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Original Article

Outcome of Patients with Locally Advanced Rectal Cancer Treated with Neoadjuvant Chemotherapy and Radiotherapy

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Abstract

Introduction: About 30% of all colorectal tumors develop in the rectum. The location of the rectum within the bony pelvis and its proximity to vital structures presents significant therapeutic challenges when considering neoadjuvant options and surgical interventions. Neoadjuvant therapy may comprise either radiotherapy (RT) alone or in combination with chemotherapy. Commonly prescribed chemotherapy agents include 5-fluorouracil and oxaliplatin. These agents act to limit tumor cell division in several ways.

Aim: The aim of this study was to study the outcome of patients with locally advanced rectal cancer treated with neoadjuvant chemotherapy and RT.

Materials and Methods: Patients with locally advanced pathologically confirmed adenocarcinoma of the rectum, without detectable distant metastasis at presentation, were included in this study. Patients underwent neoadjuvant chemotherapy and radiation therapy.

Results: In 67 patients, 63% of patients were female; Stage IIA cases were 69% followed by Stages IIB and IIC 10% in each. About 19% of patients underwent surgery and 81% of patients underwent neoadjuvant chemoradiation followed by reassessment for surgery. Overall survival in 3 years in this study was noted as 67.6%.

Conclusion: Neoadjuvant chemoradiation followed by radical surgery has shown very satisfactory results in the management of locally advanced rectal cancers.

Key words: Chemoradiation, Chemotherapy, Neoadjuvant therapy, Rectal cancer

INTRODUCTION

Cancer of the rectum is less frequent than colon cancer, accounting for 5% of malignant tumors, and ranks as the fifth most common cancer in adults.[1,2]

In India, the annual incidence rates (AARs) for colon cancer and rectal cancer in men are 4.4 and 4.1/100,000, respectively. The AAR for colon cancer in women is 3.9/100,000. Colon cancer ranks 8th and rectal cancer ranks 9th among men. For women, rectal cancer does not figure in the top 10 cancers, whereas colon cancer ranks 9th.[3]

Colorectal cancer most commonly occurs sporadically and is inherited in only 5% of cases.[4] Migrant studies indicate that when populations move from a low-risk area (e.g., Japan) to a high-risk area (e.g., the USA), the incidence of colorectal cancer increases rapidly within the first generation of migrants, and Japanese born in the USA have a higher risk than the white population.[5] Diet is definitely the most important exogenous factor identified up to now in the etiology of colorectal cancer. It has been estimated that 70% of colorectal cancers could be prevented by nutritional intervention;[6] various promoting and protective factors have been identified in prospective and case–control studies. Evidence that diets rich in vegetable protect against colorectal cancer is substantial. Among subgroups of vegetables, green leafy vegetables were associated with a lower risk of colorectal cancer for

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men, while intake of fruits was not related to the risk of colorectal cancer in men or women.[7,8]

Colon and rectal cancers are usually considered one disease in the advanced setting because the prognosis and sensitivity to antineoplastic agents are largely similar for tumors originating from different portions of the large bowel. However, the pattern of recurrence of the colon and rectal cancers differs substantially. The final outcome of rectal cancer depends far more on the skills of the surgeon than for colon cancer. Chemotherapy is given with adjuvant intent to high-risk patients with both neoplasms, but in general, radiation therapy is also necessary for rectal cancer, while it is not in colon cancer.

Aim

The aim of this study was to study the outcome of patients with locally advanced rectal cancer treated with neoadjuvant chemotherapy and radiotherapy (RT).

MATERIALS AND METHODS

This observational study was conducted in the Department of RT at Thanjavur Medical College. Patients with locally advanced pathologically confirmed adenocarcinoma of the rectum, without detectable distant metastasis at presentation, were included during the period from November 2018 to October 2019.

Patient details were collected, complete clinical examination and rectal examination were performed. Hematology, biochemistry, colonoscopy, histopathology, computed tomography scan, and carcinoembryonic antigen were performed.

Patients underwent for the 1st cycle of chemotherapy with mitomycin C and 5-fluorouracil (5-FU) from day 1 to day 5 followed by RT. At 30 Gy of RT, patients received the 2nd cycle of chemotherapy with 5-FU (×5 days) only. RT was continued to a total of 50 Gy. Patients were reassessed 6 weeks after the end of chemoradiation for surgery. In suitable patients, either an abdominoperineal resection or low anterior resection was done, depending on the clinical situation. Following surgery, they received adjuvant 5-FU-based chemotherapy, once in 3 weeks, to a total of 6 cycles.

Radiation was given with telecobalt therapy, delivering 200 cGy per fraction, to a total dose of 50 Gy to the whole pelvis after simulation.

The 1st cycle of chemotherapy included inj. mitomycin C at a dose of 6 mg/m^2 intravenous (IV) on day 1 and inj. 5-FU at a dose of 375 mg/m^2 IV on day 1–day 5 in the 2nd cycle, inj. mitomycin C was not given.

RESULTS

In this study, 67 patients with locally advanced (T2-T4/N0-N2 disease), pathologically confirmed adenocarcinoma of the rectum, without detectable distant metastasis, were included in the study. The age of these patients varied

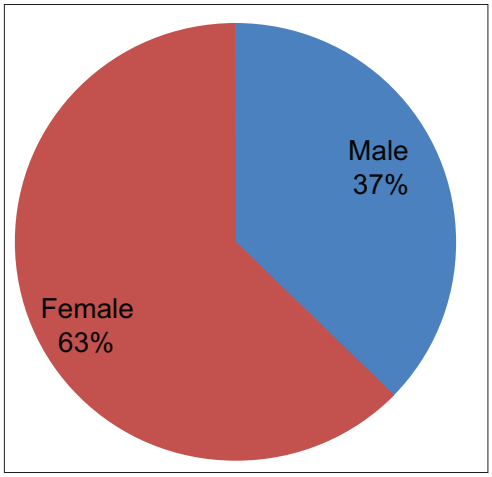

Figure 1: Gender distribution

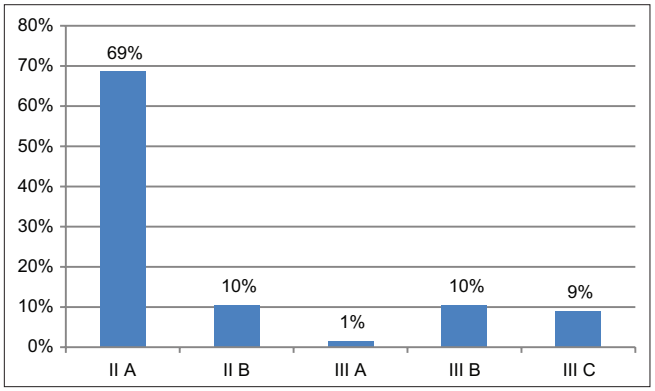

Figure 2: Stage distribution

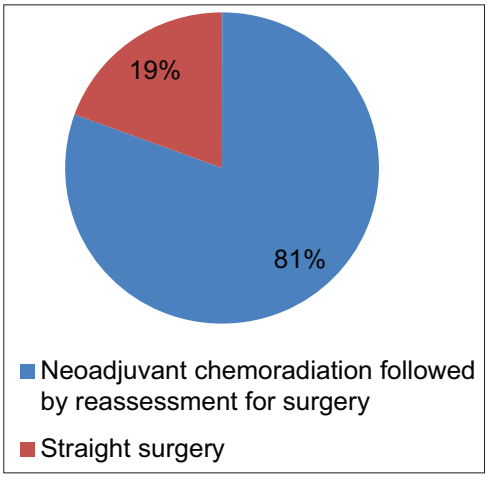

Figure 3: Treatment distribution

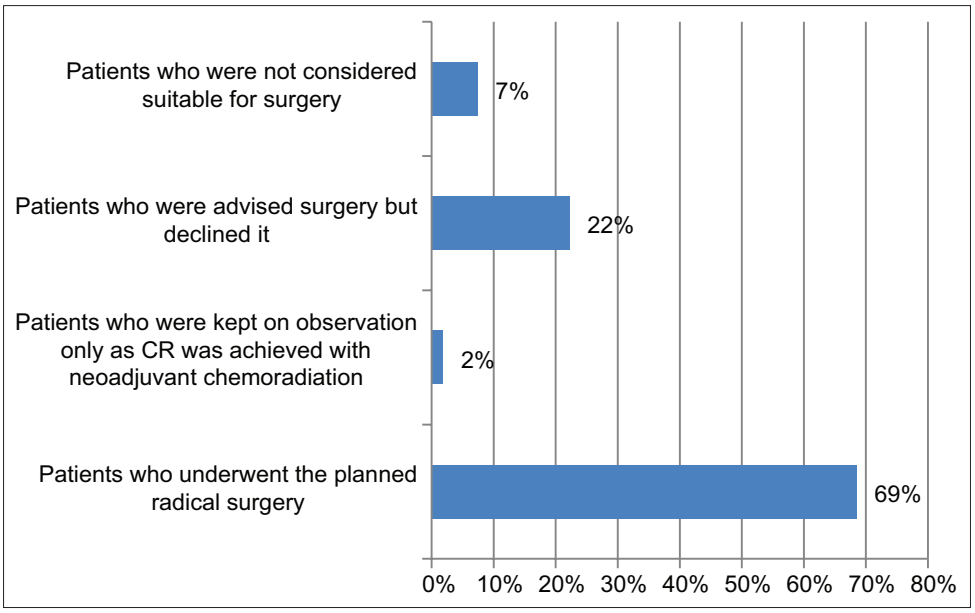

Figure 4: Patients completed neoadjuvant chemoradiation

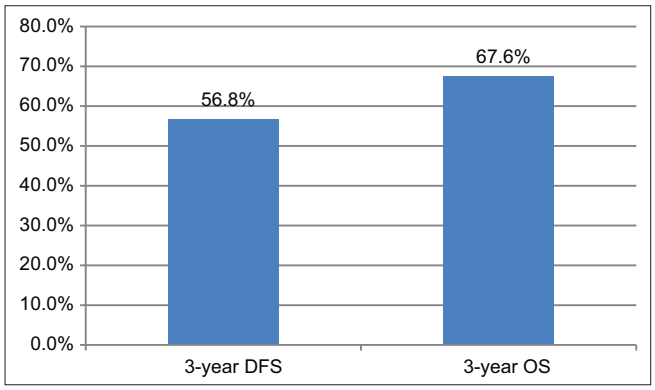

Figure 5: Outcome distribution

from 26 years to 78 years. The majority of the patients were female in our study (63%) Figure 1. Stage IIA cases were 69% followed by Stages IIB and IIC 10% in each Figure 2. About 19% of patients underwent surgery and 81% of patients underwent neoadjuvant chemoradiation followed by reassessment for surgery Figure 3. About 69% of patients underwent the planned radical surgery. 22% of patients who have advised surgery but declined it, 7% of patients who were not considered suitable for surgery Figure 4. Overall survival in 3 years in this study was noted as 67.6% Figure 5.

DISCUSSION

Colon and rectal cancers are usually considered one disease in the advanced setting because the prognosis and sensitivity to antineoplastic agents are largely similar for tumors originating from different portions of the large bowel. However, the pattern of recurrence of the colon and rectal cancers differs substantially. The final outcome of rectal cancer depends far more on the skills of the surgeon than for colon cancer. Chemotherapy is given with adjuvant intent to high-risk patients with both neoplasms, but in general, radiation therapy is also necessary for rectal cancer, while it is not in colon cancer.

Several cytotoxic agents act as radiosensitizers and hence increase the cytotoxic effect of RT. When used as adjuvant treatment, combined chemo-RT reduces the local recurrence rate and improves survival compared with RT alone. Moreover, chemotherapy may also have an effect on micrometastases and thereby reduce the frequency of distant metastases. However, cytotoxic agents also increase the side effects of RT, especially regarding the small bowel. Several drugs are being used, but 5-FU is the main component; the optimal time schedules have not yet been defined. In this respect, the continuous 5-FU infusion has been shown to be more effective than bolus 5-FU.[9] The results of a trial (INT 0144) evaluating the benefit of continuous infusion 5-FU during the entire 6 months adjuvant program versus continuous infusion 5-FU only during the period of RT do not show relevant differences between the three arms of the study.[10] Furthermore, there is no advantage of leucovorin or levamisole-containing regimens over bolus 5-FU alone when combined with irradiation. An open question has been whether radiochemotherapy is better when administered as adjuvant or neoadjuvant modality: Two trials in North America were conducted with the aim of evaluating the role of integrated strategy but were closed due to poor patient accrual. The preliminary results of the NSABP R03 trial and the German study strongly suggested a benefit for the pre-operative approach: The

neoadjuvant strategy was more active and demonstrated less risk for acute and late morbidity.[11,12]

CONCLUSION

The potential advantages of a pre-operative approach over a post-operative one are decreased tumor seeding during the operation, less acute, and late toxicity increased the efficacy of RT and, for patients who receive a conventional long course of RT, an increased rate of sphincter preservation. FU-based schemes in combination with pre-operative irradiation are employed with the aim of improving local control and reducing distant recurrence rates.

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