

ORIGINAL RESEARCH

Dynamic changes and outcomes of magnetic resonance imaging in radiotherapy-related rectal injury in cervical cancer

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Abstract

Background: To observe dynamic changes of rectal injury in patients with locally advanced cervical cancer during curative pelvic radiotherapy using magnetic resonance imaging (MRI), and to explore non-invasive radiological methods for assessing radiation-induced rectal injury (RRI). **Methods:** A retrospective analysis was conducted on pelvic MRI images from 56 patients with locally advanced cervical cancer who underwent radical radiotherapy. MRI scans were conducted at four key stages: before radiotherapy, two weeks after starting external irradiation, upon completing external irradiation, and at the conclusion of brachytherapy. Thickness of the intestinal wall from the anorectal region to the sigmoid take-off at each scanning level was measured by RadiAnt DICOM Viewer software, and the average rectal wall thickness was calculated. Statistical analysis was performed using SPSS 26. **Results:** Out of the 56 patients undergoing pelvic radiation therapy, 30 (53.6%) reported symptoms of rectal injury, including diarrhea, increased frequency of stools, loose stools, abdominal pain, tenesmus, and difficulty in defecation, typically appearing during the 3rd to 5th week of treatment. Medication-preserved enemas were administered in the 5th week of radiotherapy and at the beginning of brachytherapy. In symptomatic patients, rectal wall thickness at two weeks of radiotherapy (7.76 ± 0.96 mm) was significantly greater than that before radiotherapy (6.98 ± 0.77 mm) ($p < 0.01$). Thickness continued to increase during external irradiation, reaching its peak at the end of external irradiation (7.99 ± 0.83 mm), followed by a decrease at the end of brachytherapy (7.31 ± 0.81 mm), which was significantly reduced compared with end-of-external-irradiation values ($p < 0.01$). **Conclusions:** Patients with locally advanced cervical cancer undergoing pelvic radiotherapy exhibit significant early and time-dependent rectal imaging changes prior to the onset of evident clinical symptoms of RRI. MRI may serve as a sensitive diagnostic tool for the early detection and prediction of radiation-induced rectal injury.

Keywords

Cervical cancer; Radiotherapy; MRI; Radiation-induced rectal injury

1. Introduction

Cervical cancer is the fourth most common malignant tumor among women [1]. Benefitting from the widespread implementation of human papillomavirus vaccination and cervical cancer screening, the global incidence has declined in recent years; however, it continues to pose a significant health burden for women in China [2, 3]. Standard treatments for locally advanced cervical cancer involve pelvic external beam radiotherapy, brachytherapy, and concurrent chemotherapy [4]. Despite their therapeutic efficacy, these modalities are also associated with substantial adverse effects. Although most cases of treatment-related toxicity respond well to symptomatic management, some patients experience radiotherapy interruptions due to intestinal dysfunction, which may adversely affect treat-

ment outcomes and quality of life. Radiation-induced intestinal injury can occur in any segment of the bowel, with the rectum being affected in up to 75% of cases [4–7]. The pathogenesis of radiation-induced rectal injury is not fully understood. This condition is generally categorized as acute or chronic depending on whether symptoms develop within three months or beyond three months after radiotherapy [8–10]. Inadequate management of the acute phase may lead to chronic complications such as intestinal perforation, bleeding, obstruction, and rectovaginal fistula. Thus, the prevention of radiation-induced intestinal injury is crucial during the treatment.

Radiation-induced rectal injury (RRI) is typically managed using conservative methods such as corticosteroid therapy and antibiotic enemas; however, these approaches often demon-

strate limited efficacy and frequent recurrence [11]. For patients with cervical cancer undergoing curative pelvic radiotherapy, early prediction, and prevention of RRI are essential to reducing its incidence and severity while optimizing the overall effectiveness of radiotherapy.

Rectal injury following cervical cancer radiotherapy is clearly visualized using MRI. On T1-weighted imaging (T1WI), the affected intestinal wall typically demonstrates isointense signal, whereas T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI) show hyperintense signal, often with a distinctly layered “concentric ring” appearance. Contrast-enhanced MRI further highlights this pattern through noticeable mural enhancement. MRI findings usually include uniform, circumferential swelling and thickening of the rectal wall without discrete nodules or soft-tissue masses. However, a minority of cases exhibit irregular mural thickening accompanied by focal luminal contour irregularities or nodular protrusions along the inner margin.

This study retrospectively analyzed MRI scans of cervical cancer patients undergoing curative pelvic radiotherapy at multiple time points during and after the radiotherapy to identify early rectal changes on MRI and to provide a non-invasive method for predicting the development of RRI.

2. Materials and methods

2.1 Patients

This study included 56 patients (mean age, 51 years; range, 24–68 years) with locally advanced cervical cancer who underwent concurrent chemo-radiotherapy (CCRT) at the Department of Oncology, Nanjing Drum Tower Hospital from February 2013 to January 2017 (Table 1). The inclusion criteria were as follows: (1) women aged over 18 years with biopsy-confirmed cervical squamous carcinoma, adenocarcinoma, or adenosquamous carcinoma, and clinically staged IB–IVA according to the International Federation of Gynecology and Obstetrics (FIGO) 2009 classification; (2) no prior history of abdominal and pelvic radiation therapy; (3) no contraindication to MRI (4) completion of radiation therapy without interruption; and (5) no history of chronic diarrhea caused by Crohn’s disease, ulcerative colitis, irritable bowel syndrome and other gastrointestinal diseases. This study was reviewed and approved by the Medical Ethics Committee of Nanjing Drum Tower Hospital (ethics approval number: 2024-558-02).

2.2 Concurrent chemo-radiotherapy methods

Intensity modulated radiotherapy using the Elekta Precision linear accelerator was employed for pelvic external beam radiation therapy (EBRT). The target volumes were delineated by senior radiation oncologists following established guidelines [12] and were supervised in team discussions. The planning target volume (PTV) of whole pelvis was 44–50.4 Gy/22–28 fractions. Brachytherapy was initiated at the fifth week of pelvic EBRT, and the total dose was 22–34 Gy/6–8 fractions, prescribed to point A. Concurrent chemotherapy was administered during radiotherapy, using either platinum alone or

TABLE 1. General information of patients undergoing curative radiotherapy for cervical cancer.

Characteristics	Cases Number
Age (yr)	
<51	28
≥51	28
Pathology subtypes	
Squamous carcinoma	51
Non-squamous carcinoma	5
FIGO staging	
IB2	1
II	24
III	14
IVA	7
Other	10
Chemotherapy history before radiotherapy	
Yes	18
No	38
Synchronous chemotherapy	
Yes	49
No	7
Lymph nodes boost	35
The occurrence of intestinal reaction (Standard: RTOG/EORTC)	
1–2 wk	13
-Level 1	2
-Level 2	11
3–5 wk	30
-Level 1	4
-Level 2	26
-Level 3 and above	0
No intestinal reaction during radiotherapy	13
Intestinal reaction reduced during brachytherapy	30
Aggravated	2
No changes	3
Uncertain	15

FIGO: International Federation of Gynecology and Obstetrics; RTOG: Radiation Therapy Oncology Group; EORTC: European Organization for Research and Treatment of Cancer.

platinum in combination with paclitaxel on a weekly regimen. Patients routinely received a medication-preserved enema with active silver ion gel (YinErShu, 20162640063, Xi’an Kang-wang Antisepsis Technology Co., Ltd., Xi’an, Shannxi, China) inserted to a depth of 8–9 cm, with 3 g applied once daily. All patients receiving radiotherapy and chemotherapy for cervical cancer underwent early intervention treatment with this drug enema at the initiation of brachytherapy.

2.3 Definition and classification of RRI

Symptoms including diarrhea, increased frequency of stools, unformed stools, abdominal pain, tenesmus, and difficulty in defecation were considered indicative of RRI. During radiation therapy, patients declined colonoscopy examinations. The severity of RRI was evaluated according to the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) criteria [13].

2.4 MRI scanning methods

Pelvic MRI scans were performed using a 3.0 T Ingenia scanner (Philips Healthcare, Best, The Netherlands) at four time points during radiotherapy: before the initiation of pelvic radiotherapy, two weeks after the start of radiotherapy, at the completion of EBRT, and at the end of brachytherapy (approximately 8 weeks after the start of radiotherapy). The standard sequences included: axial T2-weighted turbo spin-echo (Repetition Time (TR) = 4500 ms, Echo Time (TE) = 90 ms, matrix size = 308×402 , field of view = $30 \text{ cm} \times 40 \text{ cm}$, slice thickness = 5 mm, intersection gap = 0.5 mm, number of signal averages (NSA) = 1), axial T2-weighted spectral presaturation attenuated in-version recovery (SPAIR) (TR = 4700 ms, TE = 70 ms, matrix size = 376×389 , field of view = $20 \times 20 \text{ cm}$, slice thickness = 5 mm, intersection gap = 0.5 mm, NSA = 1), sagittal T2-weighted turbo spin-echo (TR = 4500 ms, TE = 90 ms, matrix size = 212×209 , field of view = $30 \text{ cm} \times 40 \text{ cm}$, slice thickness = 5 mm, intersection gap = 0.5 mm, NSA = 1), sagittal T2-weighted SPAIR (TR = 4700 ms, TE = 70 ms, matrix size = 256×179 , field of view = $20 \times 20 \text{ cm}$, slice thickness = 5 mm, intersection gap = 0.5 mm, NSA = 1), Three-Dimensional (3D) T1-weighted turbo-field-echo contrast-enhanced acquisition (TR = 3.0 ms, TE = 1.42 ms, field of view = $256 \times 194 \text{ mm}$, matrix size = $30 \text{ cm} \times 40 \text{ cm}$, slice thickness = 1.5 mm, intersection gap = 0 mm, NSA = 1) [14].

2.5 Rectum thickness examination methods

MRI scanning image sequences were imported into RadiAnt DICOM Viewer software (2024.1, Medixant, Poznań, Poland) for analysis. The range of measurement extended from the anorectal area to the sigmoid take-off [15]. The MRI T2 phase cross-sectional scanning layer range comprised of 7–16 layers. Two independent researchers measured the transverse rectal thickness at each scanning level, guided by T1 contrast-enhanced sequences and observed simultaneously on sagittal and axial T2-weighted images (Fig. 1). The average rectal thickness was calculated by summing the measured values across all scanned layers within the measurement range. Data was presented as mean value $\pm$ standard deviation.

2.6 Statistical analysis

Statistical analyses were performed using SPSS version 26 (IBM, Armonk, NY, USA). Due to partial missing data of MRI parameters at four time points (before radiotherapy, 2 weeks after radiotherapy, the end of external irradiation, and the end of brachytherapy), multiple imputation were applied to address missing values. The Kolmogorov-Smirnov (KS)

test was conducted to assess the normality of data distribution. For repeated measurement data that did not follow a normal distribution, Generalized Estimating Equations (GEE) were employed. The Chi-squared test (χ^2) was used to examine the relationship between average age and the presence or absence of clinical symptoms. A p -value < 0.05 was considered statistically significant.

3. Results

3.1 Clinical symptoms

Patients with intestinal reactions of grade 1 or higher were classified as having RRI, based on the 2021 Consensus of Multidisciplinary Diagnosis and Treatment of RRI in China [16] and the RTOG/EORTC criteria [13]. Among the 56 patients, 13 (13/56, 23.2%) showed RRI symptoms within 1–2 weeks, and 30 (53.6%) developed symptoms within 3–5 weeks. The majority of patients experienced RRI within 3–5 weeks after the onset of radiotherapy (Table 1). An analysis of rectal radiation dose revealed no significant difference between patients with and without clinical symptoms of RRI.

3.2 Changes in the course of RRI under MRI imaging

In patients with clinical symptoms of diarrhea, rectal wall thickness at two weeks of radiotherapy ($7.76 \pm 0.96 \text{ mm}$) was significantly greater than that before radiotherapy ($6.98 \pm 0.77 \text{ mm}$, $p < 0.01$) (Table 2, Figs. 2,3,4). Thickness continued to increase progressively during external irradiation, reaching a peak at the end of EBRT ($7.99 \pm 0.83 \text{ mm}$), which was significantly higher compared to both baseline and two-week measurements ($p < 0.01$ and $p = 0.002$, respectively). However, the rectal wall thickness at the end of brachytherapy reduced significantly ($7.31 \pm 0.81 \text{ mm}$) compared to the end of EBRT ($p < 0.01$) (Figs. 1,2,4). Patients without RRI symptoms demonstrated similar trends in rectal wall thickness over time (Table 3, Figs. 2,3,4).

There was no significant difference in rectal thickness between patients with and without clinical symptoms of RRI ($p > 0.05$). Additionally, analysis of average age (51 years) and the presence or absence of clinical symptoms showed no significant association ($\chi^2 = 0.902$, $p > 0.05$).

4. Discussion

Pathologically, RRI is primarily characterized by the inflammation and edema of the superficial rectal mucosa [6]. The rectal mucosal epithelium consists of a single-layered columnar epithelial cells with high turnover rate [17], active proliferation, and is extremely sensitive to radiation. Radiation inhibits the proliferation of the intestinal mucosal layer and submucosal epithelial cells. Ionizing radiation generates free radicals by depositing energy in tissues, which damages DNA, proteins, and lipids, ultimately leading to cell death [18]. Damage to endothelial cells, fibroblasts, and infiltrating leukocytes triggers signaling pathways that result in cell apoptosis and impaired epithelial renewal. The early pathological manifestations of RRI include mucosal congestion, edema, and

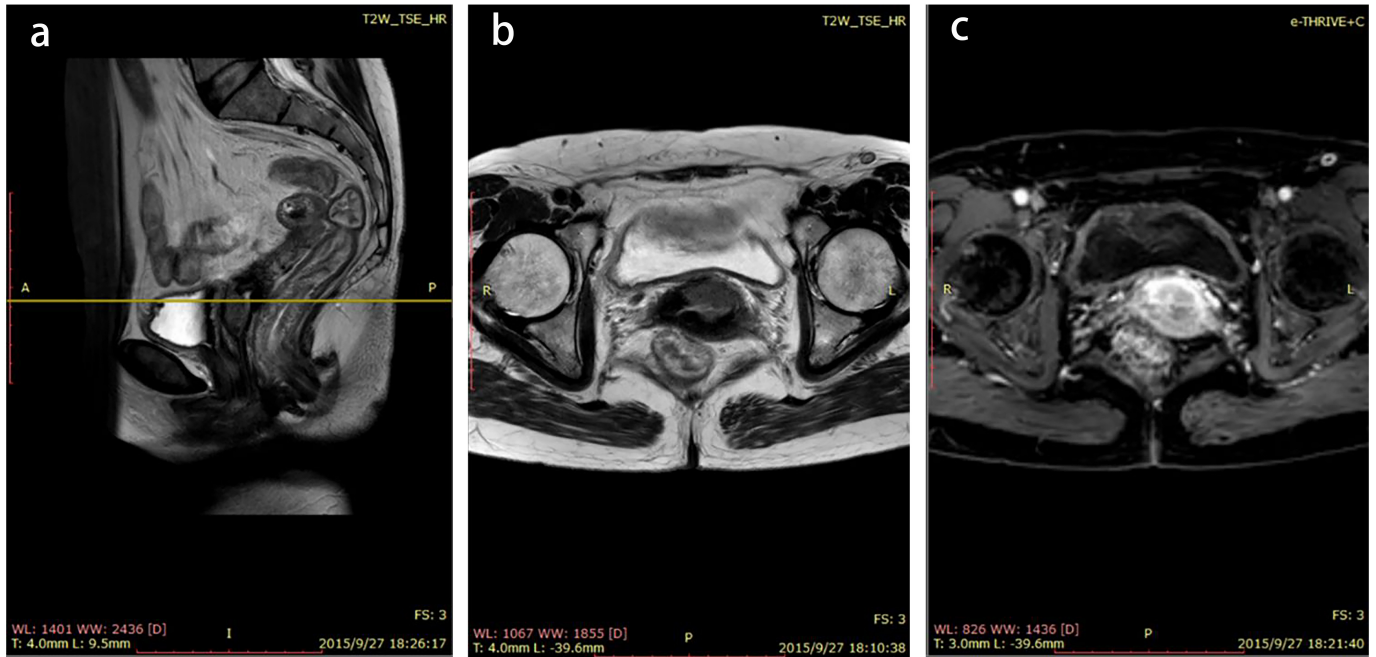


FIGURE 1. MRI Interfaces for measuring rectal wall thickness in a cervical cancer patient. (a) T2 weighted sagittal position; (b) T2 weighted transverse section; (c) T1 phase enhanced sequence. MRI: Magnetic Resonance Imaging; T2: Tissue 2; T1: Tissue 1.

TABLE 2. Rectal wall thickness observation in patients with clinical symptoms during the initial four time points of radiotherapy for cervical cancer using MRI imaging.

MRI timing	Before radiotherapy	2 weeks of radiotherapy	The end of external radiation	The end of brachytherapy
Rectal wall thickness (mm)	6.98 ± 0.77	7.76 ± 0.96	7.99 ± 0.83	7.31 ± 0.81
Mean $\pm$ SD				

SD: standard deviation; MRI: magnetic resonance imaging.

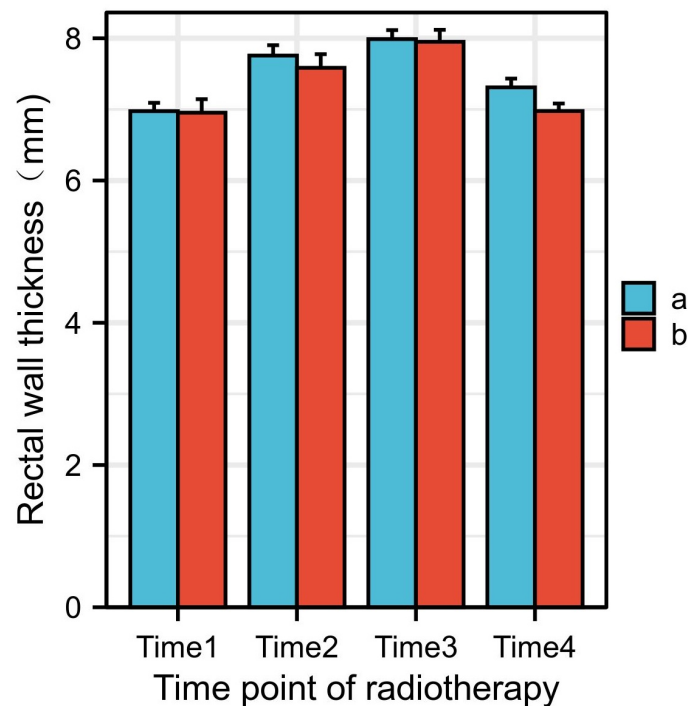


FIGURE 2. Column chart of changes in rectal wall thickness during radiotherapy for cervical cancer.

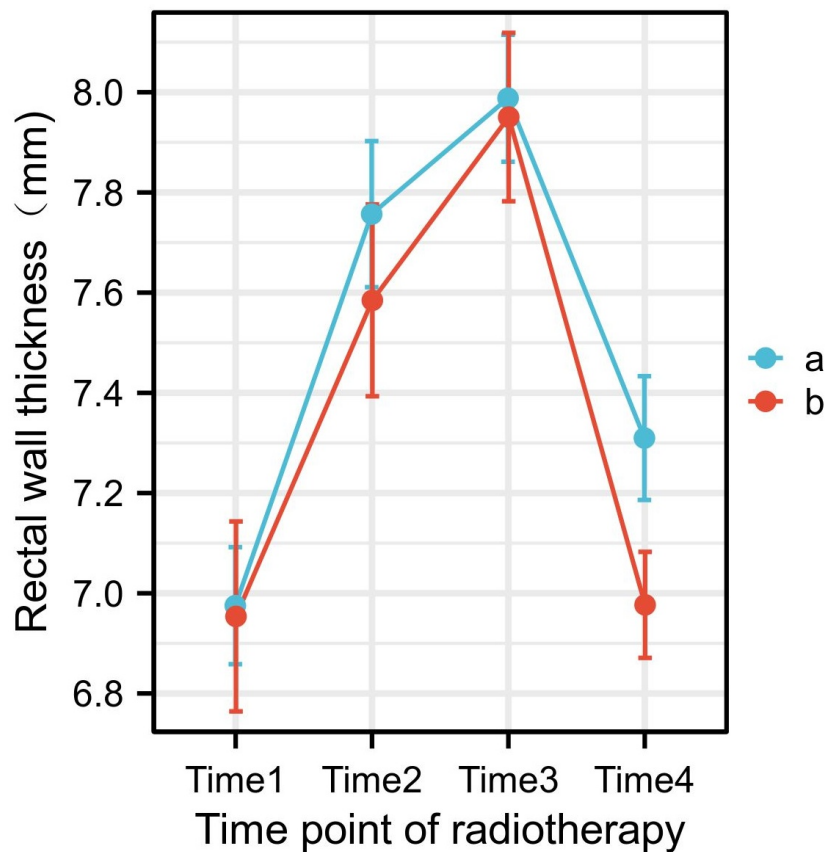


FIGURE 3. Line chart of changes in rectal wall thickness during radiotherapy for cervical cancer.

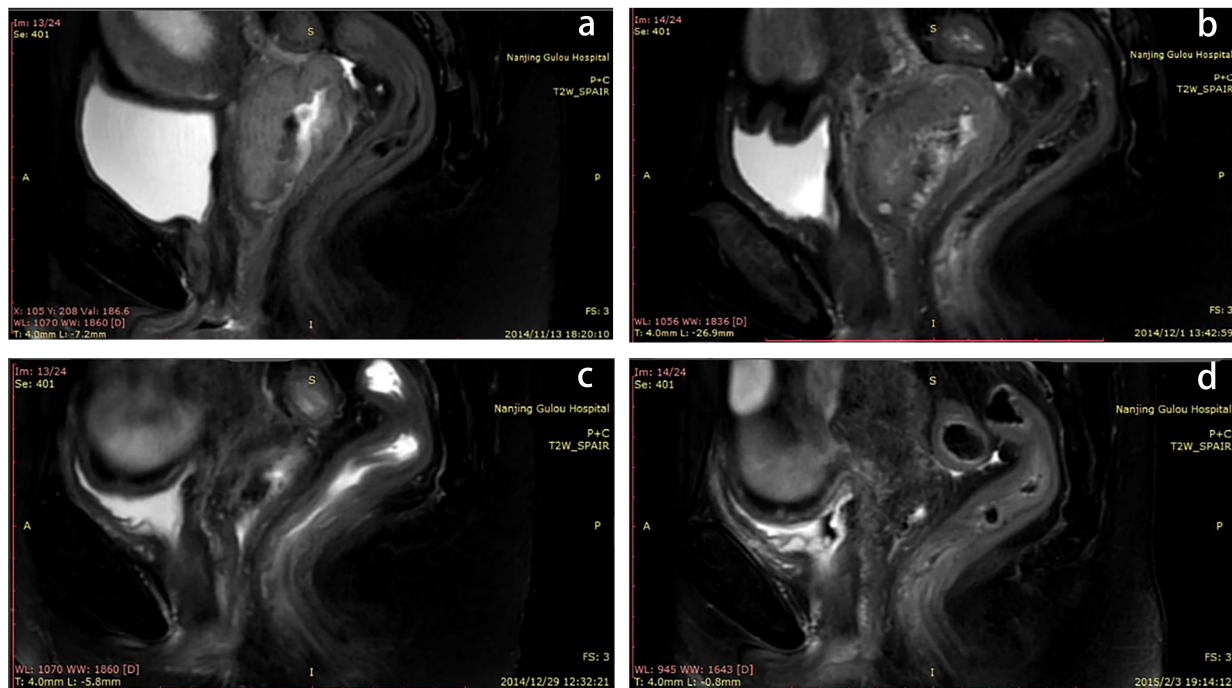


FIGURE 4. Changes in rectal MRI images of a cervical cancer patient undergoing radiotherapy at different stages. (a) Rectal scanning image of patients before radiotherapy in T2 SPAIR sequence; (b) Rectal scanning image at 2 weeks of the radiotherapy, demonstrating increased thickness compared to that before radiotherapy; (c) Significant rectal edema at the end of the external irradiation, with the rectal wall thickness reached the highest value in the course of the disease; (d) Rectal wall thinner than before after the end of brachytherapy. MRI: Magnetic Resonance Imaging; T2: Tissue 2; SPAIR: Spectral Attenuated Inversion Recovery.

TABLE 3. Observation of rectal wall thickness in patients without clinical symptoms during radiotherapy for cervical cancer using MRI imaging at the first four time points.

MRI timing	Before radiotherapy	2 weeks of radiotherapy	The end of external radiation	The end of brachytherapy
Rectal wall thickness (mm)	6.95 ± 0.68	7.58 ± 0.69	7.95 ± 0.61	6.98 ± 0.38
Mean ± SD				

SD: standard deviation; MRI: magnetic resonance imaging.

infiltration of inflammatory cells. As the injury progresses, mucosal atrophy, granulation tissue proliferation, intestinal epithelial fibrosis, and obliterative endarteritis occur sequentially [8]. Approximately 20% of patients may develop noticeable symptoms, such as diarrhea, abdominal pain, and tenesmus [19]. According to the RTOG/EORTC [13] standard, RRI is classified into 0–4 levels, with higher grades indicating more severe symptoms of rectal injury. The colonoscopy reveals extensive mucosal congestion and edema, accompanied by erosion and small ulcers.

Due to the lack of unified criteria, the diagnosis of RRI is mainly based on the comprehensive judgments of clinical symptoms, colonoscopy findings, and biopsy pathology. Colonoscopy provides the most direct method for diagnosis; however, many cervical cancer patients develop acute or chronic inflammatory changes such as rectal edema and fibrosis following radical radiotherapy. As a result, colonoscopy is generally avoided within the first year after radiotherapy to prevent procedure-related injury. Consequently, the diagnosis of RRI is often delayed, making early prediction particularly challenging. MRI, with its advantages of being non-invasive, non-radiative, high soft tissue resolution, and the ability to perform multi-directional and enabling multi-directional, multi-sequence imaging, plays a vital role in assessing the location, extent, and severity of radiation-induced intestinal injury [20].

Our study showed that during curative pelvic radiotherapy for patients with locally advanced cervical cancer, the majority of patients (53.6%) developed varying degrees of rectal injury symptoms, including diarrhea, abdominal pain, tenesmus, and difficulty in defecation, typically occurring 3–5 weeks after the start of radiotherapy. At 5 weeks of radiotherapy and at the initiation of brachytherapy, patients received daily medication-preserved enemas, which alleviated these symptoms. Notably, MRI performed at two weeks of radiotherapy revealed a significant increase in rectal wall thickness compared to baseline, indicating that imaging changes of RRI precede clinical symptoms and may provide a more sensitive means of early prediction. MRI can monitor temporal changes in rectal wall thickness during radiotherapy, serving as a valuable, non-invasive diagnostic tool for the early detection of RRI.

Preventing and treating RRI are major challenges in cervical cancer radiotherapy. Previous studies have reported the following treatments of RRI: (1) Systemic medication: using hormones, hemostatic drugs, antibiotics, probiotics, anti-inflammatory, and anti-oxidative drugs can alleviate symptoms to varying degrees [21], however, long-term efficacy remains limited, and strong evidence from high-quality clinical trials is lacking. (2) Medication-preserved enema: Local administration allows drugs to directly contact the affected rectal mucosa,

enhancing therapeutic effects. Commonly used agents include sucralfate, corticosteroids, short-chain fatty acids, metronidazole, and combination regimens; (3) Local methanol treatment: For RRI patients with severe hemorrhage, methanol can be effective [22] by inducing the formation of thrombus in newly born blood vessels through protein coagulation, achieving hemostasis. Caution is warranted in patients with complications such as rectal or anal stenosis, ulcers, or anal incontinence; (4) Endoscopic therapy: Techniques such as endoscopic argon plasma coagulation, bipolar electrocoagulation (BPEC), and endoscopic radiofrequency ablation are effective for hemorrhagic RRI [23, 24]. However, these methods are not widely used clinically due to their invasive nature; (5) Hyperbaric oxygen therapy: This approach can improve tissue ischemia, hypoxia, microcirculation disorders caused by advanced RRI and promote tissue repair [25]. However, it is less cost-effective, and some reports suggest that different dosing regimens may inadvertently promote tumor growth; (6) Fecal microbiota transplantation (FMT): FMT can benefit RRI treatment through regulating the composition and abundance of gut microbiota in patients [26], but technical details and prospective validations need further improvement. Overall, the primary focus in RRI management remains prevention. Early prediction of RRI at the onset of radiotherapy and timely application of mucosal protective measures can significantly reduce the incidence of late-onset, refractory injury. Recommended preventive strategies include: (1) Advancing radiation technologies to improve precision, including patient positioning, specialized treatment tables [27], multiportal delivery techniques [28, 29], and optimization of total and fractional radiation doses. (2) Radiation protective agents [30] such as Amifostine, an intravenously administered cytoprotective agent [31]; (3) Protection of organs at risk (OAR): Local injection of medications around the rectum can alleviate pain and inflammation, enhance neurotrophic processes, and improve tissue microcirculation [32].

5. Conclusions

Our study indicated that, with the progression of pelvic external beam radiotherapy, rectal injuries gradually aggravated. Rectal wall thickness reached its maximum at the end of EBRT but decreased significantly by the end of brachytherapy. However, rectal wall thickness did not increase consistently with cumulative radiation dose throughout the entire radiotherapy course, and this pattern was consistent with the timing of clinical symptoms. Approximately 60% of patients experienced symptomatic relief during brachytherapy, which may be attributable to the administration of active silver ion

antibacterial gel enemas at the end of EBRT and the start of brachytherapy, although further clinical trials are needed to confirm this effect. For patients with locally advanced cervical cancer undergoing curative pelvic radiotherapy, early intervention with medication-preserved enemas before the completion of radiotherapy may help alleviate rectum edema and could be considered as a routine preventive and therapeutic measure for RRI. This retrospective study is limited by a small sample size and the use of older data, which may introduce potential bias and errors. Further prospective clinical trials with larger cohorts and extended follow-up are warranted to validate and refine these findings.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

HL—Conceptualization; Methodology, Writing—original draft. MQD—Methodology, Formal analysis. FZ, LPD, ZY—Writing—original draft. JFB, LJZ—Writing—review & editing, Supervision.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study has been reviewed and approved by the Medical Ethics Committee of Nanjing Drum Tower Hospital (ethics approval number: 2024-558-02). Written informed consent was obtained from legally authorized representatives for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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