RESEARCH COMMUNICATION

Influence of Bladder Distension Control on Postoperative Intensity-Modulated Radiotherapy in Rectal Cancer Patients

Haiqin Zhang, Renben Wang*, Hongjiang Yan, Wei Zhao, Rui Feng, Shumei Jiang, Jinming Yu

Abstract

    <u>Aims</u>: A prospective study was undertaken to reduce bladder volume variation and the irradiated small bowel injury by irrigating the bladder during postoperative pelvic IMRT in rectal cancer patients. <u>Methods</u>: 12 consecutive patients underwent three sets of computed tomography scans during the treatment course: Group I, a distended (not empty) bladder before the radiation course; Group II, a distended bladder at the end of the fourth week; Group III, an irrigated bladder at the end of the fourth week. A seven-field coplanar intensity-modulated radiotherapy plan of 50.4 Gy was made to the clinical target volume. The total volume of regions of interest and volume within every isodose level, their maximum dose and mean dose were analysed. <u>Results</u>: Compared with group I, the median reduction of bladder volume was 147.7cm³ (24.3%), and the median increment of small bowel was 122.4cm³ in group II. The volume of small bowel within every isodose level was increased (P<0.05). Statistical analysis showed a correlation between the volume change of bladder and small bowel. The mean radiation dose (Dmean) of small bowel and bladder was increased in group II compared to groups I and III (P<0.05). <u>Conclusions</u>: Bladder volume declines significantly during the course of radiotherapy, leading to an increment in irradiated small bowel volume. Bladder irrigation is a feasible method to guarantee a consistent bladder volume and reduce small bowel rqadiation exposure.

Keywords: Rectal neoplasm - radiotherapy - small bowel injury - bladder irrigation - intensity-modulated radiotherapy

Introduction

    Preoperative chemoradiation has gained acceptance as the standard of care for patients with clinical stage II and III rectal cancer. However, it does not reduce distant metastases and improve survival times compared to postoperative radiotherapy. Furthermore, 20%–30% of patients will have stage I disease and will receive unnecessary treatment. Postoperative radiotherapy as an adjuvant treatment still plays an important role in the management of rectal cancer. Adjuvant chemoradiation therapy showed an advantage in local control, disease-free interval, and overall survival after surgical resection. But the toxicity of the small bowel seems to increase (Sauer et al., 2001; 2004; Baxter et al., 2007).

    After abdominoperineal or anterior resections, the small bowel settles deeper into the lower pelvis and becomes fixed by adhesions, thereby increasing the volume and toxic effects of the bowel exposed to radiation. The small bowel has potential risk for radiation injury due to lower radiation tolerance than either the urinary bladder or the rectum.

    Among various methods to reduce the irradiated small bowel volume, prone position with a belly board

and bladder distension are the most commonly applied. Bladder distention is shown to be more effective in sparing the small bowel in postoperative pelvic RT of rectal cancer patients (Kim et al., 2005). While conventional bladder distention by a 1-2h restriction in urination sometimes result in low practicability and reproducibility (Tsai et al., 2009). A consistent bladder volume is important to make a quantitative analysis. This present study compared the effects of the combination of belly board with or without bladder irrigation on reducing the irradiated small bowel volume during postoperative pelvic radiation.

Materials and Methods

Patients

    This study enrolled 12 (6 males, 6 females) consecutive patients with rectal cancer who were scheduled to receive postoperative pelvic radiotherapy. All patients underwent TME surgery (7 anterior resection, 5 abdominoperineal resection). The cancer stage of all patients was deeply invasive (pT3–T4) or regional lymph node metastasis (pN1–2). Median age distribution was 58.5 years (range 37.0-65.3). Patient with previous history of intra-abdominal surgery, urogenital system disease were
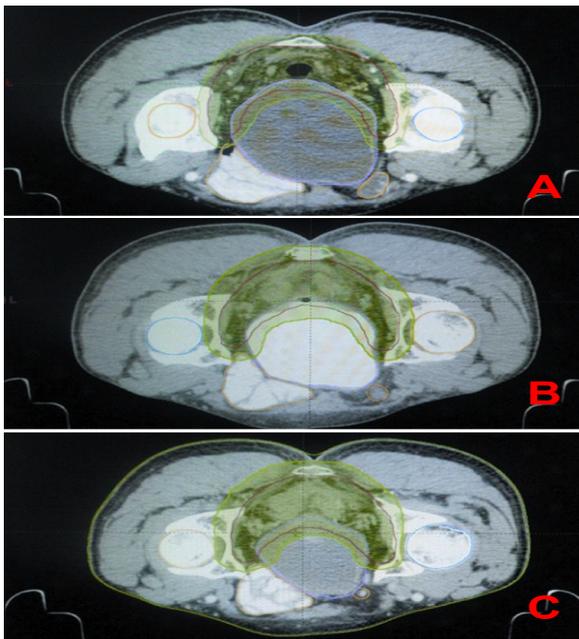
Department of Radiation Oncology, Shandong Cancer Hospital, 440 Jiyan Road, Jinan, China   **For correspondence: wangrenben@tom.com*

Figure 1. An Example of Delineation of ROI. The volume of bladder reduced in group II(B), and was equal in groupI (A) and III(C).

excluded. Patients who were unable to tolerate bladder irrigation were not enrolled in the study. No patients had undergone previous surgery. The study was performed in accordance with our institutional review board guidelines, and informed consent was obtained.

CT stimulation

All patients were asked to empty their bladders, and drink 800ml oral contrast solution (meglumine diatrizoate) before the CT scan. Then the patient was asked to maintain a upright position allowing time to visualize the small bowel and distend the bladder. Patients completed self-assessment using a scale of 1–4 for bladder comfort. A score of 1 indicated the patient's bladder was comfortably full and a score of 4 was an indicator that the bladder was uncomfortably full. Patients were asked to lay prone on the belly board and start to scan when the score was 3 (GroupI). The belly board measured 180 cm×50 cm×8 cm and with a round aperture on a diameter of 32cm. The lower border of the aperture was placed at the lower end of the sacroiliac joint. The first set of CT was taken at an interval of 3-mm thickness from the bottom of the tenth thoracic vertebra (T10) spine to 5 cm inferior to the ischial tuberosity. Then the patient underwent urethral catheterication and record the urine volume (VU1) within 10 minutes. The patient was instructed in bladder distension techniques and were told to have a full bladder for daily treatment. The second set of CT scans (Group II) was taken 4 weeks later using a same method and underwent urethral catheterication. Then VU1 ml normal saline solution was injected into urinary bladder via urethral catheter to distend the bladder. Then the patient was scaned (Group III).

IMRT Planning

All target volumes were contoured and reviewed for each slice. The bladder and small bowel were identified on each set of CT images. Clinical target volume (CTV) included the primary tumor bed and regional lymphatics. Part of posterior bladder wall and prostate or uterus were delineated. CTV plus 8 mm was planning target volume (PTV). The superior border was at the fifth lumbar vertebra/first sacral vertebra (L5/S1) and the inferior border at lower margin of the obturator foramen. The small bowel volumes consisted of individual loops of bowel, contoured up to 2-cm above the superior-most PTV slice, and the bladder was fully contoured. The identified organ volumes and the targets in 3 plans were ensured to more or less equal.

IMRT planning was performed using 15-MV photon beams and seven equispaced fields(gantry angles 0°, 51°, 103°, 154°, 206°, 257°, and 308°). The isocenter was placed at the geometric center of the PTV. The prescribed radiation dose (50.4Gy) was normalized to the isodose surface to cover 98% of the PTV. Radiation dose of PTV and critical organs were all within limits. Dose-volume histograms (DVHs) were computed for all plans.

Statistical analysis

All data were analyzed for different groups using Wilcoxon sign rank test and/or Friedman test. All tests were two-sided and analyzed using SPSS 17.0 programs. A p value of <0.05 was considered to indicate a significant difference.

Results

The summation of all regions of interest (ROI) volume are listed in table1.

The volumes of PTV and CTV were equal for all three groups (p=0.377; p=0.841).

The volume of bladder (B) differed significantly (p=0.002). It was equal in groupI and III (p=0.294), and significantly reduced in group II compared with the other groups. The median reduction of bladder volume in group II compared with groupIwas 147.74cm³ (minimum~maximum:-33.17/315.30cm³), as is shown in Figure 1.

The total small bowel (SB) volumes were 578.18±257.46 cm³ (mean±standard deviation), 708.17±334.16 cm³, and 550.37±275.31 cm³ respectively. It increased significantly in group II compared with other groups. The median increment of small bowel in group II compared with groupIwas 122.43cm³ (54.03- 441.47cm³). There was no significant difference between groupIand III(p=0.134). Statistical analysis showed there's a correlation between the reduction of bladder and the increment of small bowel (r=0.732, P<0.05).

Results of statistical analyses for small bowel volume within every isodose level are presented in Table 2. There was no significant difference between group I and III for the small bowel volume within 10Gy, 20Gy, 30Gy, 45Gy, 50Gy isodose level (V10, V20, V30, V45, V50) (p=0.078, 0.097, 0.127, 0.064, 0.133 respectively). It was increased significantly in group II. The mean irradiated small bowel DVHs for 3 groups calculated for doses between 10 and 100% of the prescribed dose at 10% intervals

Table 1. Average Volumes Including Standard Deviation (in cm³) in the Patient Groups

structure	group I	group II	group III	P value	
CTV	635.67±170.72	630.22±181.04	635.45±181.63	0.841	I:II 0.910
					I:III 0.595
PTV	1224.47±295.06	1264.68±283.07	1247.61±297.42	0.377	I:II 0.174
					I:III 0.302
SB	578.18±257.46	708.17±334.16	550.37±275.31	0.004	I:II 0.001
					I:III 0.134
B	372.48±139.30	213.83±136.92	358.75±139.26	0.001	I:II 0.001
					I:III 0.235

Table 2. Small Bowel Volume Within Every Isodose Level

SB	Minimum			Maximum			Median			Mean			P-vable
	I	II	III	I	II	III	I	II	III	I	II	III	
V10	197.59	313.25	243.06	794.75	923.42	694.59	384.76	459.84	389.56	431.75	515.72	451.31	0.025
V20	156.47	268.31	191.83	535.37	636.74	539.64	292.14	385.32	269.87	289.26	372.57	308.29	0.021
V30	113.52	175.79	132.88	363.89	476.82	346.85	189.66	275.95	198.62	197.67	281.09	203.64	0.016
V45	28.29	85.45	58.33	168.47	266.53	175.61	78.22	146.68	90.7	76.27	177.63	88.58	0.008
V50	11.58	23.63	20.18	94.36	185.84	138.64	25.48	69.04	28.47	27.05	75.13	28.62	0.006

Table 3. The Radiation Dose of Small Bowel and Bladder for 3 Groups

|	SB						B					
	Dmax			Dmean			Dmax			Dmean		
	I	II	III	I	II	III	I	II	III	I	II	III
minimum	5016.5	4959.8	5375.4	214.7	431.8	166.4	5209.7	5154.3	5435.6	1746.8	2374	1803.5
maximum	5734.5	5678.6	5825.3	3784	3821.1	4075.9	5733.8	5747.9	5632	3398.7	4873.7	3848.3
median	5457.2	5546.3	5537.8	2562.9	3034.7	2317.4	5253.6	5455.2	5501.3	3015.5	3846.2	2980.1
mean	5432	5443.4	5458.6	2477.3	3136.5	2544.4	5204.6	5374.2	5453.6	2854.7	3811.3	2975.7
P-value		0.539			0.043			0.659			0.038	
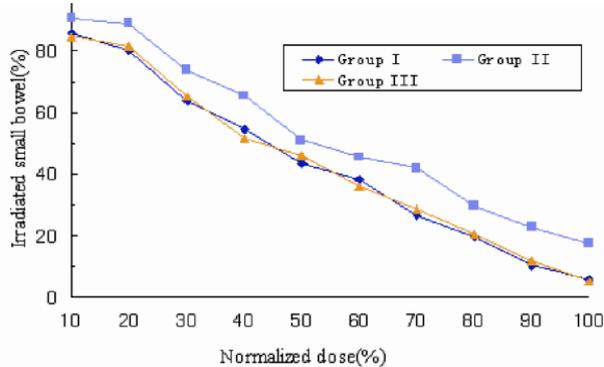
Figure 2. Irradiated Small-bowel Volumes (%) in Groups I, II, III at Various Dose Levels

are shown in Figure 2. There was a significant increase of irradiated small-bowel volume in group II at all dose levels (p < 0.001). The mean absolute increase (relative reduction) of irradiated small bowel volume at every dose levels were 4.78%, 8.44%, 9.90%, 11.09%, 7.56%, 7.15%, 15.33%, 10.18%, 12.11%, 11.85% respectively.

Both of the relative volume for bladder within 10Gy, 20Gy isodose level was 100%. There is no significant difference for mean relative bladder volume (%) within 30Gy, 40Gy and 50Gy isodose level between group I and group III. While it is significantly increased in group II, the mean relative volume increased (%) compared with group I is 12.23, 10.86, 10.84 (p=0.003, 0.015, 0.009).

As is shown in Table 3, there is no statistical significance btween the maximum radiation dose (Dmax) of small bowel and bladder in all groups (p=0.539; 0.659). While the mean radiation dose (Dmean) of small bowel

and bladder is increased in group II compared to group Iand group III (3136.5 vs. 2477.3; 3811.3 vs. 2854.7), P<0.05.

Discussion

The volume of the irradiated small bowel in pelvic carcinoma is considered to be an important factor to the severity of acute and chronic morbidity (Lebesque et al., 1995; Gunnlaugsson et al., 2007; Robertson et al., 2008; 2010; Sanguineti et al.,2009). A highly statistically significant correlation was found to exist between small bowel dose-volume and Grade 3 diarrhea. The volume of small bowel receiving at least 15 Gy (V15) was strongly associated with the degree of toxicity.

Various methods have been applied to reduce the irradiated small bowel volume, including surgical techniques such as pelvic tissue expanders for displacement of the small bowel and absorbable mesh slings, and non-surgical techniques such as bladder distension, belly boards, and small bowel displacement devices. The combination of belly board and bladder distension was mostly used methord and was reported with a mean 73.4% relative reductions of the irradiated small bowel volume. And bladder distention was more effective than belly board in reducing the irradiated small bowel volume (Kim et al., 2005).

While there is a shortcoming for bladder distention: the status of bladder distension maybe inconsistent during radiotherapy, which can cause an increase in inter-fractional set-up inaccuracy. A reduction of 16~47% of bladder volume during the whole treatment compared

to the values measured in the planning CT was reported during fractionated radiotherapy of prostate cancer patients (Fiorino et al., 2005; O'Doherty et al., 2006; Stam et al., 2006; Naoki et al., 2010). Ahmad et al. (2008) reported that population mean bladder volumes during the course of the radiotherapy treatment for uterine cervical cancer: Our study is consistent with previous analyses.

The reason for the decline in bladder volume remains unclear and may be multifactorial. Pinkawa et al. (2006) hypothesized that cystitis might lead to the declination of bladder volume, while previous study showed no significant correlation between intrapatient variations in bladder volume and the incidence of acute cystitis, and the mechanism underlying the decline in bladder volume can not be explained by cystitis alone, since previous reports showed that reductions in bladder volume occurred imediately after treatment had been initiated. In O'Doherty's study (2006), anti-muscularinic drugs and alpha-blockers are routinely prescribed, while there was a significant decrease between the volume at CT and treatment.

In order to improve bladder volume consistency, many study fixed the drinking protol through specify the volume of liquids to be consumed and the times at which such liquids should be consumed (e.g., drink 500 ml of fluid an hour before the planning CT scan and treatment) (Stasi et al., 2006; Ahmad et al., 2008). However, the bladder volume varies significantly with such protols. O'Doherty et al. (2006) claim that a fixed drinking protocol did not eliminate all variations in the bladder volume, in part due to significant individual variations in velocity of bladder filling. They also reported that patients are able to accurately judge their bladder filling state and suggested that subjective patient assessments should be taken into account during efforts to control bladder volume. So in Naoki's study (2010), the patients were told to adjust the amount of liquid ingested based on their urge to urinate. Nonetheless, it showed large variations in bladder volume .

This study is the first to quantitate the reproducibility of small bowel sparing using bladder irrigation in the radiotherapy of rectal cancer patients using belly board. We demonstrated that the volume of the bladder and irradiated small bowel can be kept consistent throughout planning and treatment to reduce positional uncertainties and the risk of increased irradiated volume and dose in the normal surrounding tissue. A consistently full bladder prevent additional small bowel settle into the pelvis due to the reduced bladder volume during the treatment course. In our study, the small bowel in every isodose level and the bladder in 30Gy, 40Gy, 50Gy were also statistically consistent to the planning CT. These findings may result in a reduction in small bowel complications. Bladder distension control is an effective and inexpensive technique in reducing small bowel radiation volume compared to belly board without bladder irrigation in pelvic radiotherapy of rectal cancer patients.

References

Ahmad R, Hoogeman MS, Quint S, et al (2008). Inter-fraction bladder filling variations and time trends for cervical cancer patients assessed with a portable 3-dimensional ultrasound bladder scanner. *Radiother Oncol*, **89**, 172-9.

Baxter NN, Hartman LK, Tepper JE, et al (2007). Postoperative irradiation for rectal cancer increases the risk of small bowel obstruction after surgery. *Ann Surg*, **245**, 553-9.

Fiorino C, Foppiano F, Franzone P, et al (2005). Rectal and bladder motion during conformal radiotherapy after radical prostatectomy. *Radiother Oncol*, **74**, 187–95

Gunnlaugsson A, Kjellén E, Nilsson P, et al (2007). Dose-volume relationships between enteritis and irradiated bowel volumes during 5-fluorouracil and oxaliplatin based chemoradiotherapy in locally advanced rectal cancer. *Acta Oncol*, **46** 937-44.

Kim TH, Kim DY, Cho KH, et al (2005). Comparative analysis of the effects of belly board and bladder distension in postoperative radiotherapy of rectal cancer patients. *Strahlenther Onkol*, **181**, 601-5.

Lebesque JV, Bruce AM, Kroes AP, et al (1995). Variation in volumes, dose-volume histograms, and estimated normal tissue complication probabilities of rectum and bladder during conformal radiotherapy of T3 prostate cancer. *Int J Radiat Oncol Biol Phys*, **33**, 1109-19.

Naoki Nakamura, Naoto Shikama, Osamu Takahashi, et al. (2010). Variability in Bladder Volumes of Full Bladders in Definitive Radiotherapy for Cases of Localized Prostate Cancer. *Strahlenther Onkol*, **186**, 637-42.

O'Doherty UM, McNair HA, Norman AR, et al (2006) Variability of bladder filling in patients receiving radical radiotherapy to the prostate. *Radiother Oncol*, **79**, 335–40.

Pinkawa M, Asadpour B, Gagel B, et al (2006). Prostate position variability and dose-volume histograms in radiotherapy for prostate cancer with full and empty bladder. *Int J Radiat Oncol Biol Phys*, **64**, 856–61.

Robertson JM, Lockman D, Yan D, Wallace M (2008). The dose-volume relationship of small bowel irradiation and acute grade 3 diarrhea during chemoradiotherapy for rectal cancer. *Int J Radiat Oncol Biol Phys*, **70**, 413-8.

Robertson JM, Söhn M, Yan D (2010). Predicting grade 3 acute diarrhea during radiation therapy for rectal cancer using a cutoff-dose logistic regression normal tissue complication probability model. *Int J Radiat Oncol Biol Phys*, **77**, 66-72.

Sanguineti G, Endres EJ, Sormani MP, Parker BC (2009). Dosimetric predictors of diarrhea during radiotherapy for prostate cancer. *Strahlenther Onkol*, **185**, 390-6.

Sauer R, Fietkau R, Wittekind C, et al (2001). Adjuvant versus neoadjuvant radiochemotherapy for locally advanced rectal cancer. A progress report of a phase-III randomized trial (protocol CAO/ARO/AIO-94). *Strahlenther Onkol*, **177**, 173-81.

Sauer R, Becker H, Hohenberger W, et al (2004). Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med*, **351**, 1731-40.

Stam MR, van Lin EN, vander Vight LP, Kaanders JH, Visser AG (2006). Bladder filling variation during radiation treatment of prostate cancer: can the use of a bladder ultrasound scanner and biofeedback optimize bladder filling? *Int J Radiat Oncol Biol Phys*, **65**, 371–7.

Stasi M, Munoz F, Fiorino C, et al (2006). Emptying the rectum before treatment delivery limits the variations of rectal dose-volume parameters during 3DCRT of prostate cancer. *Radiother Oncol*, **80**, 363–70.

Tsai CL, Wu JK, Wang CW, et al (2009). Using cone-beam computed tomography to evaluate the impact of bladder filling status on target position in prostate radiotherapy. *Strahlenther Onkol*, **185**, 588-95