This study is a part of a clinical trial in preoperative radiotherapy of low rectal cancer, conducted as a prospective and partly retrospective clinical study. It was designed to estimate the influence of long term radiotherapy on symptoms of locally advanced rectal cancer. We included 49 patients with T3/4 stage adenocarcinoma (diagnosis confirmed by clinical, pathological and CT examinations) of the lower two thirds of the rectum, who were treated with long term radiotherapy (45 Gy in 20-25 fractions) and questioned for the presentation of symptoms before and after the treatment. The chief complaints of these patients were the presence of blood in stool, abdominal and pelvic pain, straining (tenesmus) and the alteration in bowel movement. We found a significant decrease in symptoms and signs of the illness after the radiotherapy as well as the improvement of the quality of life.

Key words: long term preoperative radiotherapy, rectal cancer, symptoms, signs

INTRODUCTION

Colorectal cancer is one of the most common causes of cancer deaths in the world. Its incidence in our country is 45/100 000 inhabitants, approximately the same as in modern countries. Tumors localized in rectum represent a special part of this problem, due to the delicate pelvic anatomy and the complex position of the rectum. Locally advanced rectal cancer is alarmingly raising entity which presents with characteristic symptoms, including rectal bleeding, change in bowel movement, pelvic or abdominal pain, straining, and abscess and fistula formation.

Most of the patients do not address their doctor in the asymptomatic stage, when surgery can be the only modality of curative treatment. It is the dramatic presentation of the disease that makes them come for examination and in the majority of cases the tumor cannot be successfully removed by surgery alone. Therefore, the additional methods of treatment have been established, including radio and chemotherapy.

It has been estimated that if chemoradiotherapy alone led to the complete tumor response we can have up to 95% five year survival rate. A strict follow-up of these patients is mandatory in order to detect early recurrence or alteration in tumor size and position. Other patients may have a partial response or a progression of the disease.

Therefore radiotherapy (in further text RT) can lead to increased resectability of the tumor, and its local response to irradiation is, among other methods, estimated by presentation of the symptoms. Most of the patients have a change in bowel habit that they do not give much attention to. It appears mostly in a form of interchanging periods of diarrhea and constipation, accompanied by bloating and flatulence. These symptoms can be so discrete that the patients may not even consider as abnormal, until they start seriously influencing the quality of life.

Generally, more distant the lesion, the symptoms are more expressed. The reason for this is the obstruction of the stool that is less liquid in that segment, narrowing of the distal lumen of the colon as well as the occurrence of the other symptoms in that region (pain, bleeding, secretions, overflow incontinence). Bleeding comes as the second most frequent symptom, but also as the first chief complaint in the majority of patients. It can be obvious and occult. The blood can be red, purple, brownish, black or unapparent. As well as in bowel habit alteration, the more distant the lesion is, more severe are the symptoms.

Although the bleeding could be an early sign of rectal cancer, it is often attributed to hemorrhoids or even neglected. Therefore it is very important to investigate the cause of any kind of bleeding from the lower parts of the digestive tract.
Mucus, as an excretion (in distal localization) or mixed with stool is another important symptom and often accompanies the bleeding. The infiltration of surrounding structures in low rectal cancer can lead to abscess formation, opening of perianal fistulas, or free perforation leading to a poor prognosis with surgery alone.

Pain is not a symptom specific for rectal cancer. It is usually caused by perianal thrombosis, anal fissure or proctalgia fugax. If the tumor is the cause of pain it usually points towards its volume or distal localization, as well as towards the anal canal or sphincter infiltration. That kind of invasion can induce tenesmus (straining), again one of the most often complaints in rectal cancer patients.

Many studies have shown that neoadjuvant radiotherapy can lead to tumor fibrosis along with the decrease in symptoms, downstaging and downsizing.

The present study investigates the influence of preoperative radiotherapy on local symptom control and the improvement of the quality of life prior to surgery.

**PATIENTS AND METHODS**

In this study we included 49 patients with low rectal cancer, surgically treated at the III department of the 1st Surgical Clinic, Clinical Center of Serbia, between November 2004 and August 2006. Eligibility criteria included potentially resectable low rectal cancer and biopsy-proven adenocarcinoma. Exclusion criteria were: previous chemoradiotherapy treatments, evidence of metastatic disease and the recurrent disease.

All of them were diagnosed with T3 and T4 low rectal cancer, and were included in the protocol for the long term preoperative radiotherapy treatment (45Gy in 20-25 fractions).

High-energy photon radiation was delivered preoperatively using a 10-mV to 15-mV linear accelerator (three and four field technique), followed by an elective operation 6-10 weeks after the completion of radiation.

There were 33 males and 16 females ranging in age from 27 to 75 (mean age 57) years. All patients had potentially resectable rectal tumors located within 10 (range 0-10) cm from the anal verge (mean distance 4 cm). Patient characteristics are presented in table 1.

Pretreatment evaluation included a thorough medical history, physical examination, radiological examination, abdominal US, pelvic CT scan in all, and NMR in most of them, and the assessment of tumor characteristics by digital examination, rigid rectosigmoidoscopy, and biopsy.

Patients were followed for 2-50 months after the surgery (median 21.18 months).

The complete results of this study will be published additionally.

Patients who fulfilled the criteria were interviewed before and after the radiotherapy in order to compare any change in personal experience of the quality of life and the severity of symptoms of the illness. The details of the questionnaire involving chief complaints are listed in table 2.
RESULTS:

The most often complaint was the presence of blood in stool in various forms, including severe rectorrhagia, occasional presence of it, or even bleeding joined with abscess and fistula formations, as presented in table 3.

After the radiotherapy there was no apparent bleeding in 57.14% of patients (Chart 1), showing the statistical significance by McNemar test; $c^2=23.3103$, $p=1.379\times10^{-6}$

Pelvic and/or abdominal pain was reported by 21 (42.85%) patient, as shown in table 4 and chart 2.

Before RT 39 (79.59%) of our patients complained of tenesmus (straining), which, after the completion of RT, is lost in significant number of patients (18 (36.73%).

(Chart 3)

Change in bowel movement was as presented in table 5.

Due to the retrospective part of the study, we had no written information about the bowel function in six patients who were lost from the follow up.

After the radiotherapy there was significant normalisation of defeication in 28% of patients.

The more detailed presentation of bowel function alteration is presented in chart 4.

Shortly, by comparing symptoms and signs before and after radiotherapy, we see the significant decrease in patients complaints and improvement in the quality of life. (Table 6, chart 5)

COMPLICATIONS OF RT

During and after the radiotherapy we followed the urinary function and changes on the skin of the patients. There were 11 patients (22.45%) with urinary dysfunction, 9 of those with disuria, 1 with haematuria and 2 with urinary retention requiring intermittent catheterisation.

Changes on the skin were seen in 29 (59%) patients, 27 of those had redness of the skin with a slightly burning discomfort in the gluteal area and 2 had second degree burns requiring more attention and regular dressing.

DISCUSSION

Neoadjuvant radiotherapy has been used to enhance the resectability of the locally advanced rectal cancer, potentially increase the number of sphincter saving procedures, decrease the pelvic recurrence rates and improve overall survival. The reported advantages of preoperative radiotherapy are a reduction in tumor volume (downsizing) and in the clinical pathologic stage of the primary tumor (downstaging)6-15.

The positive effects of RT on local status of the tumor can be estimated by various means, including CT, NMR imaging, endorectal ultrasound, but, before all that, by simple digital rectal examination and above all, subjective experience of the patient.

Sometimes the patients feel so much better after the RT that they even question the necessity of the following surgery. From their point of view the pore quality of life was what brought them to their doctor in the first place. Some studies have been conducted in order to estimate the actual necessity of the surgery after the complete clinical re-
response of the primary tumor to RT. In these trials it is usually the initial stage of the tumor (T1, T2) that could respond completely to RT. But, in advanced rectal cancer, in spite of all the diagnostic methods, we cannot be completely sure that there are no malignant cells still present in the irradiated tissue of the apparently fibrozed tumor.

Therefore, RT is used mostly for the demarcation of the tumor from the surrounding structures, increase in radicality of the resection and for the improvement of the sphincter preservation. In patients who have locally advanced tumor, RT can significantly improve the quality of life during the period prior to surgery.

None of our patients refused the surgery, and they were all operated on within 6-10 weeks period after the completion of RT3,15,16,17.

In our study, after the application of long term radiotherapy we had significant decrease in rectal bleeding and tenesmus as well as normalization of defecation, showing the positive effect of the radiotherapy in symptom relief. This has been characterized by many authors as positive effects of RT on local control and improvement in quality of life even in initially inoperable patients3,14,16,17, 18,19,20.

There was also some improvement in control of pelvic and abdominal pain, although the presence of pain usually speaks for locally advanced tumor infiltrating surrounding nerves or occluding the rectum.

The symptom relief can be attributed to the alteration in tumor structure, decrease of tissue fragility and its volume. Especially the decrease in straining shows that there is less irritation of the rectum by the tumor, along with the improvement of constipation or diarrhea, leading us to assume, even before imaging or any other examination that there may be a decrease in the volume, or even the stage of the tumor.

Reduction in bleeding, or complete cessation of it, speaks in favor of the lesser fragility and the fibrosis of the timorous tissue.

One of the most severe acute side effects reported by some authors was acute neurogenic pain in the lower lumbar region with or without radiation to the legs, which can disable patients for a long time, and was observed in 10% of patients in varying degrees.

The authors from the Dutch colorectal group published their results explaining that in this case the upper border of the target volume should be lowered in order to decrease this side effect, and that the completion of radiotherapy should be aimed19,21.

In our study, luckily, there were not so severe side effects of the irradiation. Only 22.45% of patients with advanced rectal cancer complained of urinary dysfunction during or after the therapy and the changes on skin were successfully treated by topical application of ointments.

**CONCLUSIONS**

Preoperative RT has an important role in advanced rectal cancer treatment. Apart from the all the advancements of imaging and operative techniques, it is the patient’s quality of life that counts as well as the subjective experience of the illness.

**TABLE 2**

<table>
<thead>
<tr>
<th>CHIEF COMPLAINTS</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of blood in stool</td>
<td>occasional, rectorrhagia, abscess, fistula formation</td>
<td>absent</td>
</tr>
<tr>
<td>Pain (abdominal or pelvic)</td>
<td>only during defecation</td>
<td>present</td>
</tr>
<tr>
<td>Tenesmus (staining)</td>
<td>present</td>
<td>present</td>
</tr>
<tr>
<td>Bowel movement alteration</td>
<td>narrowing of the stool caliber</td>
<td>constipation</td>
</tr>
<tr>
<td></td>
<td>normal movement with the use of laxatives</td>
<td>interchanging periods of diarrhea and constipation</td>
</tr>
</tbody>
</table>

**TABLE 3**

<table>
<thead>
<tr>
<th>FORMS OF PRESENTATION OF BLOOD IN STOOL</th>
<th>Before radiotherapy</th>
<th>After radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of blood in stool</td>
<td>Absent 6 (12.24%)</td>
<td>33 (67.35%)</td>
</tr>
<tr>
<td></td>
<td>Present 43 (87.76%)</td>
<td>16 (32.65%)</td>
</tr>
<tr>
<td></td>
<td>Occasional 36 (73.47%)</td>
<td>12 (24.49%)</td>
</tr>
<tr>
<td></td>
<td>Rectorrhagia 2 (4.08%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td></td>
<td>Abscess/fistula 5 (10.2%)</td>
<td>4 (8.16%)</td>
</tr>
</tbody>
</table>

**TABLE 4**

<table>
<thead>
<tr>
<th>PRESENCE OF PELVIC AND/OR ABDOMINAL PAIN</th>
<th>Before radiotherapy</th>
<th>After radiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Absent 28 (57.14%)</td>
<td>35 (71.43%)</td>
</tr>
<tr>
<td></td>
<td>Present 16 (32.65%)</td>
<td>10 (20.41%)</td>
</tr>
<tr>
<td>Only while defecating</td>
<td>5 (10.20%)</td>
<td>4 (8.16%)</td>
</tr>
</tbody>
</table>
We must not forget one of the first lectures from the propedeutics: well taken patient history is half the diagnosis. The alteration in symptoms after the RT must not be neglected, but accepted and considered as an important sign of the tumor response to RT. Our study shows that by RT significant local control of the tumor can be reached along with the improvement in symptoms. Normalization of defecation and decrease in bleeding may even speak in favor of RT as the primary mean of palliative procedure in inoperable patients, postponing the moment when derivative ostomies may be necessary and allowing the patients more dignified lifestyle.

### TABLE 5

**ALTERATION IN BOWEL MOVEMENT**

<table>
<thead>
<tr>
<th>Change in bowel movement</th>
<th>Before RT</th>
<th>After RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avscent</td>
<td>8 (16.33%)</td>
<td>21 (42.86%)</td>
</tr>
<tr>
<td>Present</td>
<td>35 (71.43%)</td>
<td>22 (44.90%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (12.24%)</td>
<td>6 (12.24%)</td>
</tr>
</tbody>
</table>

### TABLE 6

**SUMMARY OF THE SYMPTOMS BEFORE AND AFTER RT**

<table>
<thead>
<tr>
<th>Chief complaint</th>
<th>Before RT</th>
<th>After RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of blood in stool</td>
<td>43 (87.75%)</td>
<td>16 (32.65%)</td>
</tr>
<tr>
<td>Pain</td>
<td>22 (44.89%)</td>
<td>14 (28.57%)</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>39 (79.59%)</td>
<td>18 (36.73%)</td>
</tr>
<tr>
<td>Alteration in bowel movement</td>
<td>35 (71.42%)</td>
<td>22 (44.90%)</td>
</tr>
</tbody>
</table>

### TABLE 6

**COMPLICATIONS OF RADIOTHERAPY**

<table>
<thead>
<tr>
<th>Complications</th>
<th>Pts</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>disuria</td>
<td>9</td>
<td>18.36</td>
<td></td>
</tr>
<tr>
<td>haematuria</td>
<td>1</td>
<td>2.04</td>
<td></td>
</tr>
<tr>
<td>urinary retention</td>
<td>2</td>
<td>4.08</td>
<td></td>
</tr>
<tr>
<td>Skin lesions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st degree burns</td>
<td>27</td>
<td>55.10</td>
<td></td>
</tr>
<tr>
<td>2nd degree burns</td>
<td>2</td>
<td>4.08</td>
<td></td>
</tr>
</tbody>
</table>

We must not forget one of the first lectures from the propedeutics: well taken patient history is half the diagnosis. The alteration in symptoms after the RT must not be neglected, but accepted and considered as an important sign of the tumor response to RT.

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### SUMMARY

**UTICAJ DUGOTRAJNE RO TERAPIJE NA SIMPTOME UZNAPREDOVALOG PRIMARNOG REKTALNOG KARCINOMA**

Ova studija je deo kliničkog ispitivanja preoperativne radiotherapije niskog karcinoma rektuma, koja je sprovedena kao prospektivna i delom retrospektivna klinička studija. Dizajnirana je u cilju određivanja uticaja preoperativne radiotherapije na simptome lokalno uznapredovalog karcinoma rektuma. Uključili smo 49 pacijenata T3/4 stadijuma adenokarcinoma rektuma (klinički, patohistološki i CT potvrđenih dijagnoza) distalne dve trećine rektuma, koji su preoperativno tretirani dugotrajnom radiotherapijom (45 Gy u 20-25 frakcija). Pacijenti su ispiti-vani o prezentaciji simptoma pre i posle zračenja. Glavne tegobe pacijenata bile su prisustvo sveve krvi u stolici, bol u trbuhi i karlici, lažni pozivi na pražnjenje (tenezmi) i promene u ritmu pražnjenja. Nasli smo značajno smanjenje simptoma i znakova bolesti posle radiotherapije, kao i poboljšanje kvaliteta života.

**Ključne reči:** dugoročna preoperativna radiotherapija, carcinom rektuma, simptomi, znaci

### REFERENCE


Influence of long term Ro therapy on symptoms and signs of locally advanced primary rectal cancer