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# The Comparison of Surgery and Chemo-Radio Therapy in Locally Recurrent Colorectal Cancer

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**Abstract:- Introduction: Globally, over 2 million colorectal cancer cases were diagnosed. It is the second most common cause of cancer fatalities, causing 1 million deaths annually. The current study aimed to compare surgery and chemoradiotherapy treatment outcomes in colorectal cancer recurrence. Method: The current study was conducted using a randomized clinical trial design. The study was carried out at Hayatabad Medical Complex, Peshawar. A total of 74 patients previously treated for colorectal cancer, were selected. The patients who showed recurrence, based on radiology results, were selected for the current study. Survival from the commencement of chemoradiotherapy/surgery to death from any cause or censoring at the final follow-up was defined as overall survival (OS). OS were calculated using the Kaplan–Meier technique and compared with the log-rank test. All analyses were conducted using SPSS v25 and Jamovi. Result: A total of 21 patient included in the final analysis. The mean age in the surgery group was quite higher than the chemoradiotherapy group (p = 0.31). The male to female ratio in each group was 12/4, 8/3 respectively. The timer size was quite higher than the chemoradiotherapy group (p = 0.20). Two patients were died in the chemoradiotherapy group while one patient was died in surgery group. The survival rate of the surgery was quite good as compared to the chemoradiotherapy group. In the chemoradiotherapy group the patients survived up to 30 months, however, the patient treats with surgery showed the longest survival. Conclusion: The current study compared the surgery and Chemo-radio therapy in locally recurrent colorectal cancer. Two patients in the chemoradiotherapy group and one in the surgery group was died. Compared to those who had chemoradiation, surgical patients had a much higher chance of survival. In the chemoradiotherapy group, patients lived up to 30 months; nevertheless, the surgical group had the longest survival rate.**

***Keywords:-*** *Colorectal Cancer, Recurrence, Chemoradiotherapy, Surgery.*

## I. INTRODUCTION

Globally, over 2 million colorectal cancer cases were diagnosed. It is the second most common cause of cancer fatalities, causing 1 million deaths annually. However, there are good screening approaches that potentially minimize illness fatalities globally [1].

Asia has more than half of all colorectal cancer cases and fatalities. China has more than 500,000 new cases and 280,000 fatalities every year. Japan has the second-most colorectal cancer fatalities per year, 60 000. International Agency for Research on Cancer (IARC) projects that colorectal cancer will grow by 56% between 2020 and 2040, reaching more than 3 million new cases annually [2]. The illness is expected to cause 1.6 million deaths globally by 2040, a 69% rise. Most growth is projected in high-Human Development Index (HDI) nations. IARC researchers found that many variables enhance or reduce colorectal cancer risk. Most of these variables increase or decrease the risk of other cancers [3].

In 2020, alcohol caused 165,000 new instances of colorectal cancer or 8% of all cases. Alcohol intake raises the risk of six additional cancers, including liver and breast cancer [4]. Smoking causes lung cancer [5], while HPV causes cervical cancer [6]. Both variables lead to colorectal cancer. Obesity raises colorectal cancer risk. Obesity caused 85 000 instances of colon cancer and 25 000 cases of rectal cancer in 2012, or 23% of all colorectal cancer cases. Obesity raises the risk of seven additional cancers. Weight reduction, exercise, and diets rich in fish, fruits, and vegetables reduce colorectal cancer risk [7]. Screening raises the likelihood of discovering colorectal cancer at an earlier, more controllable stage [8].

Colorectal cancer treatment is broadly divided into two categories: local and systematic. Local therapies address the tumor without impacting other organs [9]. Colorectal surgeries are the most common way to remove the tumor and surround healthy tissues to resect the affected area. In addition to surgical resection, the other options include laparoscopic surgeries, colostomy, and radiofrequency ablation. Drugs may also be used to treat colorectal cancer; they can be administered orally or straight into circulation. These are systemic therapies because they may reach almost all cancer cells in the body. Chemotherapy for Colorectal Cancer, Targeted Therapy for Colorectal Cancer, and Immunotherapy for Colorectal Cancer

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may be administered depending on the kind of colorectal cancer [10, 11]. Multiple therapy methods may be utilized concurrently or sequentially depending on the cancer stage and other parameters. Typically, stages 0, I, II, and III are surgically treatable. However, many patients with stage III colorectal cancer, and some with stage II, have chemotherapy after surgery to boost the likelihood of curing the illness. Before or after surgery, individuals with stages II and III rectal cancer will also get radiation treatment and chemotherapy. In most cases, stage IV cancer cannot be cured, but it is treated to control its progression and symptoms [12, 13]. The current study aimed to compare surgery and chemoradiotherapy treatment outcomes in colorectal cancer recurrence.

## II. METHOD

### *A. Study design and patients*

The current study was conducted using a randomized clinical trial design. The study was carried out at Hayatabad Medical Complex, Peshawar. A total of 74 patients previously treated for colorectal cancer, were selected. The patients who showed recurrence, based on radiology results, were selected for the current study. Moreover, the patients that were not eligible (stage IV) and were not willing to participate were excluded from the current study. The selected patients were randomly assigned to surgery (n =16) and chemoradiotherapy (n = 11) groups and prospectively followed for three years. The detail can be seen in Figure 1.

### *B. Chemoradiotherapy regimens*

All patients received external beam radiation (50 to 60 Gy) with concurrent chemotherapy such as 5-FU continuous infusion (ci), or S-1, weekly 5-FU ci plus oxaliplatin, modified FOLFOX6 (mFOLFOX). 5-FU ci regimen was a continuous infusion of 2500 mg/week mg/m2 of 5-FU (7 days), repeated every week. S-1 was administered orally at the dose of 80 mg/m2/day. Weekly 5-FU ci plus oxaliplatin regimen consisted of intravenous infusion of 50 mg/m2 of oxaliplatin (2 h) on day 1 and continuous infusion of 2,500 mg/week 5-FU (7 days), repeated every week. The mFOLFOX regimen consisted of intravenous infusion of 85 mg/m2 of oxaliplatin (2 h), 200 mg/m2 l-leucovorin (2 hours), and 400 mg/m2 bolus 5-FU on day 1, followed by a continuous infusion of 2,400 mg/m2 of 5-FU (46 h), repeated every 2 weeks. Chemotherapy started from the first day and was repeated to the last day of radiotherapy in all patients, and subsequent chemotherapy regimens were determined by each physician's discretion according to the efficacy and toxicities of CRT. Six patients continued to receive chemotherapy until disease progression after the completion of radiation therapy.

### *C. Statistical analysis*

Survival from the commencement of chemoradiotherapy/surgery to death from any cause or censoring at the final follow-up was defined as overall survival (OS). OS were calculated using the Kaplan–Meier technique and compared with the log-rank test. All analyses were conducted using SPSS v25 and Jamovi.

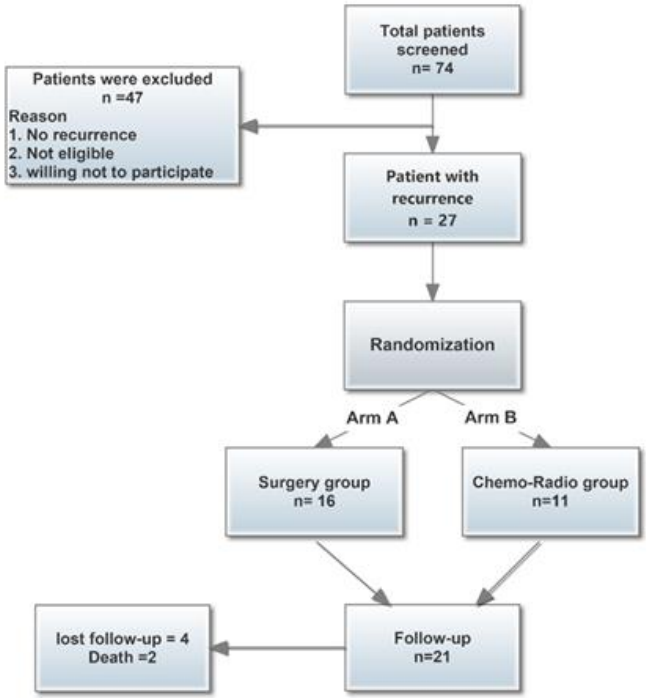


Fig 1. The detail of the patient selection and follow-up

## III. RESULTS

A total of 21 patient included in the final analysis. The mean age in the surgery group was quite higher than the chemoradiotherapy group (p = 0.31). The male to female ratio in each group was 12/4, 8/3 respectively. The timer size was quite higher than the chemoradiotherapy group ( p = 0.20). Two patients were died in the chemoradiotherapy group while one patient was died in surgery group. The detail can be seen in Table 1. The survival rate of the surgery was quite good as compared to the chemoradiotherapy group. In the chemoradiotherapy group the patients survived up to 30 months, however, the patient treats with surgery showed the longest survival as shown in Figure 2.

**Table 1. Patient characteristics and treatment outcome**

| | | Group | | | | P-value |
|---|---|---|---|---|---|---|
| | | Surgery | | CRT | | |
| | | Mean ± SD | N (%) | Mean ± SD | N (%) | |
| Age (years) | | 54 ± 14 | | 49 ± 11 | | 0.31 |
| Gender | Male | | 12 (60%) | | 8 (40) | 0.89 |
| | Female | | 4 (57.1%) | | 3 (42.9) | |
| Period of recurrence | | 32 ±8 | | 29 ± 9 | | 0.46 |
| Tumor size | | 46.09 ± 5.28 | | 42.81 ± 7.82 | | 0.20 |
| Patient status | Survived | | 15 (62.5) | | 9 (37.5) | 0.33 |
| | Death | | 1 (33.3) | | 2 (66.7) | |

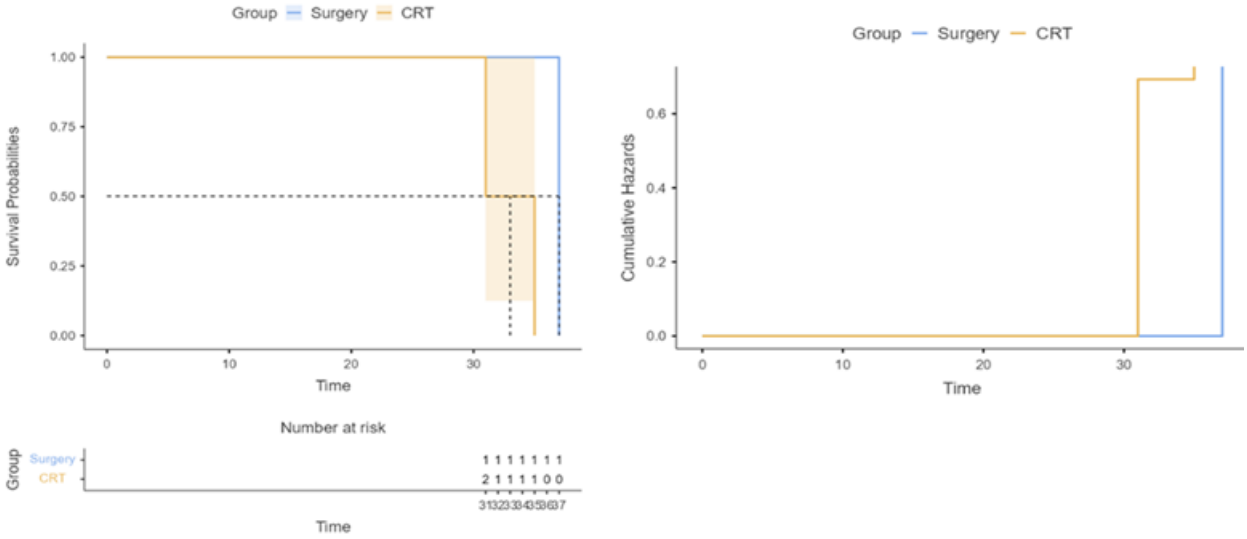


Fig 1. Treatment of the surgery and CRT.

## IV. DISCUSSION

The current study compared the surgery and Chemo-radio therapy in locally recurrent colorectal cancer. Two patients in the chemoradiotherapy group and one in the surgery group was died. Compared to those who had chemoradiation, surgical patients had a much higher chance of survival. In the chemoradiotherapy group, patients lived up to 30 months; nevertheless, the surgical group had the longest survival rate.

Regarding the treatment approach for local rectal cancer recurrence, there is no unanimity. Only 20-40% of patients with recurrent rectal cancer are suitable for curative resection (R0) resection, despite the fact that radical resection is the treatment of choice with a high cure rate [14]. It has been observed that there was no significant difference in long-term survival between R2 resection and non-surgical treatments for patients who are ineligible [15]. Consequently, if R0 cannot be done, surgical resection is not anticipated to provide a greater advantage. Radiation therapy and systemic chemotherapy alone or in combination should be considered at this point in the treatment of patients [16]. In contrast, in the current study, the survival was quite good in surgery group compared to the chemoradiotherapy.

Reportedly, the combination of 5-FU radiotherapy (RT) improves survival for locally unresectable rectal cancer over radiotherapy alone [17]. It has been observed that observed that Chemoradiotherapy (CRT) (continuous infusion of 5-FU+RT) was more effective than radiotherapy alone in 30 patients with locally recurrent rectal cancer. In addition, it has been showed increase in the median OS of patients treated with CRT over RT alone (median survival time 9.3 months). In addition, CRT was successful in relieving pain, and 5-FU-based regimens were found to be effective and safe. Compared to their findings on CRT, our results demonstrated similar survival effects of CRT. The median OS was not attained in our investigation, and survival in our group was superior to that of the CRT group in Ito's trial. This disparity in effectiveness between the Ito research and our present data may be attributable to variations in chemotherapy regimens and radiation treatment.

Since the introduction of oxaliplatin into clinical practice, colorectal cancer chemotherapy has achieved significant advances. Chemotherapy using oxaliplatin and 5-FU, such as the FOLFOX regimen, is more successful and has become the standard treatment for colorectal cancer in its later stages [18, 19]. In addition, preoperative CRT with an oxaliplatin-containing regimen demonstrated a high success rate with acceptable toxicity in patients with locally advanced rectal cancer. Hu et al. evaluated CRT [FOLFOX4+three-dimensional conformal radiation (3-DCRT)] and RT based on

prior research on CRT that included oxaliplatin-containing regimens for rectal cancer recurrence. The CRT group had a much better 2-year survival rate and a significantly greater response rate (56% vs 40%) [20]. You et al. also evaluated the efficacy of concurrent CRT with oxaliplatin (oxaliplatin+pelvic irradiation) in 96 patients with locally recurrent rectal cancer and reported a CR rate of 14% and a PR rate of 61%. (24). Cai et al. reported a CR rate of 5.6% after CRT with capecitabine and irinotecan and intensity modulated radiation treatment (IMRT) (45 Gy), which was related with a 3-year survival rate of 36.5%; the 3-year local progression-free survival rate was 33.9% after a median follow-up of 31 months. As for side effects, the incidence of grade 4 leukopenia was 4.8%, grade 3 diarrhoea was 22.5%, and the toxicity was within the allowable limit [21].

This study has several limitations. First, we only evaluated a small number of patients. Second, many of the patients were censored cases, which may have led to overestimation of the OS results.

## V. CONCLUSION

The current study compared the surgery and Chemo-radio therapy in locally recurrent colorectal cancer. Two patients in the chemoradiotherapy group and one in the surgery group was died. Compared to those who had chemoradiation, surgical patients had a much higher chance of survival. In the chemoradiotherapy group, patients lived up to 30 months; nevertheless, the surgical group had the longest survival rate.

## REFERENCES

[1]. Siegel, R.L., et al., Cancer statistics, 2022. CA: A Cancer Journal for Clinicians, 2022. 72(1): p. 7-33.
[2]. Yee, Y.K., et al., Epidemiology of colorectal cancer in Asia. Journal of gastroenterology and hepatology, 2009. 24(12): p. 1810-1816.
[3]. Onyoh, E.F., et al., The rise of colorectal cancer in Asia: epidemiology, screening, and management. Current gastroenterology reports, 2019. 21(8): p. 1-10.
[4]. Cho, E., et al., Alcohol intake and colorectal cancer: a pooled analysis of 8 cohort studies. Annals of internal medicine, 2004. 140(8): p. 603-613.
[5]. Liang, P.S., T.Y. Chen, and E. Giovannucci, Cigarette smoking and colorectal cancer incidence and mortality: Systematic review and meta-analysis. International journal of cancer, 2009. 124(10): p. 2406-2415.
[6]. Ibragimova, M.K., M.M. Tsyganov, and N.V. Litviakov, Human papillomavirus and colorectal cancer. Medical Oncology, 2018. 35(11): p. 1-6.
[7]. Jochem, C. and M. Leitzmann, Obesity and colorectal cancer. Obesity and Cancer, 2016: p. 17-41.
[8]. Montminy, E.M., et al., Screening for colorectal cancer. Medical Clinics, 2020. 104(6): p. 1023-1036.
[9]. Biller, L.H. and D. Schrag, Diagnosis and treatment of metastatic colorectal cancer: a review. Jama, 2021. 325(7): p. 669-685.
[10]. Modest, D., S. Pant, and A. Sartore-Bianchi, Treatment sequencing in metastatic colorectal cancer. European Journal of Cancer, 2019. 109: p. 70-83.
[11]. Hashiguchi, Y., et al., Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. International journal of clinical oncology, 2020. 25(1): p. 1-42.
[12]. Piawah, S. and A.P. Venook, Targeted therapy for colorectal cancer metastases: A review of current methods of molecularly targeted therapy and the use of tumor biomarkers in the treatment of metastatic colorectal cancer. Cancer, 2019. 125(23): p. 4139-4147.
[13]. Brouwer, N.P., et al., An overview of 25 years of incidence, treatment and outcome of colorectal cancer patients. International journal of cancer, 2018. 143(11): p. 2758-2766.
[14]. Bhangu, A., et al., Comparison of long-term survival outcome of operative vs nonoperative management of recurrent rectal cancer. Colorectal Disease, 2013. 15(2): p. 156-163.
[15]. Pacelli, F., et al., Locally recurrent rectal cancer: prognostic factors and long-term outcomes of multimodal therapy. Annals of Surgical Oncology, 2010. 17(1): p. 152-162.
[16]. Tanis, P.J., A. Doeksen, and J.J.B. van Lanschot, Intentionally curative treatment of locally recurrent rectal cancer: a systematic review. Canadian journal of Surgery, 2013. 56(2): p. 135.
[17]. Moertel, C., et al., Combined 5-fluorouracil and supervoltage radiation therapy of locally unresectable gastrointestinal cancer. The Lancet, 1969. 294(7626): p. 865-867.
[18]. de Gramont, A.d., et al., Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. Journal of Clinical Oncology, 2000. 18(16): p. 2938-2947.
[19]. Goldberg, R.M., et al., A randomized controlled trial of fluorouracil plus leucovorin, irinotecan, and oxaliplatin combinations in patients with previously untreated metastatic colorectal cancer. Journal of Clinical Oncology, 2004. 22(1): p. 23-30.
[20]. Hu, J.-B., et al., Three-dimensional conformal radiotherapy combined with FOLFOX4 chemotherapy for unresectable recurrent rectal cancer. World journal of gastroenterology: WJG, 2006. 12(16): p. 2610.
[21]. Cai, G., et al., CAPIRI-IMRT: a phase II study of concurrent capecitabine and irinotecan with intensity-modulated radiation therapy for the treatment of recurrent rectal cancer. Radiation Oncology, 2015. 10(1): p. 1-6.