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Effects of bladder status on cervical cancer treatment with intensity-modulated radiation therapy plans

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Abstract

Objective: The present study aimed to compare the effects of different bladder statuses on cervical cancer treatment with intensity-modulated radiation therapy (IMRT) plans.

Methods: A total of 21 cervical cancer patients who were willing to be treated with IMRT in the prone position at the Third Affiliated Hospital of Kunming Medical University from December 1, 2014 to October 31, 2015 were selected for this study. IMRT treatment plans were carried out using computed tomography images of the full and empty bladder. Data were collected to compare the differences between clinical target volume, planning target volume, and the percentage of irradiated volume of the bladder, small bowel, rectum, and caput femoris in patients with full and empty bladders.

Results: Clinical target volume, planning target volume, and the volume of organs at risk did not show obvious differences ($P > 0.05$ in all respects) in patients with different bladder statuses. The average radiation dose of the small bowel of a patient with a full bladder (2056.7 ± 364.7 cGy) was significantly lower than that of a patient with an empty bladder (2319.5 ± 451.58 cGy), $P < 0.001$. The average radiation dose of the rectum of a patient with a full bladder (4663.7 ± 68.94 cGy) was higher than that of a patient with an empty bladder (4621.6 ± 54.86 cGy), $P = 0.039$. The percentages of irradiated volume covered by the 5–45 Gy isodose curve (V5–V45) of the small bowel were lower in the full bladder patients than in the empty bladder patients ($P < 0.001$ in all respects), whereas the percentages of irradiated volume covered by the 45 Gy isodose curve (V45) of the rectum were higher in the full bladder patients ($P < 0.05$). If a patient had lymphatic metastasis, the V45 irradiated volume ratio (IVR) of the small bowel of a patient with a full bladder was lower than that of a patient with an empty bladder, $P < 0.001$, whereas the V45 IVR of the rectum increased ($P = 0.04$). For patients without lymphatic metastasis, the V45 IVR of the small bowel and bladder both decreased with a full bladder compared with an empty bladder ($P = 0.002$ and 0.01, respectively), and there was no difference in the V45 IVR of the rectum ($P = 0.275$).

Conclusions: IMRT plans delivered to patients with a full bladder in the prone position can reduce the percentage of irradiated volume in the small bowel. For patients with lymphatic metastasis, although keeping a full bladder reduces the percentage of irradiated volume in the intestine, it also increases the percentage of irradiated volume in the rectum

KEYWORDS

cervical cancer, empty bladder, full bladder, intensity-modulated radiation therapy, irradiation volume

1 | INTRODUCTION

Radiotherapy (external beam and/or brachytherapy) plays an important role in the treatment of cervical cancer. In external beam radiotherapy, factors such as fixed technology, posture (prone or supine), and volume variation in adjacent anatomical structures can affect the accuracy of the irradiation plan. For example, these factors might lead to displacement of the target volume, causing more normal tissue to be pushed into the area of irradiation.[1–3]

The bladder is a structure with a variable volume, located in front of the cervix. The status of the bladder might result in considerable tumor and/or normal organ mobility within the pelvis. If a patient whose plan is based on a full bladder keeps an empty bladder when receiving irradiation, normal tissue, such as the intestine, might be more likely to be exposed to irradiation, thus increasing toxicity. We therefore need to pay more attention to the influence of bladder status on target volume and normal tissue during irradiation. The present study compares clinical target volume (CTV), planning target volume (PTV), and dose–volume parameters of organs at risk in intensity-modulated radiation therapy (IMRT) plans for the treatment of cervical cancer, in patients with a full bladder and an empty bladder in the prone position.

2 | METHODS

2.1 | Patients

We observed 21 patients with histologically confirmed cervical cancer in the Third Affiliated Hospital of Kunming Medical University (Tumor Hospital of Yunnan Province) from December 1, 2014 to October 31, 2015. They were treated with IMRT in the prone position, and had had no previous chemotherapy or operation. The patient median age was 52 years, and the patient age ranged from 30 to 64 years. A total of 16 patients were at FIGO stage IIB and five were at stage IIIB when diagnosed. Based on their magnetic resonance imaging scans, 1 patients were shown to have regional lymphatic metastasis (six with lymphatic metastasis in the pelvic cavity; five with lymphatic metastasis in both the pelvic cavity and the para-aorta). The remaining 10 patients did not have lymphatic metastasis.

2.2 | Imaging

For each patient, two consecutive computed tomography (CT) scans (CT scanner: SIEMENS 24 row spiral CT; Siemens Medical Solutions USA, Ins. 51 Valley Stream Parkay Malvern, PA19355-1406 USA) were taken from the diaphragm to the perineum with a slice thickness of 5 mm for treatment planning. All patients were investigated in the prone position on a belly board. The CT was carried out with a full bladder (FB) first. Then, patients were asked to empty their bladders (EB) to take another set of CT images in the same position. All scans were taken by the same team of technologists.

Before CT simulation, all patients were given clear verbal and written instructions specifying fluid intake. To prepare the bladder, patients were required to drink 1000 cm^3 of water at least 1 h before the scans. The time for FB scanning depended on the patients' feeling of a strong, yet tolerable, desire for micturition. During simulation, there was no rectal preparation.

2.3 | IMRT planning

After imaging was completed, image data were sent for contouring and planning (Philips Pinnacle^3 treatment planning system; Philips Medical Systems, ADAC Laboratories, 5520 Nobel Drive, Suite 125 Fitchburg, WI 53711 USA). Target volumes (gross tumor volume [GTV], CTV, and PTV) and normal structures (bladder, rectum, bowel, renal, spinal cord, caput femoris, and bone marrow) were contoured according to radiation therapy oncology group (RTOG) contouring atlases for targets and organs at risk, respectively. The CTV was composed of data from the GTV, cervix, uterus, parametrium, vagina, and pelvic lymph nodes (common, external, and internal iliac lymph nodes, obturator lymph nodes and presacral lymph nodes).[4–6] For patients with para-aortic lymph node metastasis, the CTV also contained the para-aortic lymph nodes with the superior boundary at L1–L2. The delineation of the lymph node drainage area was outlined as 7 mm on either side of the corresponding blood vessels. The inferior boundary of the CTV was 3 cm below the tumor in patients with vaginal invasion, and 3 cm superior to the vagina in patients without vaginal invasion. The positive lymph nodes were countered as GTV-nd. Peritoneal space was contoured for the bowel and outlined on every slice, extending 1–2 cm above the PTV. Peritoneal space included the volume surrounding the loops of the bowel out to the edge of the peritoneum.

The PTV was defined as the CTV plus a 0.6-cm margin for lymph node drainage areas, and a 1-cm margin for the primary cervical tumor. The GTV-nd plus a 0.4-cm margin formed the planning gross tumor volume (PGTV)-nd.

All the IMRT plans were calculated by the same physicist. Treatment plans were optimized using seven fields, with gantry angles of 0°, 50°, 100°, 155°, 205°, 255°, and 310°, respectively. The prescription dose for PGTV-nd was 62.4 Gy, delivered as 2.4 Gy/fraction, and for PTV, the dose was 46.8 Gy, delivered as 2.4 Gy/fraction. For both, five fractions/week were given. The prescribed dose encompassed 95% of the PTV, depending on the location and proximity to critical organs. The priorities were prescribed as PGTV-nd, PTV, rectum, bladder, small bowel, caput femoris, spinal cord, and renal. The optimization parameters (dose constraint and overlap priority) were given the same consideration in both the FB and EB plans. The IMRT treatment plans were carried out with 6-MV X-rays using a Varian Trilogy linear accelerator (Varian Medical Systems, Inc. 660 North Mc Carthy Blvd. Milpitas, CA95035 USA).

2.4 | Statistical analysis

A comparison of the dosimetric parameters and PTVs between IMRT plans in the FB and EB groups was carried out with the Wilcoxon rank-sum test. Subgroup data analyses based on lymph node metastasis were calculated using the Wilcoxon signed-rank test. The significance level was set at 0.05. All analyses were carried out with SAS version 9.2 (SAS Institute, Cary, NC, USA).[7,8]

TABLE 1 Comparison of clinical target volume, planning target volume, and average radiation dosages in bladders of different statuses

Category	Position	LNs	Mean ± SD (full)	Mean ± SD (empty)	Diff[a] ± SD	*P*-value[b]
Volume (cc)	CTV	Total	953.8 ± 147.99	941.5 ± 171.52	12.3 ± 86.25	0.352
		Yes	1021.6 ± 144.72	1003.8 ± 196.13	17.9 ± 119.55	0.7
		No	879.2 ± 116.58	873.1 ± 112.66	6. 2 ± 23.93	0.375
		P-value[c]	0.032	0.062		
	PTV	Total	1622.7 ± 249.2	1577.3 ± 233.74	45.5 ± 145.33	0.154
		Yes	1691.7 ± 213.05	1667.7 ± 262.87	24 ± 144.43	0.638
		No	1546.8 ± 274.49	1477.7 ± 153.69	69.1 ± 150.25	0.049
		P-value[c]	0.13	0. 085		
Dmean (cGy)	CTV	Total	5065.9 ± 262.61	5068.7 ± 242.74	−2.8 ± 120.73	0.828
		Yes	5241.1 ± 249.72	5260.2 ± 175.59	−19 ± 144.39	1
		No	4873.2 ± 72.04	4858.2 ± 51.35	15.1 ± 92.47	0.846
		P-value[c]	0.002	0		
	PTV	Total	4990.4 ± 198.54	4993.5 ± 183.28	−3.1 ± 86.57	0.801
		Yes	5122 ± 189.33	5137 ± 134.97	−15. 1 ± 99.69	0.966
		No	4845. 6 ± 57.55	4835.6 ± 39.06	10 ± 72.42	0.625
		P-value[c]	0. 003	0		

[a]Difference (Diff), full − empty.
[b]*P*-value is calculated by using the Wilcoxon signed-rank test
[c]*P*-value is based on the comparison of values between lymph groups using the Wilcoxon rank-sum test. CTV, clinical target volume; LNs, lymph nodes metastasis; PTV, planning target volume

3 | RESULTS

3.1 | Basic information on participants

We observed 21 patients with stage IIB–IIIB squamous carcinoma of the cervix from December 2014 to October 2015. Based on their intensive CT and MRI scans, 11 of them were shown to have regional lymphatic metastasis (six with lymphatic metastasis in the pelvic cavity; five with lymphatic metastasis in both the pelvic cavity and the para-aorta). The remaining 10 patients did not have lymphatic metastasis.

3.2 | Comparison of CTV, PTV, and average radiation dosage in bladders with different statuses

In Table 1, comparing the full status and empty status of the bladders studied, CTV and PTV did not show obvious differences (CTV: $P = 0.352$; PTV: $P = 0.154$), nor did average radiation dosage (CTV: $P = 0.828$; PTV: $P = 0.801$). We further compared the groups with and without lymphatic metastasis when the bladder was full and empty, and found that CTV and PTV average radiation dosages in the group with lymphatic metastasis were higher than those of the group without lymphatic metastasis (FB CTV: $P = 0.002$, PTV: $P = 0.003$; EB CTV: $P = 0$, PTV: $P = 0$).

3.3 | Comparison of organs at risk volumes and average radiation dosages in bladders with different statuses

In Table 2, the average volume of a FB (420.5 ± 166.52 mL) is 4.22-fold that of an EB (99.7 ± 63.22 mL), $P < 0.001$. When the bladder is full or empty, the volumes of the small bowel ($P = 0.511$), rectum ($P = 0.300$), left caput femoris ($P = 0. 933$), right caput femoris ($P = 0.801$), and spinal cord ($P = 0.227$) show no obvious differences.

When the bladder is full or empty, the average radiation dosage of the bladder ($P = 0.085$), left caput femoris ($P = 0.187$), right caput femoris ($P = 0.239$), and spinal cord ($P = 0.749$) shows no obvious differences. The average radiation dosage of the small bowel with FB status is 2056.7 ± 364.7 cGy, lower than that with EB status 2319.5 ± 451.58 cGy, $P < 0.001$, whereas the average radiation dosage of the rectum with FB status is 4663.7 ± 68.94 cGy, higher than that with EB status 4621.6 ± 54.86 cGy, $P = 0.039$.

Further analysis of the groups with and without lymphatic metastasis suggested that if a patient has lymphatic metastasis, the average radiation dosage of the rectum with FB status is 4685.8 ± 66.73 cGy, higher than that with EB status 4616.2 ± 50.68 cGy, $P = 0.004$. The average radiation dosages of the small bowel with FB and EB statuses are 2111.6 ± 384.22 cGy and 2261.6 ± 565.86 cGy, respectively, $P = 0.051$, showing no obvious differences. If a patient does not have lymphatic metastasis, the average radiation dosage of the small bowel with FB status is 1996.4 ± 351.88 cGy, lower than with EB status 2383.3 ± 297.97 cGy, $P = 0.002$. Average radiation dosages of the rectum with FB and EB status are 4639.4 ± 66.03 cGy and 4627.5 ± 61.33 cGy, respectively, $P = 0.695$, showing no obvious differences. Therefore, in patients with lymphatic metastasis, FB status might cause an increase in the average radiation dosage of the rectum, but does not significantly affect that of the small bowel. In patients without lymphatic metastasis, the FB status is protective of the small bowel, but does not significantly affect the rectum. This research suggests that posture in radiation therapy should be chosen based on the specific conditions of patients with lymphatic metastasis.

TABLE 2 Comparison of organs at risk volumes and average radiation dosages in bladders with different statuses

Category	Position	LNs	Mean ± SD (full)	Mean ± SD (empty)	Diff[a] ± SD	*P*-value[b]
Volume (cc)	Bladder	Total	420. 5 ± 166.52	99.7 ± 63.22	320.8 ± 166.63	<0.001
		Yes	444 ± 152.76	83.7 ± 48.37	360.3 ± 168.14	<0.001
		No	394.6 ± 185.11	117.3 ± 74.99	277.3 ± 162.09	0.002
		P-value[c]	0.46	0.245		
	Intestine	Total	1323.8 ± 463.53	1281.9 ± 391.97	42 ± 182.98	0.511
		Yes	1512.7 ± 545.79	1420.1 ± 445.81	92.6 ± 235.11	0.354
		No	1116.1 ± 234.42	1129.9 ± 267.55	−13.8 ± 80.01	0.77
		P-value[c]	0.084	0.13		
	Rectum	Total	79.2 ± 45.14	68.8 ± 39.38	10.4 ± 42.83	0.300
		Yes	92.1 ± 51.72	64.8 ± 34.58	27.2 ± 48.02	0.116
		No	65 ± 33.61	73.2 ± 45.57	−8. 2 ± 28.02	0.922
		P-value[c]	0.218	0.916		
	R-femur head	Total	113.1 ± 21.04	113.2 ± 17.99	−0.1 ± 10.84	0.801
		Yes	110.7 ± 20.81	113 ± 13.5	−2.2 ± 12. 4	0.27
		No	115.8 ± 22.09	113.5 ± 22.72	2.3 ± 8.86	0.432
		P-value[c]	0.503	0.597		
	L-femur head	Total	114.4 ± 18.87	114.6 ± 17.4	−0.2 ± 8.79	0.933
		Yes	114.1 ± 18.53	114 ± 12.75	0.1 ± 8.91	0.563
		No	114.7 ± 20.24	115.2 ± 22.16	−0.5 ± 9.13	0.846
		P-value[c]	0.751	0.751		
	cord	Total	25 ± 9.59	23.7 ± 8.86	1.3 ± 5.19	0.227
		Yes	29.2 ± 10.83	28.2 ± 8.68	1 ± 6.66	0.683
		No	19.9 ± 4.28	18.1 ± 5.43	1.8 ± 2.85	0.098
		P-value[c]	0.033	0.012		
Dmean (cGy)	Bladder	Total	4655.7 ± 95.04	4698.4 ± 76.16	−42.7 ± 102.12	0.085
		Yes	4662.5 ± 115.97	4712.2 ± 96.31	−49.6 ± 129.03	0.27
		No	4648.1 ± 70.78	4683.3 ± 45.82	−35.2 ± 67.48	0.084
		P-value[c]	1	0.13		
	Intestine	Total	2056.7 ± 364.7	2319.5 ± 451.58	−262.8 ± 420.89	<0.001
		Yes	2111.6 ± 384.22	2261.6 ± 565.86	−150 ± 527.51	0.051
		No	1996.4 ± 351.88	2383.3 ± 297.97	−386.9 ± 227.66	0.002
		P-value[c]	0.647	0.751		
	Rectum	Total	4663.7 ± 68.94	4621.6 ± 54.86	42.1 ± 73.14	0.039
		Yes	4685.8 ± 66.73	4616.2 ± 50.68	69.6 ± 65.4	0.004
		No	4639.4 ± 66.03	4627.5 ± 61.33	11.9 ± 72.11	0.695
		P-value[c]	0.149	0.46		
	R-femur head	Total	2189.6 ± 309.56	2174.7 ± 287.53	14.9 ± 296.92	0.239
		Yes	2200.3 ± 299.81	2165.8 ± 342.05	34.5 ± 178.33	0.75
		No	2177.9 ± 335.82	2184.4 ± 231.36	−6.6 ± 399.5	0.275
		P-value[c]	1	1		
	L-femur head	Total	2095.6 ± 305.86	2074.2 ± 268.3	21.4 ± 340.96	0.187
		Yes	2098.3 ± 304.91	2029.8 ± 259.9	68.5 ± 195.69	0.269
		No	2092.6 ± 323.37	2123.1 ± 282.58	−30.5 ± 458.36	0.492
		P-value[c]	0.972	0.503		
	Cord	Total	2103 ± 655.47	2103.3 ± 748.76	−0.3 ± 643.62	0.749
		Yes	2290.4 ± 730.64	2437 ± 700.21	−146.6 ± 394.3	0.354

(Continues)

TABLE 2 (Continued)

Category	Position	LNs	Mean ± SD (full)	Mean ± SD (empty)	Diff[a] ± SD	*P*-value[b]
		No	1874.1 ± 495.87	1695.5 ± 615.19	178.6 ± 850.92	0.652
		P-value[c]	0.362	0.048		

[a]Difference (Diff), full – empty.
[b]*P*-value is calculated by using the Wilcoxon signed-rank test
[c]*P*-value is based on the comparison of values between lymph groups using the Wilcoxon rank-sum test. Dmean, mean dose; L, left; LNs, lymph nodes metastasis; R, right.

3.4 | Comparisons of the irradiated volume ratios in at-risk organs at certain doses in bladders with different statuses

As shown in Table 3, compared with EB status, the irradiated volume ratio (IVR) in the small bowel from V5 to V45 decreases ($P < 0.05$); IVR in the bladder from V5 to V40 shows no significant difference ($P > 0.05$), and V45 IVR decreases ($P < 0.001$). In the rectum, V45 IVR increases, and from V5–V40, IVR shows no significant difference. IVRs in the left caput femoris, right caput femoris, and spinal cord show no significant differences.

4 | DISCUSSION

Complications of cervical cancer radiotherapy, such as radiation cystitis, radiation enteritis, and radiation proctitis, are key factors that can affect the success of radiotherapy and quality of life after treatment. It has always been a research focus to reduce irradiated volume ratios and doses in at-risk organs while guaranteeing the target dose.

Compared with two-dimensional radiation therapy and three-dimensional radiation therapy, IMRT shows advantages in effectively decreasing the radiation dosage of organs in the pelvic cavity and the incidence of complications.[9–11] While researching how posture influenced the small bowel in IMRT, Adli *et al.* discovered that radiation dosages of the small bowel in patients in a prone posture were less than those of patients in a supine posture.[12] Therefore, prone IMRT is more protective to the small bowel in pelvic cavity radiation therapy. Related research of pelvic cavity radiation therapy in prostate cancer and rectal cancer suggested that a FB can protect the small bowel by decreasing radiation dosage and volume.[13,14]

As the bladder is directly in front of the cervix, changes in bladder volume can greatly influence the effects of cervical cancer radiotherapy. Mao *et al.* analyzed 15 postoperative cervical cancer patients who received pelvic cavity IMRT in the prone position, and compared the dosage and volume changes of at-risk organs in bladders of different statuses. The results showed that for the same patient receiving IMRT in the prone position, when the bladder was full, irradiated volume ratios of the bladder, small bowel, and rectum were lower than when the bladder was empty, ($P < 0.05$); radiation dosages of the bladder and small bowel with FB status were less than those with EB status ($P < 0.05$).[15] Lu *et al.* analyzed data from 15 postoperative cervical cancer patients who received pelvic cavity IMRT in the prone position, comparing dosage and cubage changes of the intestines of patients with bladders of different statuses. When the bladder was full, irradiated cubage ratios of the bladder, small bowel, and colon were lower than with EB status ($P < 0.05$).[16] Fu *et al.* analyzed 30 postoperative cervical cancer patients, and found that when the bladder was full, radiation dosages of the bladder and small bowel were significantly less than for those with EB status ($P < 0.05$), whereas radiation dosages of the CTV, PTV, rectum, and caput femoris for patients with FB status and EB status were not statistically different ($P > 0.05$).[17] The aforementioned research showed that for postoperative cervical cancer patients who received pelvic cavity IMRT, FB status can be protective to the small bowel, bladder, and colon. However, the anatomical structure of a postoperative patient is different from that of a patient who has not had an operation. The effects of bladder status on pelvic cavity radiotherapy in patients without an operation have not yet been reported.

In the present study, pelvic cavity IMRT in a prone position was adopted, and radiation dosages and volumes of targets and at-risk organs (small bowel, rectum, etc.) in cervical cancer patients before operation were compared. The results showed that in conditions when 95% of the PTV reached the prescription dose, the PTV average doses, CTVs, PTVs, and volumes of the small bowel, rectum, left and right caput femoris, and spinal cord were not significantly changed. In addition to the bladder itself, volumes of targets or at-risk organs did not change as the bladder status changed. Therefore, changes in bladder status do not cause changes in radiotherapy targets or organ volumes.

The results also suggested that, compared with EB status, average radiation dosage (ARD) of the small bowel from V5 (percentage of the volume covered by certain isodose curve) to V45 is lower than with FB status. From V5 to V40 in the bladder, ARD shows no significant difference, and in V45, ARD decreases; in the rectum V45, ARD increases. ARDs and IVRs in the left caput femoris, right caput femoris, and spinal cord (V5–V50) show no significant difference. That is, FB status can protect the small bowel to a certain extent and can lower the high-dose IVR of the bladder, but can also increase the high-dose IVR of the rectum. Further analysis of lymphatic metastasis subgroups shows that in the group with lymphatic metastasis, IVR of the small bowel V45 with FB status is lower than that with EB status ($P < 0.001$), whereas IVR of the rectum and V45 increase significantly ($P = 0.04$) with EB status, and IVR of the small bowel and bladder V45 were not influenced by bladder status ($P > 0.05$). In the group without lymphatic metastasis, when the bladder is full, ARD of the small bowel is less ($P = 0.002$); high-dose IVR V45 of the bladder is lower ($P = 0.002$, $P = 0.01$). However, ARD of the rectum and bladder, and the rectum V45 do not show significant changes in bladders of different statuses. Whether the patient has

TABLE 3 Comparison of irradiated volume ratios in organs at risk with a certain dose in bladders with different statuses

Category	Position	LNs	Mean ± SD (full)	Mean ± SD (empty)	Diff[a] ± SD	*P*-value[b]
V5 (%)	Bladder	Total	100 ± 0	100 ± 0	0 ± 0	NA
		Yes	100 ± 0	100 ± 0	0 ± 0	NA
		No	100 ± 0	100 ± 0	0 ± 0	NA
		P-value[c]	1	1		
	Intestine	Total	81.2 ± 11.96	83.1 ± 11.16	−1.9 ± 4.29	0. 022
		Yes	86.7 ± 10.81	87.3 ± 11.84	−0.6 ± 3.22	0. 334
		No	75.2 ± 10.58	78.6 ± 8.75	−3.3 ± 5.03	0. 064
		P-value[c]	0.053	0.062		
	Rectum	Total	100 ± 0	100 ± 0	0 ± 0	NA
		Yes	100 ± 0	100 ± 0	0 ± 0	NA
		No	100 ± 0	100 ± 0	0 ± 0	NA
		P-value[c]	1	1		
V15 (%)	Bladder	Total	100 ± 0	100 ± 0	0 ± 0	NA
		Yes	100 ± 0	100 ± 0	0 ± 0	NA
		No	100 ± 0	100 ± 0	0 ± 0	NA
		P-value[c]	1	1		
	Intestine	Total	59.7 ± 12.92	65.3 ± 12.79	−5.7 ± 6.46	<0.001
		Yes	64.3 ± 14.23	68.7 ± 15.62	−4.5 ± 6.06	0.04
		No	54.6 ± 9.54	61.6 ± 7.89	−7 ± 6.93	0.02
		P-value[c]	0.193	0.378		
	Rectum	Total	100 ± 0	100 ± 0	0 ± 0	NA
		Yes	100 ± 0	100 ± 0	0 ± 0	NA
		No	100 ± 0	100 ± 0	0 ± 0	NA
		P-value[c]	1	1		
V25 (%)	Bladder	Total	99.9 ± 0.42	100 ± 0	−0.1 ± 0.42	1
		Yes	100 ± 0	100 ± 0	0 ± 0	NA
		No	99.8 ± 0.6	100 ± 0	−0.2 ± 0.6	1
		P-value[c]	0.34	1		
	Intestine	Total	33.4 ± 7.58	42.2 ± 8.1	−8.8 ± 4.72	<0.001
		Yes	33.5 ± 8	41.8 ± 9.29	−8.4 ± 3.9	<0.001
		No	33.3 ± 7.54	42.7 ± 7.04	−9.4 ± 5.66	0.002
		P-value[c]	0.86	0.972		
	Rectum	Total	100 ± 0	100 ± 0	0 ± 0	NA
		Yes	100 ± 0	100 ± 0	0 ± 0	NA
		No	100 ± 0	100 ± 0	0 ± 0	NA
		P-value[c]	1	1		
V35 (%)	Bladder	Total	99.1 ± 2.69	99.9 ± 0.23	−0.8 ± 2.72	0.056
		Yes	99.5 ± 0.54	99.8 ± 0.3	−0.3 ± 0.7	0.195
		No	98.7 ± 3.92	100 ± 0	−1.3 ± 3.92	0.125
		P-value[c]	0.133	0.094		
	Intestine	Total	20.1 ± 7.93	30.4 ± 8.88	−10.3 ± 4.71	<0.001
		Yes	18.3 ± 7.22	27.4 ± 8.57	−9.2 ± 4.79	<0.001
		No	22.2 ± 8.54	33.6 ± 8.45	−11.5 ± 4.57	0.002
		P-value[c]	0.342	0.13		
	Rectum	Total	99.8 ± 0.43	99.9 ± 0.29	−0. 1 ± 0. 55	0.922
		Yes	99.8 ± 0.45	99.8 ± 0.38	0 ± 0.65	1
		No	99.9 ± 0.43	100 ± 0.09	−0.1 ± 0.45	0.875

(Continues)

TABLE 3 (Continued)

Category	Position	LNs	Mean ± SD (full)	Mean ± SD (empty)	Diff[a] ± SD	*P*-value[b]
		P-value[c]	0.383	0.895		
V45 (%)	Bladder	Total	70.6 ± 11.31	79.4 ± 11.15	−8.8 ± 11.14	<0.0001
		Yes	64.2 ± 10.03	74.9 ± 12.48	−10.8 ± 14.28	0.053
		No	77.6 ± 8.19	84.2 ± 7.28	−6.6 ± 6.26	0.01
		P-value[c]	0.007	0.032		
	Intestine	Total	10.4 ± 6.08	18.5 ± 7.82	−8.1 ± 5.11	<0.001
		Yes	7.9 ± 3.34	14.5 ± 7.1	−6.6 ± 4.76	<0.001
		No	13.2 ± 7.33	22.9 ± 6.23	−9.8 ± 5.19	0.002
		P-value[c]	0.032	0.012		
	Rectum	Total	78.2 ± 11.95	69.6 ± 16.37	8.6 ± 14.62	0.023
		Yes	77.6 ± 13.76	67.7 ± 12.99	9.9 ± 12.6	0.04
		No	78.8 ± 10.3	71.6 ± 19.98	7.2 ± 17.15	0.275
		P-value[c]	0.916	0.379		

[a]Difference (Diff), full – empty.
[b]*P*-value is calculated by using the Wilcoxon signed-rank test
[c]*P*-value is based on the comparison of values between lymph groups using the Wilcoxon rank-sum test. V5–V45 are the percentages of irradiated volume covered by the 5–45 Gy isodose curve. NA, not applicable.

lymphatic metastasis or not does not influence low-dose IVR (V5–V40) of the small bowel, bladder, or rectum. For patients with lymphatic metastasis, a FB can increase ARD of the rectum, but does not affect ARD of the small bowel. For patients without lymphatic metastasis, a FB can protect the small bowel, but does not affect ARD of the rectum.

The research results did not suggest that a FB would protect the bladder or rectum. Comparatively, when we carried out lymphatic metastasis subgroup analyses, radiation dosages of the rectum increased. The result was different from previous research, potentially because the research participants of other studies were postoperative cervical cancer patients.[15–18] When the bladder of a postoperative cervical cancer patient was full, displacement of organs in the pelvic cavity, such as the small bowel, rectum, and bladder, was rather obvious, thus resulting in greater radiation dosages of those organs.

In conclusion, when carrying out radical IMRT on patients with stage IIB–IIIB cervical cancer, bladder filling could protect the small bowel; however, if pelvic lymph node metastasis occurs, bladder filling could lower the radiation dosage of the small bowel while increasing that of the rectum. Consequently, it is necessary to suggest bladder status based on specific patient conditions.

CONFLICT OF INTEREST

The authors declare that they had read the article and there are no competing interests.

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