

# Preoperative Short-Course Radiation Therapy in Rectal Cancer

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**Abstract:** Purpose: To evaluate the benefits of preoperative short-course radiotherapy in locally advanced rectal cancer. Patients and methods: A prospective study of 30 rectal cancer patients at T3-4M0 stage and ECOG 0-2 performed preoperative short-course radiation therapy at Hue Central Hospital Vietnam between June 2016 and July 2018, using pelvic 3D-Conformal Radiation Therapy with the total radiation dose being 25 Gy in 5 fractions over five days. Results: Mean age  $57.1 \pm 13.6$  with 46.7% of patients in the range of 41-60 year-old. Male/female ratio: 2/1. Tumour stage T3 and T4 was 70% and 30%, respectively; stage III and stage IV was 86.7% and 13.3%, respectively. Positive lymph node rates on endoscopic ultrasound were 85.7% in T3 and 77.8% in T4. Downstaging rate for stage III, T4 and T3 was 65.4%, 65.4% and 4.8%, respectively. For upper third of the rectum: 100% of T3 stage patients got no downstaging. For middle rectum: downstaging rate for stage III, T4 and T3 was 55.6%, 57.1% and 7.1%, respectively. For lower rectum: downstaging rate for stage III, T4 was 50.0% and 100.0%, respectively. No acute toxicity was seen, 86.7% of the patients performed laparoscopic sphincter-preserving surgery. Conclusion: For the treatment of locally advanced rectal cancer, neoadjuvant therapy is standard. Preoperative short-course radiation therapy is a reasonable therapeutic option because it demonstrates benefits in tumour downstaging especially for middle and lower rectum.

**Key words:** Rectal cancer, short-course radiation therapy, preoperative, downstaging, pelvic 3D-conformal radiation therapy.

## 1. Background

Colorectal cancer is one of the common cancers in the world, including Vietnam, the incidence rate is keeping increase. In developed countries, colorectal cancer ranks the second among all cancers in both sexes, which listed only after lung cancer in men and breast cancer in women. In Vietnam, colorectal cancer ranks the 6th in the most common 10 cancers with the ASR of 9.2/100,000 and the mortality rate of 5.0/100,000 people [8, 10]. One-third of colorectal tumours arise in the rectum, more commonly in men. Most rectal cancer patients were at the advanced stage at time of diagnosed.

Radiation therapy plays an important role in rectal cancer management. Preoperative adjuvant radiotherapy is used in high-risk cases to improve

resectability, reduce local recurrence, increase sphincter preservation, and improve overall survival and quality of life.

In Vietnam, there have been some studies of preoperative radiotherapy in locally advanced rectal cancer, applying long-course concurrent chemoradiation therapy. In this study, we applied preoperative short-course radiation therapy to evaluate the effectiveness in T3-4 stage rectal cancer management.

## 2. Patients and Method

A prospective study of 30 rectal cancer patients at T3-4M0 stage and ECOG 0-2 performed preoperative short-course radiation therapy at Hue Central Hospital Vietnam between June 2016 and July 2018, using pelvic 3D-conformal radiation therapy with the total radiation dose being 25 Gy in 5 fractions over five days.

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Assessment of toxicity based on Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 of the National Cancer Institute (2009). Data were processed using SPSS 16.0 for Windows.

### 3. Results

#### 3.1 Patients Characteristics

**Table 1 Patients characteristics.**

Patients characteristics	No.	%
Age	56.73 ± 14.34 (29-77)	
Age group		
≤ 40	4	13.3
41-60	14	46.7
60-80	12	40.0
Gender		
Male	20	66.7
Female	10	33.3
Rectal tumour location		
Upper third	5	16.7
Middle third	21	70.0
Lower third	4	13.3
Histopathology		
Adenocarcinoma	29	96.7
Mucous adenocarcinoma	1	3.3
Stage		
Tumour		
T3	21	70.0
T4	9	30.0
Node		
N0	5	16.7
N1	13	43.3
N2	12	40.0
Stage		
II	4	13.3
III	26	86.7

#### 3.2 Treatment Outcomes

**Table 2 Symptom response after radiation.**

Symptoms	Before radiotherapy		After radiotherapy	
	No.	%	n	%
Rectal bleeding	26	86.7	6	20.0
Mucus in stool	10	33.3	0	0
Abdominal pain	15	50	8	26.7
Constipation	13	43.3	5	17.2

**Table 3 The change of CEA level after radiotherapy.**

CEA level (ng/mL)	Before radiotherapy		After radiotherapy	
	No.	%	n	%
≤ 5	17	56.7	23	76.7
> 5	13	43.3	2	23.3

$p = 0.006$

**Table 4 The change of disease stage.**

Stage		After radiotherapy					Total	
		0	I	II	III	IV	No.	%
Before radiotherapy	II	0	0	2	1	1	4	13.3
	III	1	4	13	8	0	26	86.7
Total	n	1	4	15	9	1	30	
	%	3.3	13.3	50.0	30.0	3.3		

Downstaging rate for stage III was  $(26-9)/26 = 65.4\%$ .

**Table 5 The change of stage T and CEA level related to tumour location.**

Rectal tumour location	T stage and CEA (ng/mL)	Before radiotherapy		After radiotherapy	
		No.	%	No.	%
Upper third	T3	5	100	5	100
	T4	0	0	0	0
	CEA $\leq 5$	5	100	5	100
	CEA $> 5$	0	0	0	0
Middle third	T2	0	0	5	23.8
	T3	14	66.7	13	61.9
	T4	7	33.3	3	14.3
	CEA $\leq 5$	10	47.6	15	71.4
	CEA $> 5$	11	52.4	16	28.6
Lower third	T0	0	0	1	25
	T2	0	0	1	25
	T3	2	50	2	50
	T4	2	50	0	0
	CEA $\leq 5$	2	50	3	75
	CEA $> 5$	2	50	1	25

With middle third: downstaging rate for stage T4 and T3 was  $(7-3)/7 = 57.1\%$  and  $(14-13)/14 = 7.1\%$ , respectively.

With lower third: downstaging rate for stage T4 was  $(2-0)/2 = 100.0\%$ .

**Table 6 The change of disease stage.**

Tumour location	Stage		After radiotherapy			Total	
			II	III	IV	No.	%
Higher rectum	Before radiotherapy	II	0	0	1	1	20
		III	3	1	0	4	80
	Total	n	3	1	1	5	
		%	60	20	20		
Middle rectum	Stage		I	II	III	n	%
	Before radiotherapy	II	0	2	1	3	14.3
		III	3	8	7	18	85.7
	Total	n	3	10	8	21	
		%	14.3	47.6	38.1		
Lower rectum	Stage		0	II	III	n	%
	Before radiotherapy	III	1	1	2	4	100.0
		n	1	1	2	4	
		%	25.0	25.0	50.0		

For upper third of the rectum, after radiation, stage III remained only one case (four before) while the stage II case transferred to stage IV.

Downstaging rate for stage III for middle and lower third was  $(18-8)/18 = 55.6\%$  and  $(4-2)/4 = 50.0\%$ , respectively.

**Table 7** Rate of laparoscopic surgery of sphincter preservation.

Tumour location	sphincter- preserving surgery <sup>*</sup> /number of patients	%
Upper rectum	4/5	
Middle rectum	19/21	
Lower rectum	3/4	
Total	26/30	86.7

(\*) Low anterior resection, Anterior resection, Pull-through.

## 4. Discussion

### 4.1 Patients Characteristics

In this study, the mean age was  $56.73 \pm 14.34$  (29-77), 86.7% of the patients were above 40 years old in which 46.7% of the patients were in the range of 41-60 year-old. Male/female ratio was 2/1. The location of upper, middle and lower third of rectal cancer was 16.7%, 70.0% and 13.3%, respectively. Histopathology was adenocarcinoma, accounting for 96.7%, was similar to some Vietnamese studies such as Vo Van Xuan 83.9% [10], Vo Quoc Hung 87.4% [6], Pham Cam Phuong (89.6%) [8], Nguyen Van Hieu (89.8%) [5].

And 83.3% of the patients had positive lymph nodes on endoscopic ultrasound; 70% at T3 and 30% at T4 stage; and then 13.3% at stage II and 86.7% at stage III.

### 4.2 Treatment Results

Surgery is the mainstay of rectal cancer treatment. However, for locally advanced stages, the combination of treatment modalities including neoadjuvant therapy is necessary in reducing the risk of cancer recurrence and shrinking the cancer prior to surgery.

#### 4.2.1 Symptom Response

Table 2 showed that the majority of patients had significantly improved symptoms after radiotherapy. The symptom improvement demonstrated the role of short-course radiotherapy and was a greatly spiritual support for patients before surgery.

#### 4.2.2 Biochemistry Response

Carcinoembryonic antigen (CEA), whose main application is mostly in gastrointestinal cancers, especially in colorectal malignancy, is one of the most widely used tumor markers worldwide. The clinical

value of CEA in colorectal cancer is contributing to evaluating treatment outcomes and prognosis. In this study, we tried assessing the treatment response through the change of CEA concentration for each patient before and after treatment. The result showed that the highest reduction rate was 36.7%, the difference is statistically significant.

#### 4.2.3 Stage Response

Response rate relating to disease stage III was 65.4%. For upper third of the rectum, at tumour stage T there was no change for 5 cases of T3. After radiation, there was only one case at stage III (four cases before radiation).

For middle third of the rectum, one remarkable thing was that 4 patients downstaged from T4 to T2, downstaging rate was 57.1%. The stage III before and after radiation accounted for 85.7% and 38.1%, respectively. After treatment, the proportion of patients with  $\text{CEA} \geq 5 \text{ ng/mL}$  decreased from 52.4% to 28.6%. These results demonstrated a significant improvement in downstaging and CEA concentration reduction in middle rectum.

For lower rectum, two T4 cases downstaged. After treatment, the proportion of patients with  $\text{CEA} \geq 5 \text{ ng/mL}$  decreased from 50% to 25%. Downstaging rate for stage III was 50%. According to Nguyen Van Hieu's study, the T3 stage decreased from 67.7 to 61.3%, T4 stage decreased from 32.3% to 9.6%, the rate of T4 tumors decreased by 70% [5]; higher than the rate in Vo Quoc Hung's study (51.8%) [6]. According to Pham Cam Phuong's study, the overall downstaging rate was 46%, including 61.5% at stage IV and 39.3% at stage III [8].

The results of this study showed that lower and middle rectal tumours got response rate better than

ones in upper third of the rectum.

#### 4.2.4 Toxicity and Sphincter-Preserving Surgery

In this study, 26 patients performed sphincter-preserving surgery including low anterior resection, anterior resection and Pull-through operation, accounting for 86.7%. According to Manisha Palta et al., a number of clinical trials showed that after short-course preoperative radiotherapy, the rate of sphincter-preserving surgery ranged from 61.2 to 63% [7]. Also according to Manisha Palta, the rate of grade 3-4 toxicity ranged from 1.9 to 3.2%, much lower than the rate in long-course concurrent chemoradiation therapy (18.2-28%). In this study, no acute toxicity was recorded. Because of the short follow-up duration, this study has not been able to assess local recurrence as well as progressive-free survival and overall survival.

## 5. Conclusion

Short-course preoperative adjuvant radiotherapy in stage T3-4 rectal cancers demonstrated benefits in improving symptoms, tumour downstaging and increasing sphincter preservation. Tumours in the middle and lower thirds of rectum got treatment response better than ones in upper rectum.

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