

## Radiotherapy Role in Rectal Cancer at Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia

Jeffri,<sup>1</sup> Ferdinand Tjandra,<sup>2</sup> Michael Tendean,<sup>2</sup> Toar Mambu,<sup>2</sup> Enrico Napitupulu<sup>3</sup>

<sup>1</sup>Surgery Department, Faculty of Medicine, Universitas Sam Ratulangi - Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia

<sup>2</sup>Digestive Surgery Division, Surgery Department, Faculty of Medicine, Universitas Sam Ratulangi - Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia

<sup>3</sup>Radiotherapy Department, Faculty of Medicine, Universitas Sam Ratulangi - Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia

Email: [nigatsu\\_month@gmail.com](mailto:nigatsu_month@gmail.com)

Received: January 6, 2023; Accepted: April 12, 2023; Published online: April 15, 2023

**Abstract:** Rectal cancer (RC) remains as a major health burden, being the 3<sup>rd</sup> most common form of cancer and leading cause of death. RC affects as much as 12.8 per 100 adult population with a mortality rate as high as 9.5%.<sup>1</sup> Efforts were made to reduce morbidity and mortality due to rectal cancer. One of them is radiotherapy acting as both neoadjuvant and adjuvant. Thus study aimed to emphasize the role of radiotherapy in treating rectal cancer patients at Prof. Dr. R. D. Kandou General Hospital, Manado. This was a retrospective study using data of all rectal cancer outpatients seeking at Prof. Dr. R. D. Kandou General Hospital, Manado. from 2017-2020 especially of those receiving radiotherapy treatment in radiology department. The results obtained a total 119 patients, 28 of them received radiotherapy based on staging and clinical judgement. From the radiotherapy group, 46.4% patient received neoadjuvant radiotherapy primary to surgical procedure, and among the neoadjuvant group 71.4% received long course radiotherapy. From the neoadjuvant radiotherapy group, 46.4% became resectable and 46.4% among them underwent Miles Procedure. In conclusion, rectal cancer is still a health problem, and radiotherapy as one of the modality play major role as neoadjuvant and adjuvant treatment.

**Keywords:** rectal cancer; mortality; radiotherapy

## INTRODUCTION

Rectal cancer (RC) remains as a major health burden, being the 3<sup>rd</sup> most common form of cancer and leading cause of death. Rectal cancer affects as much as 12.8 per 100 adult population with a mortality rate as high as 9.5%.<sup>1</sup> An estimated 27.150 men and 23.110 woman will die from RC in 2017.<sup>2</sup>

Radiotherapy (RT) treatment using high energy rays or particles to destroy cancer cells, either before and/or after surgery along with chemotherapy (CT) aims to prevent cancer recurrency. When administered before surgery, it relieves cancer removal by reducing its size and chances of sphincter muscle trauma in surgery, called neoadjuvant treatment. It could also administered to the tumor area intra surgery to kill any rectal cancer cells left behind, called intraoperative radiation therapy (IORT).<sup>3</sup> There are also different types of radiation therapy used to treat colon and rectal cancers: external-beam radiation therapy (EBRT) using machine outside the body; internal radiation therapy (brachytherapy) still in research to understand its role in rectal cancer treatment; endocavitary radiation therapy using small balloon-like device placed into the rectum to deliver high intensity radiation for a few minutes; and interstitial brachytherapy using a tube placed into the rectum and right into the tumor in a form of small pellets of radioactive material for several minutes.<sup>3</sup>

Adjuvant therapy for rectal cancer consist of regiments including both concurrent chemotherapy or radiotherapy and adjuvant chemotherapy, with approximately six months therapy was preferred, targeting to prevent distant metastases and local recurrences.<sup>4,5</sup> Several studies comparing administration of RT preoperative vs postoperative showed that RT preoperative therapy was associated with a significant reduction in local recurrence (6% vs 13%;  $p=0.006$ ) and treatment-associated toxicity (27% vs 40%;  $p=0.001$ ). Surveillance, Epidemiology, and End Results (SEER) database analysis of 4724 patients with T3, N0, found that radiation given after resection was associated with a significant decrease in risk of cancer death compared to cancer death without radiation (HR, 0.69; 95 CI. 0.58-0.82;  $p<.001$ ) while radiation given before resection was not ( $p=0.13$ ).<sup>4</sup>

Due to the high mortality and morbidity burden of rectal cancer, the authors try to demonstrate and emphasize the role of radiotherapy management in rectal cancer patients at Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia.

## METHODS

This study used medical records of all rectal cancer outpatients at Prof. Dr. R. D. Kandou General Hospital from 2017 to 2020, especially of those receiving radiotherapy treatment in the radiology department. This was a descriptive and analytical study using the chi-square and SPSS statistical software for Windows. A p-value less than 0.05 was considered to be significant. Data were presented in total (%) and mean  $\pm$  standard deviation.

## RESULTS

There were a total of 119 patients diagnosed with rectal cancers based on medical history, physical examination, laboratory value (CEA value), colonoscopy, and pathological results. The highest incidence was in the age group of 50-60 years old (38.7%) and more than 60 years old (33.6%). The incidence was higher in male (58.8%) than in female (41.2%). The main chief complaint was hematochezia (65.5%). Most patients were admitted at stage 4A (31.9%), while overall mortality was as high as 12.6%. Among all rectal cancer patients, 30.3% received chemotherapy, 16% radiotherapy, and 7.6% both chemotherapy and radiotherapy as adjuvant and neoadjuvant.

Table 2 showed that out of all rectal cancer patients, 28 received radiotherapy based on staging and clinical judgement in order to help tumor downsizing in order to relieve its removal. From the radiotherapy group, 46.4% patient received neoadjuvant radiotherapy primary to surgical procedure, and among the neoadjuvant group 71.4% received long course radiotherapy.

From the neoadjuvant radiotherapy group, 46.4% became resectable and 46.4% among them underwent Miles Procedure.

**Table 1.** Characteristics of rectal cancer patients

Characteristic (n=119)	Total	(%)	Characteristic (n=119)	Total	(%)
<b>Age</b>			<b>Stadium</b>		
>30	4	3.4	2a	6	5.0
30-40	11	9.2	2b	13	10.9
40-50	18	15.1	3a	7	5.9
50-60	46	38.7	3b	31	26.1
>60	40	33.6	3c	15	12.6
<b>Sex</b>			4a	38	31.9
Male	70	58.8	4b	9	7.6
Female	49	41.2	<b>Surgical procedures</b>		
<b>Chief Complaint</b>			None	47	39.5
Hematochezia	78	65.5	Colostomy	10	8.4
Lower abdominal pain	9	7.6	Ileostomy	7	5.9
Chronic diarrhoea	4	3.4	Abdomino- perineal resection (Miles)	21	17.6
Lower abdomen tenderness	2	1.7	Sigmoidectomy	14	11.8
Anal pain	7	5.9	Hartman Procedure	8	6.7
Anal lump	10	8.4	Low Anterior Resection (LAR)	9	7.6
Constipation	9	7.6	Others	3	2.5
<b>Neoadjuvant/Adjuvant Therapy</b>			<b>Status</b>		
None	55	46.2	Deceased	15	12.6
Chemotherapy	36	30.3	Live	104	87.4
Radiotherapy	19	16.0			
Both	9	7.6			

**Table 2.** Rectal patients' characteristics with Radiotherapy

Characteristics (n=28)	Total	(%)	Characteristics (n=28)	Total	(%)
<b>Stadium</b>			<b>Surgical Procedures</b>		
2b	3	10.7	Colostomy	6	21.4
3a	2	7.1	Sigmoidectomy	2	7.1
3b	6	21.4	LAR	3	10.7
3c	4	14.3	Abdomino- perineal resection (Miles)	8	28.6
4a	13	46.7	No Surgery performed	6	32.1
<b>Adjuvant vs Neoadjuvant</b>			<b>Recurrency</b>		
Adjuvant	15	53.6	No	19	67.9
Neoadjuvant	13	46.4	Yes	9	32.1
<b>Short course vs Long course</b>			<b>Status</b>		
Short course	8	28.6	Deceased	6	10.7
Long course	20	71.4	Live	22	78.6
<b>Resectability</b>					
Non-resectable	15	53.6			
Resectable	13	46.4			

## DISCUSSION

Based on American Cancer Society, in 2017 there were 39,910 new rectal cancer cases diagnosed in the US and a larger number of men (23,720 cases) than women (16,190 cases).<sup>2</sup> Several risks of rectal cancer incidence include ages more than 50, male sex, and ethnicity.<sup>2</sup> Those findings were similar to this study findings, as follows: incidence was higher in male group (58.8%), the highest incidence was in age group 50-60 years old (38.7%) and more than 60 years old (33.6%), with overall mortality as high as 12.6%. Serious concern should be put on the causes of diagnosis delay in rectal cancer patients, seeing that most patients that sought treatment were already in stage 4a (31.9%).

In order to treat rectal cancer patients, local and systemic approaches should be considered. Local treatment performing without affecting the rest of the body is more useful in earlier stage cancers including surgery of rectal cancer and RT. While systemic treatment given per oral or directly into the bloodstream, affects cancer cells throughout the body, including CT, targeted therapy, and immunotherapy.<sup>3,5</sup> Consideration in choosing treatment modality depends on the stage of the cancer, suitability for surgery, and other considerations in team approach including gastroenterologist, surgical oncologist, colorectal surgeon, and radiation oncologist assisted by general physician, nurse, psychologist, nutritionist, social worker, and other health professionals.<sup>3,5,6</sup>

Radiotherapy is a treatment using high-energy rays (such as x-rays) or particles to destroy cancer cells. It is often used to treat rectal cancer than colon cancer. For some colon and rectal cancers, certain simultaneous chemotherapy induced radiotherapy has a better result.<sup>3</sup> In general, radiotherapy could be used in different steps of treatment: (1) Either before and/or after surgery, often along with CT, to prevent recurrences. Many doctors now favor giving radiation therapy before surgery, as it may relieve cancer removal especially if the cancer's size and/or location might make the surgery difficult; this is called *neoadjuvant* treatment. Giving chemoradiation before surgery can also help lowering the chances of damaging the sphincter muscles in the rectum when surgery is performed. In either case, adjacent lymph nodes are also commonly treated; (2) During surgery, to the exact tumor area was, to obliterate any rectal cancer cells that may be left behind. This is called intraoperative radiation therapy (IORT); (3) With or without chemotherapy to help control rectal cancer progression if a person is not healthy enough for surgery or to ease symptoms if advanced rectal cancer is causing intestinal blockage, bleeding, or pain; (4) To retreat rectal tumors recurrences after previous radiation; (5) To treat rectal cancer that has spread to other areas, such as the bones, lungs, or brain.<sup>3</sup> In this study, the radiotherapy in rectal cancer patients has reduced overall mortality from 12.7% in all rectal cancer patients to 10.7% in RT recipients.

Advantages that have often been associated with preoperative radiotherapy as neoadjuvant, are simply as efforts to both reducing tumor and preservation of normal tissue. As radiotherapy administration preoperative allowing tumor to: first, reducing its volume to facilitate resection and increase the likelihood of a sphincter-sparing procedure; second, irradiating tissue that has not undergone any surgery and thus better oxygenated may result in increased sensitivity to RT; third, preoperative radiotherapy can avoid the occurrence of radiotherapy-induced injury to the small bowel trapped in the pelvis by postsurgical adhesions. Finally, the anastomosis remains unaffected by the effects of radiotherapy because irradiated tissue is resected. As for optimal timing of surgery after preoperative radiation, it must allow tumor to downstage, as long as 6-8 weeks from the end of preoperative radiotherapy.<sup>5,7</sup> Due to its favorable effect, in some countries, RT in combination with CT has been considered the standard care for RC patients in stage II and III.<sup>5</sup> National Comprehensive Cancer Network (NCCN) guidelines put forward the facts that

50-60% of patients are downstaging following neoadjuvant therapy<sup>4</sup> which is in line with the result of this study that showed 46.4% patient receiving RT became resectable.

Adjuvant therapy is recommended for all patients with stage II/III rectal cancer following neoadjuvant (both CT and RT) and surgery regardless the surgical pathological results. It has provided benefit to limit local recurrence.<sup>4</sup> The result of this study showed recurrency in 32.1% patients.

In Europe, a short course of RT (25 Gy), followed by extirpative surgery (low anterior resection or abdominal perineal resection), is the most common approach. Several European studies have looked at the efficacy of a shorter course of preoperative RT (25 Gy over five days), not combined with chemotherapy, for the treatment of rectal cancer. In a Swedish rectal cancer trial, the results showed a survival advantage and a decreased rate of local recurrence with this approach compared with surgery alone.<sup>4,5,8</sup> Despite improvements in local control of disease, some studies have demonstrated that preoperative short-course RT for rectal cancer patients does not affect their overall survival (OS) significantly.<sup>5</sup> Other studies found that short-course RT appeared to provide effective local control and the same OS as more long-course chemo RT schedules and, therefore, may be an appropriate choice in some situations.<sup>4,5</sup>

Possible side effects determining patient's quality of life should also come to our consideration, including skin irritation at the site where radiation beams were aimed which can range from redness to blistering and peeling, problems with wound healing if radiation was given before surgery, nausea, rectal irritation which can cause diarrhea, painful bowel movements, or blood in the stool, bowel incontinence (stool leakage), bladder irritation which can cause problems like feeling like have to go often (called frequency), burning or pain while urinating, blood in the urine, fatigue/tiredness, sexual problems (erection issues in men and vaginal irritation in women), scarring, fibrosis (stiffening), and adhesions that cause the tissues in the treated area to stick to each other.<sup>3,9,10</sup> These possible side effects should get better overtime after treatment ends, but some problem may not go away completely.

## CONCLUSION

Rectal cancer is still a health problem, and radiotherapy has shown its important role as adjunction in rectal cancer treatment as neoadjuvant and adjuvant treatment. It is expected that in the near future, patients with rectal cancer could be optimally treated using the best combination of surgery, chemotherapy and radiotherapy.

## Conflict of Interest

The authors affirm no conflict of interest in this study.

## REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, Eser S, Mathers C, Rebelo , Parkin DM, et al. Cancer incidence and mortality worldwide: Source, methods and major patterns in GLOBOCAN 2012. *Int. J. Cancer* 2015;136(5): E359–E386.
2. American Cancer Society. *Colorectal Cancer Facts & Figures 2017-2019*. Atlanta: American Cancer Society; 2017
3. American Cancer Society. The American Cancer Society medical and editorial content team. 2020. Available on: <https://www.cancer.org/cancer/colon-rectal-cancer/treating/radiation-herapy.html#references>
4. National Comprehensive Cancer Network (NCCN). NCCN Guidelines Version 6.2020 Rectal cancer. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/rectal.pdf](https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf) (accessed on Sept 20, 2020)
5. Kye BH, Cho HM. Overview of radiation therapy for treating rectal cancer. *Ann Coloproctol.* 2014; 30(4):165-174.

6. Myint AS, Gerard JP. Role of radiotherapy in the treatment of rectal cancer in older patients. *Eur J Surg Oncol.* 2020;46(3):349-57.
7. Feeney G, Sehgal R, Sheehan M, Hogan A, Regan M, Joyce M, et al. Neoadjuvant radiotherapy for rectal cancer management. *World J Gastroenterol.* 2019;25(33):4850-69.
8. Sebag-Montefiore D, Stephens RJ, Steele R, Monson J, Grieve R, Khanna S, et al. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. *Lancet.* 2009;373(9666):811-20
9. Couwenberg AM, Burbach JPM, van Grevenstein WMU, Smits AB, Consten ECJ, Schiphorst AHW, et al. Effect of neoadjuvant therapy and rectal surgery on health-related quality of life in patients with rectal cancer during the first 2 years after diagnosis. *Clin Colorectal Cancer.* 2018;17(3):e499-e512.
10. Li Y, Wang J, Ma X, Tan L, Yan Y, Xue C, et al. A review of neoadjuvant chemoradiotherapy for locally advanced rectal cancer. *Int J Biol Sci.* 2016;12(8):1022-31.