

# Chapter 06



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# Role of Neoadjuvant Radiotherapy in the Management of Rectal Cancer

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## ABSTRACT

Preoperative radiotherapy is highly effective in the treatment of rectal cancer. It is the single modality that has been shown to lower local recurrence rates. Radiation therapy enhances treatment effectiveness by three main mechanisms: (1) downstaging the tumors to allow surgical resection, (2) decreasing local recurrence rates by eliminating microscopic foci of tumor in the operative field, and (3) improving sphincter preservation due to disease invading levator ani or muscle external anal sphincters. The current study included a total of 289 patients diagnosed with rectal cancer, out of which 80 (27,6 %) were treated with preoperative radiotherapy. Of these, 30 (37,5 %) received short-course radiotherapy and 50 (62,5 %) long-course radiotherapy. In the long course group, 22 patients (44 %) were in laparoscopic surgery and 28 (56 %) for open surgery. The long-course consisted of 2 Gy per session, every day, for four weeks, and the short-course radiotherapy involved five sessions of 5 Gy each, over five days. The long-course outcome was evaluated 8 weeks after the end of radiotherapy.

Short-course RT was performed predominantly in patients with suspected mesorectal lymph node metastases, followed by TME surgery done in the following week. In long-course radiotherapy patients, three patterns of response were detected: complete radiosensitivity (n = 9), partial sensitivity not warranting further surgery (n = 22), or radioresistance (n = 21).

In totally radiosensitive cases, the tumor completely regressed; however, this did not occur in partially irradiosensitive ones. Radiotherapy did not achieve a significant reduction in tumor size in cases that were radioresistant. Tumor responsiveness was quantitatively evaluated by comparing the rates of tumor shrinkage.

After long-course radiotherapy, 4 (18,2 %) patients in the laparoscopic group were susceptible to radiotherapy, while 15 (68,2 %) were partially sensitive and 3 (13,6 %) were resistant to radiation treatment. 5 (17,9 %) patients achieved complete radiosensitivity, and 19 (67,9 %) reached partial radiosensitivity, whereas there were 4 (14,3 %) cases in the radioresistant group from open surgery (p = 0,998).

For tumor regression grading, in the laparoscopic group, the percentages were as follows: Grade 1, 19,1 ± 5,7 %; Grade 2, 51,0 ± 7,3 %. Among patients with MRD > yT, the percentages for Grade yT were: G3, 17,0 ± 5,5 %; and G4, 12,8 ± 4,9 %. In the open surgery group, these numbers were 23,2 ± 5,6 %, 44,6 ± 6,6 %, 17,9 ± 5,1 %, and 14,3 ± 4,7 %.

Long-course radiotherapy was found to be effective in reducing tumor size, leading to a complete response, a decrease in local recurrence, and an increased likelihood of surgery being a viable option. There were no statistically significant differences between the laparoscopic and open groups in terms of radiosensitivity and tumor response rate (P > 0,05). The most common result observed with respect to regression was Grade 2, which was seen in (51,1 ± 7,3 %) and (44,6 ± 6,6 %) of laparoscopic and open cohorts, respectively.

**Keywords:** Radiotherapy; Short-Course Radiotherapy; Long-Course Radiotherapy; Rectal Cancer;

## Circumferential Excision Margin

### INTRODUCTION

The radical surgical excision is the treatment of choice for malignant rectal tumors.<sup>(1,2)</sup> Nevertheless, surgery alone frequently carries a high risk of local recurrence and is sometimes technically impossible because of tumor spread or architectural reasons. Moreover, treatment options for this type of local recurrence are limited, presenting a significant therapeutic challenge. Among the possibilities, preoperative radiotherapy is the most effective measure for decreasing locally recurrent rates.<sup>(3)</sup>

Nowadays, NACRT, followed by total mesorectal excision (TME), is accepted as the standard of care for LARC and is primarily practiced internationally.<sup>(1,2,3,4)</sup> The use of chemoradiotherapy in addition to surgery has several aims: it decreases the risk of local recurrence, shrinks the tumor to allow complete resection, and increases the possibility of sphincter preservation in low-lying tumors.<sup>(3,5)</sup> The purpose of this study is to determine the degree of tumor shrinkage, changes in depth of invasion, and reduction in recurrence rates associated with neoadjuvant radiochemotherapy in patients with rectal cancer.

### DEVELOPMENT

This study involved 80 of the 103 patients with rectal adenocarcinoma who were diagnosed from 2016 to 2021. Thirty-five of these patients were female, and 45 were male, with ages ranging from 19 to 78 years. The distance to the anal verge was used to classify tumor localization as lower (0-6 cm), middle (7-12 cm), and upper rectum (>12 cm) (table 9.1).

**Table 9.1.** Patients' Distribution according to Tumor Localization, According to the Distance from the Anal Verge

| Distance from Anal Verge | Laparoscopic Group (n=47)        |      | Open Group (n=56) |      |
|--------------------------|----------------------------------|------|-------------------|------|
|                          | n                                | %    | n                 | %    |
| 0-6 sm                   | 13                               | 27,7 | 16                | 28,6 |
| 7-12 sm                  | 18                               | 38,3 | 22                | 39,3 |
| >12 sm                   | 16                               | 34,0 | 18                | 32,1 |
| x <sup>2</sup> ; p       | x <sup>2</sup> =0,042; p = 0,979 |      |                   |      |

Note: P-value is the level of significance computed through Pearson's polychoric correlation coefficient for the analyzed trait indicators\_MANOVA.

The T-stage distribution in laparoscopic vs open surgery groups was as follows: T1 (3 patients [6,4 %] vs 2 patient [3,6 %]), T2 (11 [23,4 %] vs 10 [17,9 %]), T3 (29 [61,7 %] vs 36 [64,3 %]), and T4 (4[8,5 %] vs 8[14-3 %]).

The stage of disease was distributed as follows: seven (14,9 %) versus five (8,9 %) (Stage I), 12 (25,5 %) versus 16 (28,6 %) patients (Stage II), and 28(59,6 %) versus 35 (62,5 %) (Stage III) patients (p=0,637). We further classified patients with T3 and T4 tumors as a separate subgroup for additional analysis, given the clinical importance of extensive tumor invasion (table 9.2).

In most cases, pathohistological examination of the surgical specimens documented adenocarcinoma of different grades (table 9.3). Moderately differentiated adenocarcinoma was more common in both groups (p = 0,998) (57,4 % for laparoscopic and 55,4 % for open, respectively). The least common histological cell types were mucinous adenocarcinoma and squamous cell carcinoma, at 2,1 % and 1,8 %, respectively, in both the laparoscopic and open

surgery groups.

| T (mm) |                         | n  | Laparoscopic Group n=33 |      | n  | Open Group n=42 |      |
|--------|-------------------------|----|-------------------------|------|----|-----------------|------|
|        |                         |    | n                       | %    |    | n               | %    |
| pT3    | pT3a (<1)               | 29 | 6                       | 18,2 | 36 | 7               | 16,7 |
|        | pT3b (1-5)              |    | 6                       | 18,2 |    | 8               | 19,1 |
|        | pT3c (5-15)             |    | 8                       | 24,2 |    | 11              | 26,3 |
|        | pT3d (>15)              |    | 9                       | 27,3 |    | 10              | 23,8 |
| pT4    | pT4a (i.v.)             | 4  | 1                       | 3,0  | 8  | 3               | 7,2  |
|        | Pt <sub>4b</sub> (i.y.) |    | 3                       | 9,1  |    | 5               | 11,9 |

**Note:** Depth of tumor spread in the mesorectum was grouped into pT3a- invasion up to 1 mm, pT3b- invasion of 1-5 mm, pT3c- invasion of 5-15 mm, and pT3d - invasion greater than or equal to 15.

| Morphological Type           |                            | Laparoscopic Group n=47           |      | Open Group n=56 |      |
|------------------------------|----------------------------|-----------------------------------|------|-----------------|------|
|                              |                            | No.                               | %    | No.             | %    |
| Adenocarcinoma               | High-grade differentiation | 13                                | 27,7 | 16              | 28,6 |
|                              | Moderate differentiation   | 27                                | 57,4 | 31              | 55,4 |
|                              | Low-grade differentiation  | 5                                 | 10,6 | 7               | 12,5 |
| Mucinous carcinoma (colloid) |                            | 1                                 | 2,1  | 1               | 1,8  |
| Squamous cell carcinoma      |                            | 1                                 | 2,1  | 1               | 1,8  |
| x <sup>2</sup> ; p-value     |                            | x <sup>2</sup> = 0,134; p = 0,998 |      |                 |      |

TNM staging was based on a classification system. The locations of the tumors were the upper rectum (20 patients), mid-rectum (36 patients), and lower rectum (24 patients). Thirty-five patients in the laparoscopic group underwent preoperative radiotherapy, consisting of 13 short-course and 22 long-course treatments. In the open subgroup, 45 patients received radiotherapy: 17 received short-course and 28 received long-course treatment.

For upper rectal cancer patients, 6 and 3 patients in the laparoscopic group received short-course and long-course radiotherapy separately, while these numbers for open surgery were 7 and 4. For middle rectal tumors, eight and 10 patients in the laparoscopic and open group underwent short-course radiotherapy; 8 patients in each group received long-course radiotherapy. In the low rectum tumor group, none of the patients received definitive short-course radiotherapy; however, 11 patients in the laparoscopic group and 13 patients in the open operation group underwent long-course radiotherapy (table 9.4).

The long-course radiotherapy involved fractions of 2 Gy over a period of 4 weeks, while the short-course consisted of 5 Gy fractions administered daily for five consecutive days. The treatment efficacy of long-course radiotherapy was evaluated 8 weeks after the completion of treatment.

Among patients treated with radiotherapy, 13 were stage T1-T2, 55 were stage T3, and the remaining 12 were stage T4. Although the division of the rectum into upper, middle, and lower thirds is essential for preoperative MRI-based assessment, we consider that the anatomical site in relation to the peritoneal reflection is a crucial factor in accurately determining tumor

position during surgery.

**Table 9.4.** Distribution of Patients in the Laparoscopic versus Open Surgery Groups According to Type of Radiotherapy and Location of Tumor According to TNM Classification

| Localization | TNM                                                                                    | Laparoscopic Group (n=35) |      | Open Group (n=45) |      |
|--------------|----------------------------------------------------------------------------------------|---------------------------|------|-------------------|------|
|              |                                                                                        | Short                     | Long | Short             | Long |
| High         | T <sub>1-2</sub> N <sub>1-2</sub> M <sub>0</sub> (within the mesorectum)               | 1                         | -    | 2                 | -    |
|              | T <sub>1-2</sub> N <sub>1</sub> -N <sub>2</sub> M <sub>0</sub> (within the mesorectum) | -                         | -    | -                 | -    |
|              | T <sub>3</sub> N <sub>0</sub> (SRS-)                                                   | -                         | -    | -                 | -    |
|              | T <sub>3</sub> N <sub>1-2</sub> (SRS-) (within the mesorectum)                         | 5                         | -    | 5                 | -    |
|              | T <sub>3</sub> N <sub>1-2</sub> (SRS-) (outside the mesorectum)                        | -                         | -    | -                 | 1    |
|              | T <sub>3</sub> SRS+                                                                    | -                         | -    | -                 | -    |
|              | T <sub>4</sub> N <sub>x</sub>                                                          | -                         | 3    | -                 | 3    |
| Middle       | T <sub>1-2</sub> N <sub>1-2</sub> (within the mesorectum)                              | 2                         | -    | 2                 | -    |
|              | T <sub>1-2</sub> N <sub>1-2</sub> (outside the mesorectum)                             | -                         | -    | -                 | 1    |
|              | T <sub>3</sub> N <sub>0</sub> (SRS-)                                                   | 3                         | -    | 6                 | -    |
|              | T <sub>3</sub> N <sub>1-2</sub> (SRS-) (within the mesorectum)                         | 2                         | -    | 2                 | -    |
|              | T <sub>3</sub> N <sub>1-2</sub> (SRS-) (outside the mesorectum)                        | -                         | 6    | -                 | 4    |
|              | T <sub>3</sub> SRS+                                                                    | -                         | 1    | -                 | 2    |
|              | T <sub>4</sub> N <sub>x</sub> (0.1.2)                                                  | -                         | 1    | -                 | 3    |
| Low          | T <sub>1-2</sub> N <sub>1-2</sub> (within the mesorectum)                              | -                         | 3    | -                 | 1    |
|              | T <sub>1-2</sub> N <sub>1-2</sub> (outside the mesorectum)                             | -                         | 1    | -                 | -    |
|              | T <sub>3</sub> N <sub>0</sub> (SRS-)                                                   | -                         | 4    | -                 | 5    |
|              | T <sub>3</sub> N <sub>1-2</sub> (SRS-) (within the mesorectum)                         | -                         | 1    | -                 | 3    |
|              | T <sub>3</sub> N <sub>1-2</sub> (SRS-) (outside the mesorectum)                        | -                         | 1    | -                 | 2    |
|              | T <sub>3</sub> SRS+                                                                    | -                         | 1    | -                 | 1    |
|              | T <sub>4</sub> N <sub>x</sub>                                                          | -                         | -    | -                 | 2    |
| Total        |                                                                                        | 13                        | 22   | 17                | 28   |

In this context, for tumor site location, we specifically registered tumors in the area above and below the peritoneal reflection, as well as their distance from the corresponding peritoneal fold to the rectosigmoid junction. All patients determined to have enrolled in this study (n = 80) underwent TME with a double-lumen loop ileostomy. Patients with tumors and distant metastasis were ineligible.

According to the literature and our personal experience, preoperative radiochemotherapy should be applied in all cases with lymph node-positive rectal cancer. For T3N0M0 and T4N0M0 disease, especially when abdominoperineal resection is the plan, preoperative therapy should follow standardized clinical guidelines.

For operative classification, we divided the rectum anatomically into two major compartments:

(1) supralelevator and (2) infralelevator. The supralelevator component was composed of three subcomponents: the upper, middle, and lower rectum. One notable fact is that the middle and lower rectum are primarily situated below the peritoneal reflection, whereas the upper rectum lies above it.<sup>(6,7,8)</sup> We believe that the inclusion of the peritoneal reflection as a landmark in classifying rectal valuable tumors is for clinical use, especially for planning surgery and stage categorization.

Tumors originating from the sublevator (pelvic-floor) gutter were not part of the study. Both short-course Swedish protocols and long-course English treatment protocols of preoperative radiochemotherapy were used, adjusted to the stage and anatomical site of the tumor.

For all the primary colorectal cancer centers, the T3aN tumor was classified as locally advanced. The general guideline for T3 and T4 tumors is neoadjuvant therapy.<sup>(9)</sup> If operated unprocessed, adjuvant treatment after surgery would not be omitted.<sup>(10)</sup> Surgeon One hundred preoperatively irradiated patients undergoing resection for extremity STS had a statistically significant decreased rate of local recurrence and less radiation-associated toxicity compared with 79 similarly treated postoperatively.

The best approach to T3M0 tumors, particularly those evaluated by MRI, remains a subject of active debate. Because the T3 lesions are quite heterogeneous, their prognosis is also much worse for those with T3c and T4 tumors. An interesting finding from our study is that 4 of 17 patients (23,5 %) who were clinical T3N0 had pathologic node involvement after surgery. This is evidence for the use of preoperative radiotherapy, also in T3N0M0 tumors.

Furthermore, 12 patients with nodal involvement (T1-T2 tumors) were treated preoperatively with radiotherapy. In 15 patients who had suspected mesorectal fascia involvement and in whom the risk of a positive CRM was high, we gave long-course neoadjuvant chemoradiation to overcome this risk.

The SCSP, consisting of 25 Gy in five fractions, was prescribed for the neoadjuvant treatment of 30 patients. Long-course chemoradiotherapy was given simultaneously to 50 patients with locally advanced (T3N1-T4) and low-lying rectal tumors. Pretreatment tumor size on MRI and histopathological tumor regression were used to assess the response of patients who had undergone long-course preoperative radiotherapy.

Their response to long-course radiotherapy was classified as radiosensitive, partially radiosensitive, or radioresistant (table 9.5).

**Table 9.5.** Treatment Response of the Tumor Tissue to Long-Course Radiotherapy for Laparoscopic and Open Surgery Patient Cohorts

| Response Type     | Laparoscopic Group (n=22)    |      | Open Group (n=28) |      |
|-------------------|------------------------------|------|-------------------|------|
|                   | n                            | %    | n                 | %    |
| Complete Response | 4                            | 18,2 | 5                 | 17,9 |
| Partial Response  | 15                           | 68,2 | 19                | 67,9 |
| Radioresistant    | 3                            | 13,6 | 4                 | 14,3 |
| $\chi^2$ ; p      | $\chi^2=0,005$ ; $p = 0,998$ |      |                   |      |

After long-course radiotherapy, four patients (18,2 %) in the laparoscopic group had a complete response, and 15 patients (68,2 %) had a partial response. In comparison, 3 patients (13,6 %) were classified as non-responders or resistant to radiation therapy. In the OS group, five patients

(17,9 %) were completely radiosensitive, 19 patients (67,9 %) were partially radiosensitive, and 4 patients (14,3 %) were radioresistant ( $p = 0,998$ ).

Among patients who received long-course radiotherapy as sole treatment, 18,2% of cases with pathological complete regression (PCR) subsequently required proctectomy. The complete clinical response rate in the laparoscopic group (17,9 %) was higher than that observed in the open surgery group.

Total mesorectal excision (TME) was performed in all patients. Pathological examination of the resected specimens showed tumor regression in those who had received an extended course of radiotherapy, with the most dramatic regression observed in grade 2 (table 9.6).

| Indicator                   |                | Laparoscopic Group         | Open Group                 | $p$   |
|-----------------------------|----------------|----------------------------|----------------------------|-------|
|                             |                | n (P±mp %) / M (min - max) | n (P±mp %) / M (min - max) |       |
| TME Quality                 | High Quality   | 23 (48,9±7,3 %)            | 26 (46,4±6,7 %)            | 0,952 |
|                             | Medium Quality | 15 (31,9±6,8 %)            | 18 (32,1±6,2 %)            |       |
|                             | Low Quality    | 9 (19,1±5,7 %)             | 12 (21,4±5,5 %)            |       |
| SRS Positivity              | High $1/3$     | 2/13 (15,4±10,0 %)         | 2/16 (12,5±8,3 %)          | 0,751 |
|                             | Medium $1/3$   | 3/18 (16,7±8,8 %)          | 3/22 (13,6±7,3 %)          | 0,859 |
|                             | Low $1/3$      | 3/16 (18,8±9,8 %)          | 3/18 (16,7±8,8 %)          | 0,771 |
| SRS Median                  | High $1/3$     | 1,3 (0,7-2,0)              | 1,2 (0,6-1,8)              | 0,259 |
|                             | Medium $1/3$   | 1,4 (0,6-2,1)              | 1,2 (0,7-1,9)              | 0,126 |
|                             | Low $1/3$      | 1,1 (0,5-1,6)              | 1,2 (0,4-1,8)              | 0,214 |
| Tumor regression rate       | 1              | 19,1±5,7 %                 | 23,2±5,6 %                 | 0,925 |
|                             | 2              | 51,1±7,3 %                 | 44,6±6,6 %                 |       |
|                             | 3              | 17,0±5,5 %                 | 17,9±5,1 %                 |       |
|                             | 4              | 12,8±4,9 %                 | 14,3±4,7 %                 |       |
| Resection margin (Proximal) | High $1/3$     | 12 (7,0-17,0)              | 14 (10,5-22,5)             | 0,529 |
|                             | Medium $1/3$   | 17,5 (11,5-22,7)           | 18,0 (13,5-25,7)           | 0,185 |
|                             | aşağı $1/3$    | 22,2 (16,5-26,8)           | 24,2 (18,0-28,5)           | 0,221 |
| Resection margin (Distal)   | High $1/3$     | 5,5 (4,5-6,5)              | 5,6 (4,6-6,8)              | 0,852 |
|                             | Medium $1/3$   | 3,6 (2,8-4,7)              | 3,8 (3,0-5,5)              | 0,106 |
|                             | Low $1/3$      | 1,9 (1,0-3,0)              | 2,0 (1,2-3,5)              | 0,174 |
| Lymph nodes removed         |                | 14,8 (10-19,0)             | 15,2 (12-22)               | 0,157 |
| Local recurrence            |                | 7/47 (14,9 %)              | 8/56 (14,3 %)              |       |
| Distant metastasis          |                | 3/47 (6,3 %)               | 4/56 (7,1 %)               |       |
| Survival                    |                | 81 %, (71,5 %)             | 80 % (68,7 %)              |       |

In addition to these results, other clinical factors were thoroughly studied in patients treated with TME and radiotherapy.

Locoregional recurrence occurred in all radioresistant patients after prolonged radiotherapy, as determined by treatment outcome. Local recurrence occurred in 3 (13,6 %) LWRs group patients and 4 (14,3 %) OWRs group patients (table 9.7).

| Response Type     | Laparoscopic Group (n=22) |                           | Open Group (n=28) |      |
|-------------------|---------------------------|---------------------------|-------------------|------|
|                   | n                         | %                         | n                 | %    |
| Complete Response | -                         | -                         | -                 | -    |
| Partial Response  | 2                         | 9,09                      | 3                 | 10,7 |
| Radioresistant    | 3                         | 13,6                      | 4                 | 14,3 |
| $\chi^2; p$       |                           | $\chi^2=0,005; p = 0,998$ |                   |      |

A presumed therapeutic option for T3a N1 - T4 tumors can be preoperative chemotherapy with extended CRT, and finally, surgery. For patients with partial resection (i.e., incomplete) and microscopically residual tumor (13 of our cohort), postoperative radiotherapy was administered following the surgical procedure. Of these patients, seven experienced local recurrence within 23 months, and the three-year survival was 41 %. There were 6 recurrences of large residual tissue in the first 12-16 months. In this cohort, adjuvant radiotherapy did not appear to reduce the risk of local recurrence or improve survival.

Patients thought to have microscopic residual disease were subsequently treated with radiotherapy (dose of 60 Gy). For patients with residual microscopic disease, the 3-year survival rate was a mere 10 %. High-dose radiotherapy: Although low-dose radiotherapy decreases local recurrence, high-dose therapy does not benefit patients with bulky residual disease.

In patients with perirectal tumors who underwent pre- or neo-adjuvant radiotherapy (45–50 Gy), tumors shrank and were in a more advantageous state for operation. In 43 % of the locally advanced tumors, we found that the tumor size decreased, making surgery more feasible. There were three groups of treatment outcomes in patients undergoing radiotherapy, categorized by the degree of response.

Patients were divided into three groups according to the neoadjuvant treatment response: Patients who had achieved complete response, (2) Patients who reached partial response, (3) Patients with no response.

Fifty patients had received long-term radiochemotherapy before operation, and nine of them (18 %) showed a complete tumor response with no residual macroscopical tumor observed by reassessment. A total of seven patients (14 %) failed to exhibit a reduction in tumor volume and were considered radiotherapy-resistant. Tumor size decreased to some extent in 34 patients (68 %), and they underwent successful surgical resection.

Refusal of radiotherapy - refractory or resistant to radiotherapy. In this cohort, even those with positive CRM still underwent TME. They have had a local recurrence after adjuvant chemotherapy, and all refractory patients in 3 3-year period after findings have 0 % relapse-free survival.

In contrast, TME was successfully performed in all patients who achieved a complete response to neoadjuvant therapy (figure 9.1).

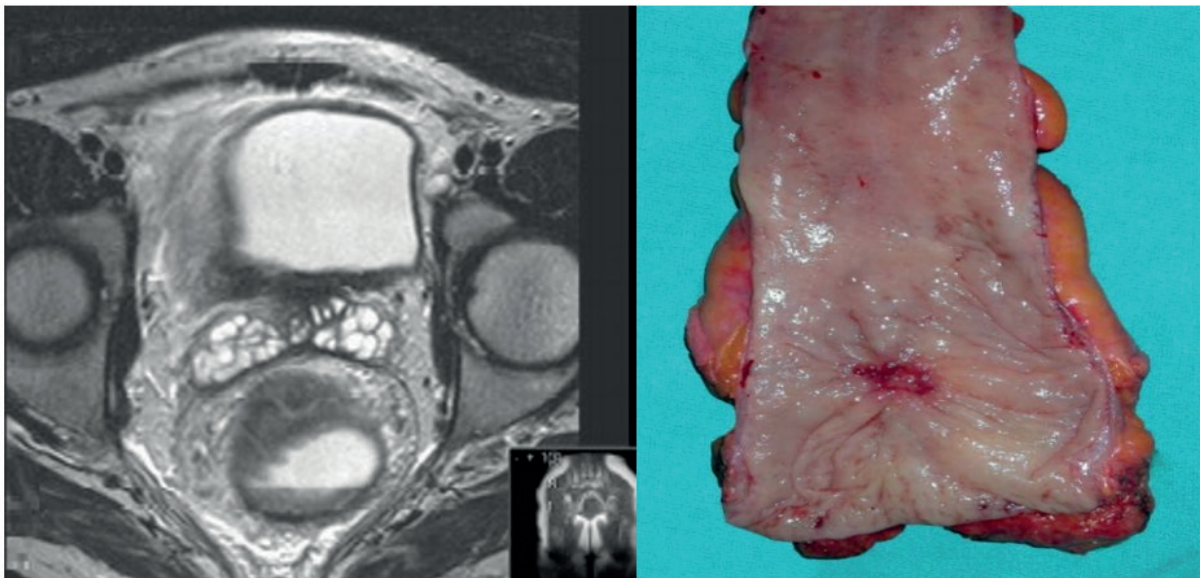


**Figure 9.1.** Tumor shrinkage following long-term radiotherapy

The magnetic resonance imaging of patients with a complete response to radiotherapy showed total clinical regression of the tumor, with no visible residual mass (figure 9.2). Gross examination of the resected specimen also revealed no gross tumor involvement in the mucosal face (figure 9.3) with his treatment response (i.e., pathological complete remission).

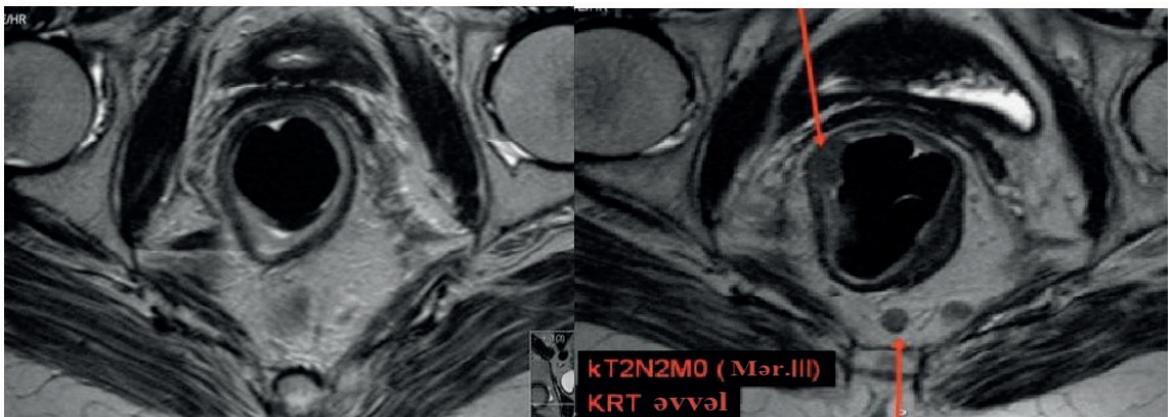


**Figure 9.2.** MRI images after radiotherapy

While the effectiveness of neoadjuvant radiotherapy for rectal cancer is well established, especially in terms of resectability and local recurrence rates, there are limitations to its use. Preoperative chemoradiotherapy plays a role in postoperative morbidity by inducing radiation injuries such as anorectal dysfunction, sphincter damage, and sexual dysfunction.



**Figure 3.** Surgical specimen from a patient who exhibited a complete response to radiotherapy

Radiotherapy is used in cases when there are no other options for treating bone-marrow lesions.<sup>(5)</sup> The ictal expressions of these disorders were present to varying extents in 52 cases (65 %). We found a significant reduction in anal sphincter resting and contractile pressures in patients with uncomplicated cryptorchidism. Sexual dysfunction is a frequent sequela of rectal cancer therapy. We speculate that surgical trauma-induced damage to the afferent nerves is, similar to radiotherapy, a significant risk factor for developing these complications.

Based on our experience and that of others, we recommend treating all eligible patients with long-term radiochemotherapy (45-50 Gy; 225 mg/m<sup>2</sup> 5-fluorouracil/day) followed by resection. Concomitant with radiotherapy, chemotherapy aims to increase the radiosensitivity of tumor cells. This joint technique reduces the local recurrence rate. Preoperative chemoradiotherapy is followed by an interval of 6-8 weeks before the patient undergoes surgery. Radical excision should be emphasized in the surgery. We feel that the idea of attempting to improve an incompetently performed mesorectal excision by adjuvant postoperative radiochemotherapy is misguided. All patients were treated with 4-6 courses of chemotherapy after surgery.

## CONCLUSION

Preoperative radiotherapy is indicated for T1-T2 N+ and T3N0-1, as well as T4N0-2. For locally advanced rectal adenocarcinoma (T3a N1-T4), preoperative chemoradiotherapy followed by surgery is the standard prophylactic approach. After long-term radiotherapy, in the laparoscopic group, 4/22 (18,2 %) patients were susceptible to radiation, and 15/22 (68,2 %)/3/22 (13,6 %) patients had partial/radioresistant RTEC, respectively. In the open group, 5 (17,9 %) patients showed full radiosensitivity, 19 (67,9 %) were partially sensitive, and 4 (14,3 %) were radioresistant ( $p = 0,998$ ). In patients with no radiosensitivity (9 patients in all), FFULL did not occur within the first 3 years (0 %). The local tumor recurrence appeared in 5 (14,7 %) partially radiosensitive patients and in all 7 resistant patients during the first 3 years. Radiotherapy resulted in the following tumor shrinkage: in patients after LAP, 1st-degree shrinkage was seen on average in 16,3 %, 2nd-degree shrinkage—17,3 %, and so on, decreasing by two degrees (in this case, up to its disappearance)—84,9 %. In the open group, these fractions were 23,2±5,6 %, 44,6±6,6 %, 17,9±5,1 %, and 14,3±4,7 %. Where there is complete absorption of the neoplasm, one should not take a wait-and-see attitude. 6-8weeks should delay TME.

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## **CONFLICT OF INTEREST**

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## **AUTHORSHIP CONTRIBUTION**

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