

## MULTIDISCIPLINARY MANAGEMENT OF RECTAL CANCER – A RETROSPECTIVE STUDY –

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**MULTIDISCIPLINARY MANAGEMENT OF RECTAL CANCER – A RETROSPECTIVE STUDY – (Abstract):** *Background:* The procedure of low or very low anterior resection of the rectum with total mesorectal excision (TME) it is now widely accepted for tumours of the middle and lower third of the rectum. It has become the gold standard for the treatment of cancer of the rectum, except where the tumor is close to or is involving the anal sphincter complex. *Patients and methods:* A retrospective study on 120 patients diagnosed with colorectal cancer and operated on between 2000 and 2004 was carried out. There were 120 anterior resection of the rectum, in 34 cases the total mesorectal excision has been performed and in 11 cases a very low anterior resection was made. All 45 cases where total mesorectal excision was made, had undertaken preoperative radiotherapy, surgery being performed after 4 to 6 weeks from the last session of radiotherapy. *Results:* The overall operative morbidity rate was 16.10% in direct relation with the distal limit of dissection. Postoperative complications that we note: anastomotic leakages, recto-vaginal fistulas, evisceration, peritonitis, occlusion, urinary dysfunctions. *Conclusions:* For the total mesorectal excision to be effective an early diagnosis is necessary, and a tumor which is not local invasive, the use of preoperative radiotherapy decreasing the local recurrence.

KEY WORDS: RECTAL CANCER, RADIOTHERAPY, TOTAL MESORECTAL EXCISION

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### INTRODUCTION

The real problem of the rectal cancer treatment is represented by the local recurrences which are difficult to treat [1]. A high incidence of local recurrence, 15-45%, was reported after conventional surgery, in which blunt dissection of the rectal fascia often fails to remove the entire tumoral tissue [2].

The current surgical management of the rectal cancer is based on new, improved rectal anatomy elements (mesorectum), revealed to the surgeons on the last 20 years. This combined with an accurate preoperative assessment of the cancer and radiotherapy had increased the patient's outcome [3].

The operation of anterior resection of the rectum with total mesorectal excision (TME) has become the gold standard for the rectal cancer treatment, except where the tumour is close or involves the anal sphincter complex. Tripartite Consensus Conference held in Washington, DC, in 1999 defined TME as being the complete excision of visceral mesorectal tissue to the level of the levators [4].

Although controversy still exists around the role of TME in tumours of the upper rectum, it is now widely accepted for tumours of the middle and lower third. The TME

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concept is based on the loco-regional recurrence preference of rectal carcinoma. It follows intuitively that adequate en bloc clearance of the mesorectum, including its blood supply and lymphatic drainage, could minimize the possibility of recurrence [5].

Postulated by Heald in early 80`s, now the TME accompanied by preoperative radiotherapy diminishes to 4% the recurrence rate in patients who underwent a curative resection [6].

The long-term preoperative radiotherapy and the TME each have been shown to improve local control of disease in patients with resectable rectal cancer [6, 7].

We conducted a retrospective clinical study to determine whether the addition of preoperative radiotherapy increases the benefit of TME in patients with rectal cancer.

### **PATIENTS AND METHODS<sup>†</sup>**

We had chosen to analyze patients diagnosed with rectal cancer in the last five years. The patients considered to enter in this clinical study were represented by 120 patients who underwent anterior resection of the rectum, from these 45 with total mesorectal excision, 75 with partial or no excision of the mesorectum and 69 with preoperative radiotherapy. We had consulted medical records from January 2000 to January 2005. To be eligible, the patients had to have histologically confirmed adenocarcinoma of the rectum, without evidence of distant metastases, and the inferior margin of the tumor had to be located not farther than 15 cm from the anal verge. Patients with fixed tumours or tumours in a local advanced stage were excluded. The 120 anterior resections of the rectum cases had a relative equal distribution by years. The male/female ratio was 1.17.

The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All persons gave their informed consent prior to their inclusion in the study.

The preoperative assessment was represented by digital rectal examination, flexible recto-sigmoidoscopy, colonoscopy with biopsy, chest X-ray, abdominal/pelvic CT (computed tomography) or MRI (magnetic resonance imaging) and endorectal US (ultrasonography) (Table I).

**Table I Preoperative assessment of rectal cancer for the study group**

	Digital rectal exam	Flexible recto-sigmoidoscopy	Colonoscopy	Biopsy	Chest X-ray	CT	MRI	Endorectal US
No. of patients	120	120	90	120	120	74	7	45

The paraclinical features established that the tumoral process was localised in 32 cases at the rectum-sigmoid junction level, in 43 cases at the superior part of the rectum ampulla, in 34 cases at the middle part of the rectum ampulla and in 11 cases at the lower part of the rectum ampulla's. After the clinical and the histological diagnosis were established just 69 patients underwent preoperative radiotherapy at the surgeon's and oncologist's indication. The radiotherapy was not indicated in rectal polyps with localised dysplasia or in cases with multiple metastatic lesions.

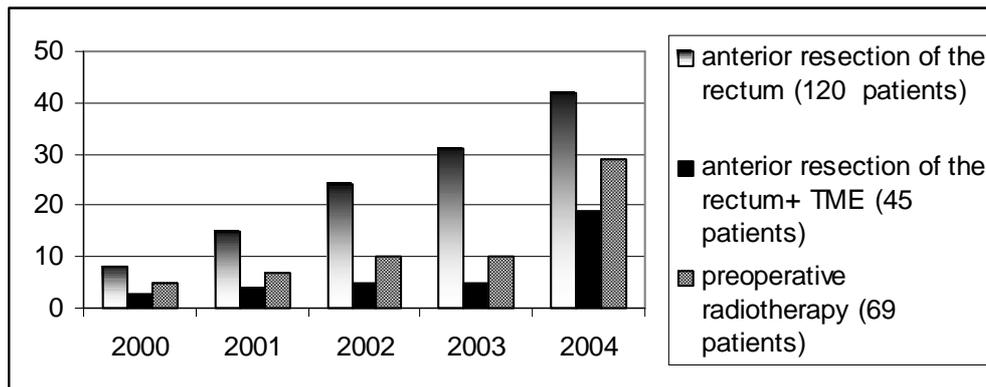
#### ***Preoperative radiotherapy***

It was performed a long course radiotherapy using fields that were including the tumor, with a 2-5 cm margin, the presacral nodes and the internal iliac nodes. Multiple

<sup>†</sup> Part of this article reflects data presented at the Second Joint Meeting ECCP/EACP in Bologna, Italy, on September 15 - 17, 2005.

radiation therapy fields (anterior and sacral) were used (2 or 3). Radiation doses: 45-50 Gy. The patients were referred to the surgeon again after a 4 to 6 weeks period of waiting. According to the international studies it is necessary to have this free of radiation period before surgery to devitalize primary and metastatic cells and to down-size the tumor to facilitate the resection [8-10].

From those 45 patients with anterior resection of the rectum and TME, all of them underwent preoperative long course radiotherapy. To the rest of 24 patients from those 69 that underwent preoperative radiotherapy it was performed anterior resection of the rectum with partial or no mesorectal excision.



**Fig. 1 The management of rectal cancer for the studied period**



**Fig. 2 Surgical specimens (rectum and mesorectum)**

### ***Surgical treatment***

In the cases where TME was performed it was done by sharp dissection under direct visualization of the plane between the endopelvic fascia and the mesorectum. The removal of the mesorectum with its intact fascia propria, and preservation of the pelvic fascia and the autonomic nerve plexuses was revealed by the macroscopic aspect of the surgical specimen and by the result of the histological examination (Fig. 2). The TME was performed in 45 cases from which in 11 cases the tumour was situated in the lower third of the rectum at 5 to 7 cm from the anal verge, tumours not locally advanced. The colorectal anastomosis was done manually except for 19 cases in which the mechanical suture was used by “double stapled technique”. In all 11 cases in which the low anterior resection with TME was performed it was accompanied by a lateral ileostomy (for the protection of the anastomosis). This

ileostomy was closed after a month from the moment of the patient discharge (almost 6 weeks from the day one postoperatively). In cases with a very low anterior resection, the anastomosis line was situated just above the anal channel so, we can not affirm that it was a colo-anal anastomosis. No colonic pouch was performed and no endoanal anastomosis.

The histological examination of the rectum mesentery showed in cases with partial excision of the mesorectum the presence of metastatic nodules in all cases. In 14 cases where TME was performed the metastatic nodules were present into the rectum mesentery.

### ***Follow-up***

Clinical evaluation was made every three months during the first year after surgery and after that once a year for at least two. The postoperative assessment included clinical examination, transabdominal US for the detection of secondary lesions, rectal digital examination and flexible rectal-sigmoidoscopy. Local recurrence was defined as evidence of a tumor of the anastomosis line or the perineal wound level. Distant recurrence was defined as evidence of a tumor in any other area. Local and distant recurrences were confirmed radiologically and/or histologically and checked by the oncologist.

## **RESULTS**

Lately we witness an increased tendency of the distal limit resection extension, especially for tumours of the lower third of the rectum. Prognosis factors are in the case of rectal cancer in a permanent reassessment. We evaluate a part of these factors like: TME, neoadjuvant radiotherapy, mechanical suture, tumour location and ileostomy used for the low anastomosis protection.

### ***Postoperative morbidity***

The patients that underwent radiotherapy and anterior resection of the rectum with TME lost slightly more blood during the operation than those assigned just to surgery (median loss, 800 vs. 600 ml;  $p < 0.001$ ). No perioperative death was marked.

In 11 cases anastomotic leakage developed, those with high flow (5 after radiotherapy and TME) necessitating a derivative ileostomy for the anastomosis protection. These leakages were closed in 8 to 10 days. In 4 cases after TME and preoperative radiotherapy recto-vaginal fistulas were developed, a lateral ileostomy being performed for the anastomosis protection. The ileostomy in these cases was closed after 3 months but, not before a complete clinical and paraclinical re-evaluation.

We did not notice any dysfunctions of the anal sphincter not even in cases with very low anastomosis, mechanically performed. Urinary dysfunctions, manifested by acute urine retention after the removal of the urinary tube, were noted in 8 cases (7 after TME). We did not observe long term urinary and sexual dysfunctions.

### ***Local recurrence***

The rate of local recurrence at two years was 7.6 % in the population who underwent preoperative radiotherapy and partial or no TME. The rate of local recurrence at two years was 4.7% in the group that underwent preoperative radiotherapy and TME and 10.5% in the group referred to surgery ( $p < 0.001$ ). We observed that preoperative radiotherapy reduced the risk of local recurrence significantly in patients who had tumours with an inferior margin to 5-7 cm ( $p = 0.05$ ) to 10-15 cm ( $p < 0.001$ ) from the anal verge. Radiotherapy had no significant effect on tumours located 10 to 15 cm from the anal verge ( $p = 0.17$ ). For TNM stage II and III tumours, preoperative radiotherapy had a significant beneficial effect ( $p = 0.01$  and  $p < 0.001$ , respectively), which was not observed for TNM stage I ( $p = 0.15$ ), the stage IV patients were not eligible to enter the study.

### ***Distant Recurrence***

The rate of distant recurrence at two years was 16.8% in the group assigned to radiotherapy and TME and 18.8% in the group that underwent anterior rectal resection without TME or radiotherapy (p=0.87).

### **DISCUSSION**

The difference in approaches is due to the fact that until a few years ago we did not have a clear treatment guideline for the rectal cancer [9,10]. Even now when the role of the TME and the chemotherapy and radiotherapy are becoming more and more justified the patients are not always undergo a correct type of therapy.

The study limitations were represented by the small size of the study group and the short period of follow up. Because of these we could not concluded on the long term prognosis of the combined therapy of preoperative adjuvant radiotherapy and TME. After two years of follow up we could observe that the patients assigned to preoperative radiotherapy, combined with anterior resection of the rectum and TME had much more immediate local complications than the others and allowed us to speculate on the long term outcome. It seemed that local recurrence was relatively decreased in these patients. The patients expressed no overall decrease in quality of life.

### **CONCLUSION**

The College of American Pathologists has created a protocol for examining colorectal cancer specimen [11].

The collaboration between the oncological surgeons, oncologists and the pathologists should develop the management of the rectal cancer involving a multidisciplinary team. By examining the macroscopic aspect of the mesorectum, after removal, the pathologist could provide information regarding the quality of the surgical procedure. That allows the re-evaluation of the surgical act. Even though for a successfully outcome it is absolutely necessary an early diagnosis of the rectal cancer [12]. The resection line must be well determined especially by imagistic techniques, a correct preoperative stadialization being cardinal for the therapeutical plan [13]. Observed by us and suggested by international studies the immediate complications rate increased due to the use of TME and the very low anterior resection of the rectum [14]. The long term preoperative radiotherapy seems to have an active role at least for the down-sizing if not, for the down-staging of the tumor [15].

International studies are concluding that the preoperative radio and chemotherapy combined with TME are representing the future in the management of the locally non advanced rectal cancer.

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