40 consecutive patients met the following inclusion criteria: (i) more than one typical endoscopic finding, such as congested mucosa, telangiectasia, ulceration, stricture and necrosis; (ii) endoscopy examination within 1 wk of the ERUS examination. Patients were excluded if (i) ERUS could not be successfully performed because of poor bowel preparation, poor tolerance of patients or intestinal stenosis; (ii) patients had other diseases such as tumor recurrence and hemorrhoids diagnosed by endoscopy and magnetic resonance imaging (MRI); and (iii) patients had undergone invasive treatments such as argon plasma coagulation (APC) and transverse colostomy.

During the same period, 30 patients who had had constipation or perianal discomfort and had no obviously abnormal rectal findings, as confirmed by endoscopy or rectal digital examination, were recruited into the control group.

ERUS examination

Endorectal ultrasound was performed by one experienced investigator (F.C.) who had more than 2 y of experience with ERUS and who was blinded to the results of other investigations, such as endoscopy and MRI. All ERUS examinations were performed with a MyLab 60 scanner (Esaote, Genoa, Italy) equipped with a TRT33 bi-planar endorectal probe (frequency range between 3 and 13 MHz). All patients underwent preparation of the rectum with an enema 1 h before the examination. ERUS was usually performed with patients in the left lateral decubitus position. Rectal wall thickness and layers, ulcers and rectovaginal fistulas were evaluated by B-mode ultrasound. Power Doppler was used to evaluate the vascularity of the rectal wall. For ease of description, the rectum was divided into four parts: proximal rectum (>12 cm proximal to the anus), middle rectum (8–12 cm proximal to the anus), distal rectum (4–8 cm proximal to the anus) and anorectal transition (0–4 cm proximal to the anus). The rectum circumference was divided into anterior wall (AW), posterior wall (PW) and left/right lateral rectal wall (LW/RW). Before the procedure, a digital examination was performed to exclude stenosis, and then 50 mL of coupling gel was injected into the rectum. The probe was inserted into the distal rectum subsequently. First, the condition of the distal rectal wall was observed by rotating the probe. Then, the distal rectal wall was evaluated by using both gray-scale and power Doppler ultrasound at the points corresponding to 12, 3, 6 and 9 o'clock in the lithotomy position. B-Mode ultrasound and power Doppler settings were the same for all examinations (Table 1). All images were stored in the hard disk of the scanner.

ERUS image analysis

Normally, five layers of the rectal wall can be visualized with ERUS: interface of the probe and mucosa

Table 1. Imaging settings of ultrasound scanner

Parameter	B-mode	Power Doppler
Probe	TRT33	TRT33
Frequency	Resolution mode	5.6 MHz
Pulse repetition frequency	Non	750 Hz
Depth	22 mm	22 mm
Grain	59%	66%
Number of focus	1	1
Position of focus	4 mm	4 mm