

Original article

To compare survival outcomes in preoperative versus postoperative chemoradiation in stage III rectal cancer

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Abstract

Background: Management of locally advanced rectal cancer requires a multidisciplinary strategy involving surgical resection with total mesorectal excision and combined use of radiotherapy and chemotherapy.

Aim and Objective: To compare survival outcomes in Preoperative versus postoperative chemoradiation in Stage III Rectal cancer.

Material and Methods: Fifty two patients of rectal cancer who received preoperative CRT (25 patients) or postoperative CRT (27 patients) of previously untreated stage III rectal cancer were analyzed retrospectively. All patients were treated at the department of Radiation Oncology, Pt B D Sharma PGIMS Rohtak between 2012 and 2018.

Results: The median locoregional recurrence free survival in the preoperative group was 33 months whereas it was 32 months in the postoperative group ($p=0.585$). The median distant metastases free survival was 17 months in the preoperative group versus 35 months in the postoperative group ($p=0.039$). The mean survival in the preoperative group was 33.927 months versus 49.519 months in the postoperative radiotherapy group ($p=0.129$). Sphincter preservation rate of 51% in the preoperative CRT group.

Conclusion: The present study concludes that there are no statistically significant differences in mean survival and median locoregional recurrence-free survival between the two groups. However, contrary to current literature, our findings show that the postoperative chemoradiation group had significantly better median distant metastasis-free survival. These results warrant further investigation through larger randomized studies.

Keywords: Survival, Outcomes, Chemoradiation, Rectal Cancer

INTRODUCTION

Management of locally advanced rectal cancer requires a multidisciplinary strategy involving surgical resection with total mesorectal excision and combined use of radiotherapy and chemotherapy. The sequence of treatment can either be preoperative chemoradiation

followed by surgery or upfront surgery followed by postoperative chemoradiation. As per Globocan 2022 Colorectal cancer accounts for 70038 (5.0%) new cases and sixth most common cancer in India [1]. Adjuvant chemoradiotherapy (CRT) is performed as the standard

treatment following radical surgery in locally advanced rectal cancer to improve local control and overall survival (OS) [2,3]. In particular, it has been proposed that preoperative CRT is a better treatment than postoperative CRT to enhance the rate of overall compliance, local control, and sphincter preservation and to reduce the risk of toxicity [4]. Due to these outcomes, preoperative CRT followed by radical surgery is widely regarded as the preferred treatment of choice for locally advanced rectal cancer. Several randomized studies have found lower rates of local failure with preoperative radiotherapy than with surgery alone. However, only the Swedish Rectal Cancer Trial, which evaluated a short course of preoperative irradiation (25 Gy, delivered in five fractions), found an advantage in overall survival [5]. The authors of a subsequent meta-analysis also concluded that the combination of preoperative radiotherapy and surgery, as compared with surgery alone, significantly improves local control and overall survival [6]. The Dutch Colorectal Cancer Group reported that the addition of short-course preoperative radiotherapy to optimal surgery with total mesorectal excision reduced the rate of local recurrence but did not improve two-year survival [7].

AIM AND OBJECTIVE

To compare survival outcomes in Preoperative versus postoperative chemoradiation in Stage III Rectal cancer

MATERIAL AND METHODS

Fifty two patients of rectal cancer who received preoperative CRT (25 patients) or postoperative CRT (27 patients) of previously untreated stage III rectal cancer were analyzed retrospectively. All patients were treated at the department of Radiation Oncology, Pt B D Sharma PGIMS Rohtak between 2012 and 2018. Eligibility criteria included histologically confirmed stage III rectal cancer. Patients with a history of chemotherapy, radiotherapy, any other malignancies, or presence of distant metastasis at diagnosis were excluded. The median age of the patients was 60 years. Of all the patients, 55% were from rural area and 45% are from urban area. Clinical staging was classified by rectosigmoidoscopy, computed tomography (CT) scan, and magnetic resonance imaging (MRI) of the abdomen and pelvis. 5-Fluorouracil (5-FU) or a precursor of 5-FU-based chemotherapy was conducted concurrently with radiotherapy for all patients. Most patients were treated using pelvic radiotherapy with the three- or four-field box techniques. Preoperative radiotherapy was delivered with a median total dose of 50.4 Gy (range, 45 to 55.8 Gy) in a median of 28 fractions (range, 24 to 31 fractions). Meanwhile, postoperative radiotherapy was delivered with a median total dose of 50.4 Gy (range, 41.4 to 60.4

Gy) in a median of 28 fractions (range, 23 to 33 fractions). The median duration of radiotherapy was 37 days (range, 21 to 56 days). All patients underwent total mesorectal excision. Surgical resection was performed at median 8 weeks (range, 5 to 12 weeks) after completion of radiotherapy in the preoperative CRT group. All patients of the preoperative CRT group received three or four cycles of adjuvant chemotherapy with the same preoperative regimen after the surgical resection. Postoperative radiotherapy was delivered at median 9 weeks (range, 1 to 14 weeks) following the surgical resection. Most (81.7%) of the postoperative CRT group were administered one or two cycles of 5-FU or a precursor of 5-FU-based adjuvant chemotherapy before CRT.

RESULTS

The median locoregional recurrence free survival in the preoperative group was 33 months whereas it was 32 months in the postoperative group ($p=0.585$). The median distant metastases free survival was 17 months in the preoperative group versus 35 months in the postoperative group ($p=0.039$). The mean survival in the preoperative group was 33.927 months versus 49.519 months in the postoperative radiotherapy group ($p=0.129$). Sphincter preservation rate of 51% in the preoperative CRT group.

DISCUSSION

Preoperative CRT results in higher rate of sphincter preservation than does postoperative CRT [4,8]. The rate of sphincter-preserving surgery after preoperative CRT varies widely [4,9]. Among the patients who were considered to require an abdominoperineal resection in preoperative CRT group of German rectal cancer trial, the rate of sphincter preservation was 39% [10]. However, we observed a sphincter preservation rate of 51% in the preoperative CRT group. Preoperative CRT in the German trial could not bring significant advantages to DFS or OS: Five-year OS was 76% vs. 74% ($p = 0.80$) and 5-year DFS rate was 68% vs. 65% ($p = 0.32$) in the preoperative and postoperative CRT group, respectively. The results of the present study correspond well with the findings of earlier experimental studies that documented high rate of tumor regression. Accordingly, tumor size decrease leads to sphincter preservation and tumor respectability [11,12]. Tumor response after preoperative CRT is known as a prognostic factor in rectal cancer [13-16]. The level of response (CR vs. partial response vs. no response) significantly influences local recurrence, DFS, freedom from distant metastases, and cancer specific survival [17,18]. Park et al. [19] suggested that the patients who had good response (ypT0-2, N0) to preoperative CRT have a lower risk than poor responders in local and distant failure. In the National Surgical

Adjuvant Breast and Bowel Project (NSABP) R-03 trial, 5-year OS was 74.5% vs. 65.6% ($p = 0.065$) and 5-year DFS was 64.7% vs. 53.4% ($p = 0.011$) in the preoperative and postoperative CRT group, respectively [10]. Roh et al. [10] attributed the prolonged DFS of NSABP R-03 to patient eligibility, timing of radiotherapy, radiation dose, type of surgery, and the length of follow-up. In the current study, The median locoregional recurrence free survival in the preoperative group was 33 months whereas it was 32 months in the postoperative group ($p=0.585$). The median distant metastases free survival was 17 months in the preoperative group versus 35 months in the postoperative group ($p=0.039$). The mean

survival in the preoperative group was 33.927 months versus 49.519 months in the postoperative radiotherapy group ($p=0.129$).

CONCLUSION

The present study concludes that there are no statistically significant differences in mean survival and median locoregional recurrence-free survival between the two groups. However, contrary to current literature, our findings show that the postoperative chemoradiation group had significantly better median distant metastasis-free survival. These results warrant further investigation through larger randomized studies.

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