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The Factors Affecting Small Bowel Volume in the Pelvis of Patients Receiving Radiotherapy for Rectal Cancer

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Abstract

Purpose: Radiation (RT)-Induced Gastrointestinal (GI) toxicities are associated the small bowel volume irradiated and the dosage received. However, rectal cancer patients treated with neoadjuvant Chemoradiotherapy (CRT) experience less GI toxicities compared to adjuvant chemoradiotherapy. The purpose of this study was to explore the factors which are associated with the small bowel volume in the pelvic radiation fields.

Materials and methods: Patients with rectal cancer who had pre- or post-surgery CRT and were treated by a single radiation oncologist were included. All patients were treated with 3-D conformal radiotherapy. The volume of the organs was determined from planning CT scans. Acute toxicity was graded using Radiation Therapy Oncology Group (RTOG) Common Toxicity Criteria. Acute GI toxicity and its associated determinants such as age, bladder volume, gender, Body Mass Index (BMI), and type of surgery were documented.

Results: A total of 119 patients (71 males, 48 females) 35 to 88 years of age were recruited. Sixty one out of 119 patients had pre-surgery RT or CRT and 58 patients had post-surgery therapy. Single predictors for greater irradiated small bowel volume were post-surgery treatment, female sex, smaller bladder volume and older age. The small bowel volume tended to increase with lower BMI and abdominoperineal resection. Multivariate analysis indicated that post-surgery treatment, being a female, and having a smaller bladder volume were predictors of greater irradiated volume of the small bowel.

Conclusion: Factors such as pelvic surgery, being female, flat bladder, and older age are associated with increased small bowel volumes in pelvis. These would increase the irradiated small bowel volumes in patients receiving radiotherapy for rectal cancer. Therefore, giving radiotherapy before the surgery or using technical such as IMRT or Rapid Arc to avoid or reduce the small bowel volumes being irradiated is warranted.

Keywords

Chemo-Radiotherapy; Dose-Volume Histogram; Multivariate Analysis; Rectal Cancer; Small Bowel

Introduction

Neoadjuvant chemoradiotherapy was shown to improve local control, and to decrease toxicities as compared to adjuvant chemoradiotherapy [1,2] though both neoadjuvant and adjuvant chemoradiotherapy are associated with improving overall survival as well as local control in patients with locally advanced rectal cancer [3-6] compared to surgery alone. Both neoadjuvant and adjuvant chemoradiotherapy have been associated with acute diarrhea [5-7] but it has been demonstrated that neoadjuvant treatment is superior to adjuvant treatment with respect to the decreased bowel toxicities [5]. Although diarrhea can be caused by chemotherapy [8] surgery [9] or radiotherapy [10] small bowel toxicity resulting from irradiation has been shown as part of the causes of acute diarrhea during the treatment [11]. However, there are no published data on the factors that may affect the small bowel volume irradiated, and this study was conducted to analyze the factors which are associated with the small bowel volume in the pelvis.

Methods and Materials

Patient eligibility

Eligibility criteria included consecutive patients with Stage I and Stage IV rectal cancers who received either neoadjuvant chemoradiotherapy or neoadjuvant radiotherapy alone or adjuvant

chemoradiotherapy in a single institute during the period of 2005 to 2010.

Study design

The patients were immobilized in supine position. The small bowel contrast (telebrix 38 Oral, tyco/healthcare) was given orally 1 hour before treatment planning computed tomography scan. Transverse images at 3 mm intervals were obtained. The volume of small bowel was outlined by contouring the small bowel loops 1 cm above the superior edge of the Planning Target Volume (PTV) and the absolute volume quantified (cm3) using Eclipse or Pinnacle planning software (Figures 1 and 2). The volumetric assessment of small bowel dose was performed based on the actual Dose Volume Histogram (DVH) of the three dimensional conformal radiotherapy treatment planning for each patient prospectively. The majority of patients received three-fields (posterior-anterior and opposed lateral fields). Most of the patients received 50.4 Gy in 28 fractions. Acute diarrhea was graded per RTOG Criteria [12].

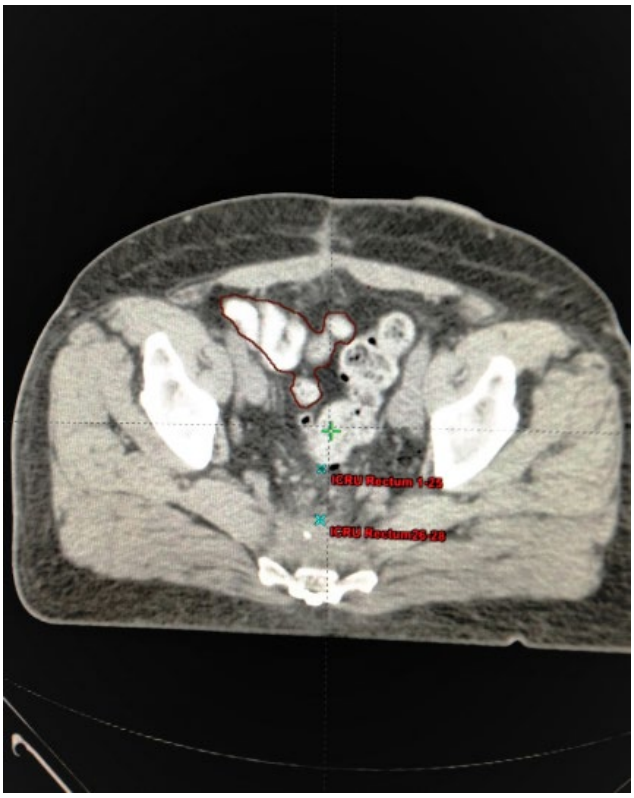

Figure 1: Radiotherapy simulation CT scan of a 67 year old man with a resected upper rectal cancer. The contrast-filled small bowel loops are contoured.

Statistical methods

Patients were divided into neoadjuvant treatment (including four patients who received radiotherapy alone) and adjuvant groups. Data were analyzed using Chi-Square, Wilcoxan Rank test, and linear regression. A P-value of 0.05 or less was considered statistically significant.

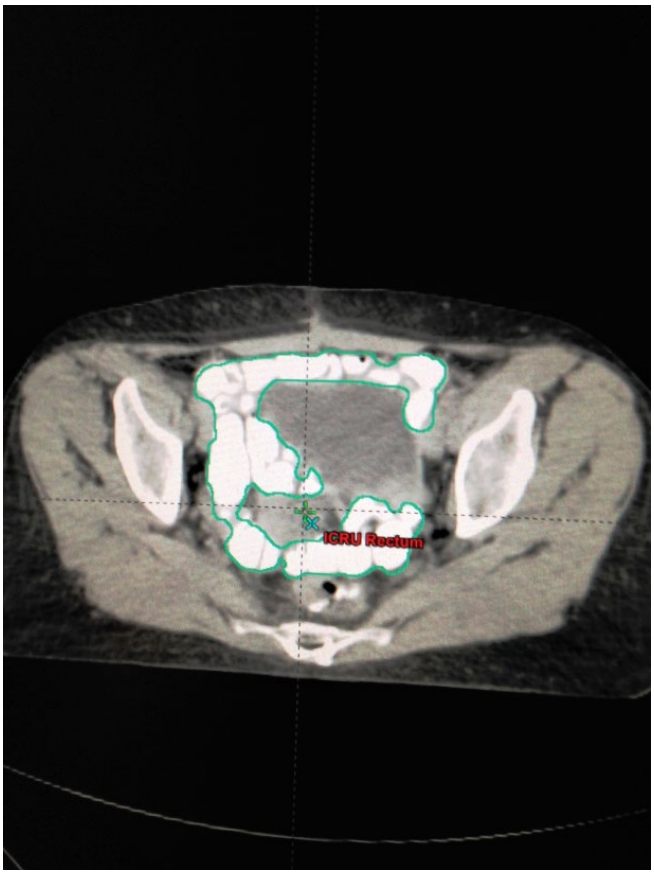

Figure 2: Radiotherapy simulation CT scan of a 66 year old woman with a resected upper rectal cancer. The contrast-filled small bowel loops are contoured.

Results

A total of 119 patients (71 males, 48 females) 35 to 88 years of age were treated by a single radiation oncologist. Sixty one patients had neo-adjuvant and 58 had adjuvant radiotherapy. One hundred and six of patients had concomitant chemotherapy (Table 1). The acute diarrhea was grade 1 in 42 patients (35.3%), grade 2 in 12 patients (10.1%), grade 3 in 7 patients (5.9%), and grade 4 in 8 patients (6.7%). The volume of the small bowel in the radiation fields was significantly increased in patients receiving adjuvant treatment (Table 2). Interestingly, small bowel volume in the pelvis was higher in female patients than in male patients (Table 3). Univariate analysis showed that adjuvant RT, female gender, smaller bladder volume, and older age were significant determinants related to increased small bowel volume in the pelvis while there was a trend for increased small bowel volume in the pelvis for patients with lower BMI (Table 4). Multivariate analysis confirmed adjuvant RT, female gender, and smaller bladder volume were statistically significant factors affecting the pelvic small bowel volume (Table 5). There was no significant difference of Planning Target Volume (PTV) between patient groups (neo-adjuvant versus adjuvant or female versus male) (Table 6).

Characteristic	Neoadjuvant (n=61)	Adjuvant (n=58)
Age (years)		
Median	62	68
Range	35-84	35-88
Gender (male: female)	1.44:1	1.52:1
Stage		
I	2	2
II	23	19
III	35	37
IV	1	0
Radiation dose		
25 Gy/5 fractions	4	0
45 Gy/25 fractions	3	6
50.4 Gy/28 fractions	52	41
54 Gy/30 fractions	0	4
Unfinished	2	7
Concomitant Chemo	55	51

Table 1: Clinical and tumor characteristics for all patients (n=119).

Factors	Neoajuvant (n=61)	Adjuvant (n=58)	P Value
Small bowel volume (ml)	197	325	0.0033
Bladder volume (ml)	219 (n=54)	171 (n=49)	0.68
Diarrhea (%)			
Grade 1	19	23	0.34
Grade 2	6	6	
Grade 3	2	5	
Grade 4	6	2	
Small bowel volume (ml)			
At RT dose			
V5 Gy	185	325	0.0016
V10 Gy	161	301	0.0008
V15 Gy	112	192	0.0018
V20 Gy	73	160	0.0016
V25 Gy	63	140	0.0009
V30 Gy	48	118	0.0002
V35 Gy	37	107	0.0002
V40 Gy	33	98	<0.0001
V45 Gy	20	66	<0.0001

Table 2: Clinical and relevant dosimetric results for all patients (n=119, median value).
Abbreviation: RT= Radiotherapy

Factors	(Male (n=71	Female ((n=48	P Value
Small bowel (volume (ml	213	335	0.0015
Bladder (volume (ml	(n=60)191	(n=43) 171	0.63
(%) Diarrhea			
Grade 1	27	15	0.89
Grade 2	7	5	
Grade 3	4	3	
Grade 4	6	2	
Small bowel (volume (ml			
At RT dose			
V5 Gy	197	321	0.0045
V 10 Gy	165	310	0.0012
V 15 Gy	117	229	0.0011
V 20 Gy	87	185	0.0014
V 25 Gy	69	161	0.0011
V 30 Gy	51	141	0.0005
V35 Gy	45	131	0.0004
V 40 Gy	40	121	0.0006
V 45 Gy	23	64	0.0023

Table 3: Small bowel volume in patients of different gender.
Abbreviation: RT= Radiotherapy

Factors	Slope	P Value
(Age (years	(ml) 2.81	0.032
(BMI (Kg/m2	(ml) 0 -3.1	0.2400
(Bladder volume (ml	(ml) -0.31	0.0015
Female (1) vs. Male ((0	(ml) 94	0.0019
Neo-adjuvant (1) vs. (adjuvant (0	(ml) -93	0.0017

Table 4: Single predictors for small bowel volume in the pelvis of patients with rectal Cancer
Abbreviation: RT= Radiotherapy

Factors	Slope	P Value
(Age (years	1.9	0.15
Bladder volume ((ml	-0.27	0.0029
(BMI (Kg/m2	-0.87	0.71
Female	86	0.0039
Neo-adjuvant	-91	0.0024

Table 5: Multivariate predictors for small bowel volume in patients with rectal Cancer.

Patient group	(PTV 45 Gy (ml	P Value
Neoajuvant	1492	
Adjuvant	1466	0.4400
Male	1469	
Female	1494	0.5600

Table 6: PTV 45 Gy in different group of patients with rectal cancer (median ml).

Discussion

Our data clearly shows that small bowel volumes in the pelvis are affected by different factors including pelvic surgery, gender, bladder volume, and patient age [13]. The volumes in the pelvis are increased when RT is given after definitive surgery in patients with rectal cancer. Pelvic surgery with abdominoperineal resection in particular causes small bowel shifts down into the pelvis (personal observation). This might be one of the reasons for the increased bowel toxicities of patients receiving post-surgery RT, as reported previously [5]. Our current study did not observe a statistically significant increase of acute bowel toxicities in patients who received adjuvant chemoradiotherapy as compared to those patients who received neoadjuvant treatment. This might be due to the sample size of this cohort was not large enough to see the clinical difference

It is commonly acknowledged that there is a direct connection between the irradiated small bowel volumes and the severity of treatment related diarrhea [14]. Our finding of the increased small bowel volume in the radiation fields in the specified conditions may draw attention to avoid such conditions or to use technical such as Intensity Modulated Radiotherapy (IMRT) or Rapid Arc to avoid or reduce small bowel volumes being irradiated.

The small bowel has been estimated to have a 5% risk of late toxicity at 5 years with doses between 45-50 Gy [15,16]. Previous studies showed a relationship between small bowel dose-volume and the development of acute diarrhea in patients receiving pelvic irradiation [16,17]. The alternative explanation for our data not showing statistically significant differences in incidence of acute diarrhea to correlate with the increased small bowel volume in the irradiation fields might be due to the dominating effects of the concomitant chemotherapy 5-FU which affects the entire GI system and its effects shadowed the role played by the small bowel volume in the radiation fields. It would be interesting to see if there is a correlation between the irradiated small bowel volume and the incidence of long term small bowel toxicities such as bowel stenosis and obstruction in our patients since it has been suggested that the absolute volume of small bowel irradiated to 45 Gy or higher is associated with an increased risk of late GI toxicity [18,19].

We report that adjuvant RT, female gender, smaller bladder volume, and older age are predictors of the increased small bowel volumes being irradiated. This gives concrete anatomic evidence to prove the superiority of neoadjuvant RT over adjuvant RT especially for female or older patients.

The German trial showed that neo-adjuvant chemoradiotherapy not only increased local control but also decreased GI toxicities [5]. The mechanism for this was not fully explored. It is highly likely that less small bowel volumes being irradiated in the neoadjuvant setting, as demonstrated in our study, might be part of the explanations for the decreased GI toxicities.

The increased small bowel volume in the pelvis of female patients and post-surgery patients in our study is not related to a larger PTV volume.

Although there are large number of confounding variables for diarrhea in patients with rectal cancer, confirmation of the existence of a relationship between the irradiated small bowel volume and the incidence of acute diarrhea or late bowel toxicities is important. Through radiotherapy technical improvements, such as IMRT, small bowel dose volume may be reduced [20-23].

Conclusion

The results of our study demonstrate that factors such as pelvic surgery, being female, flat bladder, and older age are associated with increased small bowel volumes in pelvis. These would increase the irradiated small volumes in patients receiving radiotherapy for rectal cancer. Therefore, giving radiotherapy before the surgery or using technical such as IMRT or Rapid Arc to avoid or reduce the small bowel volumes being irradiated is warranted.

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