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Rectal Cancer Treatment and Survival – Comparison of Two 5 – Year Time Intervals

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A B S T R A C T

In last two decades there was a huge step forward concerning rectal cancer treatment. The aim of our study was comparison of two time intervals regarding the methods of treatment and results of radical rectal cancer surgery. 407 patients operated on for rectal cancer were included in study. Those were patients with elective radical resection of solitary rectal tumor who survived first month after the operation. Patients were divided in two groups regarding the time of operation. In group one were patients operated on between 1996 and 2000 and in group two patients operated on between 2001 and 2005. We compared our results in both intervals with special interest about type of operation considering localization of the tumor, local recurrence and cancer related survival. Significant differences were found between two groups. There were more sphincter saving operations in second group, less local recurrences and better survival than in first group. This study observed significant improvements at recurrence rates and total survival for patients operated on rectal cancer.

Key words: *rectal cancer, rectal surgery, mortality, recurrence, locoregional neoplasm, survival*

Introduction

Rectal cancer has become one of the most frequent types of cancers among men and women in the majority of European industrialized countries and represents an important factor of morbidity and mortality.

Presently, it accounts for one third of all colorectal carcinomas. In Slovenia during 2004, we diagnosed 582 patients with carcinoma of the rectum and rectosigmoid colon[1].

Despite all progress in the development of conservative therapy (i.e., radiation and chemotherapy), radical surgical removal of the tumor is the only chance of permanent cure of the disease. Survival is also directly connected with the stage of the tumor, assessed by indicating the depth of penetration of the tumor into the bowel wall (T stage), the extent of lymph node involvement (N stage), and the presence of distant metastases (M stage). All those are the major threats for patients afflicted, leading to locoregional as well as distant recurrences.

The highly disappointing rates of local failure after curative resection in rectal cancer not only led to the development of adjuvant therapies but were also a strong motor for surgical refinements. Although the importance of clear distal, proximal, and circumferential margins and proposals to achieve them were postulated long ago, it took more than a decade to integrate those principles, performed as total mesorectal excision (TME), into surgical routine in curative resections of cancer of the mid and lower third of the rectum[2–7]. In the meantime, not only expert series on the benefits of total mesorectal excision have been published. It has been stated that surgical teaching initiative had a major effect on cancer outcomes. The proportion of abdominoperineal procedures and the local recurrence rate decreased by more than 50% and there is already evidence of a decline in rectal-cancer mortality. Regional or even nationwide surveys as well have documented a marked decrease of local recurrences up to 50% and potentially even a survival benefit[8–12].

Adjuvant systemic therapy for rectal and colon cancer was introduced by a national consensus conference in the USA in 1990. Shortly thereafter and mainly based on two rather small trials, the postoperative simultaneous com-

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bination of radiotherapy and chemotherapy became a standard in most western countries, as a survival benefit of up to 20–40% seemed achievable by combined modality treatment[13–15]. In 1994, continuous application of 5-Fluorouracil (CI) proved to be superior given simultaneously to adjuvant radiation. As uncomplicated central venous access lines nowadays are broadly available and due to its favorable toxicity profile, CI is an established standard, although the survival benefit attributed to it could not be reproduced in the recently published GI INT 0144 study on more than 1,900 patients[16–17]. A further change of the strategy was introduced by a large phase-III study demonstrating the superiority of preoperative over postoperative chemoradiation in terms of local recurrence rates (6 *vs*. 13%) as well as severe late side effects (14 *vs*. 24%). The risk of overtreatment of up to 20% of the patients due to inadequate preoperative staging inherent in this strategy was considered to be acceptable[18].

Materials and Methods

From 1996 data of all rectal cancer patients are simultaneously registered in specially designed protocols which contain preoperative, operative and postoperative part and detailed pathological report. Data of all patients operated on between January 1996 and December 2005 were analyzed. In this period 628 patients with rectal carcinoma were operated on but only 406 patients were eligible for study which included patients with elective radical resection of solitary rectal tumor who survived first month after the operation.

The ten year period 1996–2005 was divided in two time intervals. First 5-year interval between 1996–2000 and second interval between years 2001–2005. It was in the year 2000 when we have started more profound with TME surgical technique and also with neoadjuvant therapy which had represented in those times mostly short term preoperative radiotherapy.

We compared our results in both intervals with special consideration about the type of operation considering localization of the tumor, local recurrence and cancer related survival.

TNM staging system for rectal cancer was used during this study. All patients underwent liver ultrasound and chest radiogram before surgery and border cases were further examined using a CT scan. Final liver status has been confirmed by bimanual intraoperative palpation or even intraoperative ultrasound.

The majority of operations were performed by abdominal surgeons with a special interest in colorectal surgery.

The surgical procedure was termed curative if there was complete macroscopic removal of the tumor, as con-

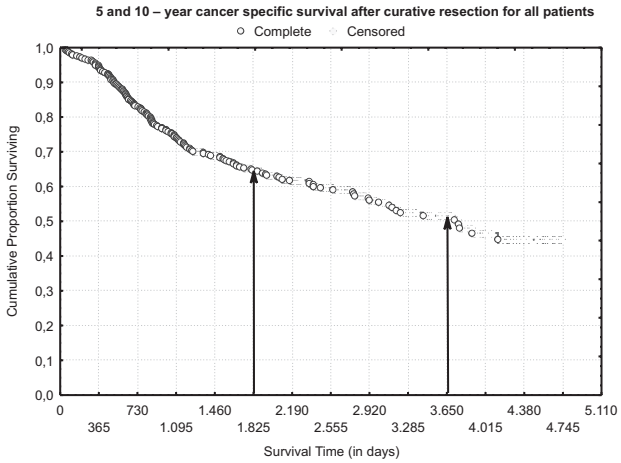

Fig. 2. 5 and 10 – year cancer specific survival after curative resection for all patients.

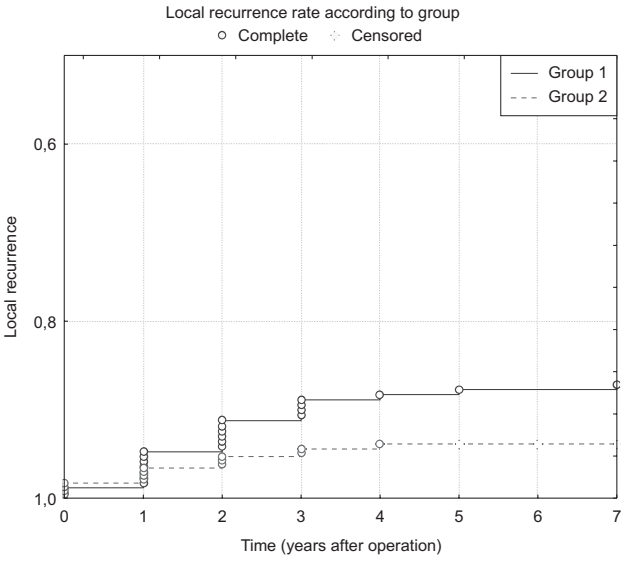

Fig. 1. Local recurrence rate according to group.

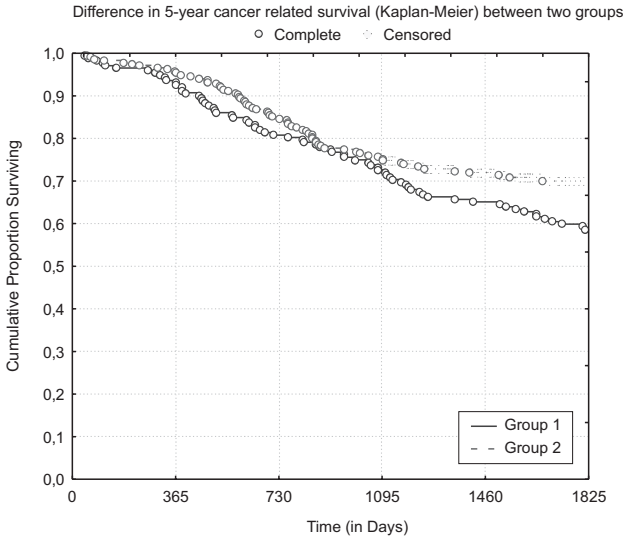

Fig. 3. Difference in 5-year cancer related survival (Kaplan-Meier) between two groups.

firmed by a pathologist, and there were no signs of metastatic disease. The radicality of the operation was accessed according to R classification, which was confirmed in 1987 by UICC.

All patients were followed up on a regular basis according to our national recommendation: at 3 month intervals during the first two years, at 6 month intervals until the5th year, and then annually[19]. Clinical examination, tumor markers (CEA and CA19-9) and ultrasound were performed at each appointment. A chest X-ray was performed every 6 months during the first two years and then annually. Colonoscopy was performed once a year after the operation. Follow up was updated on December 31st 2008.

Recurrence was defined as cancer detected in the pelvis regardless of whether some other metastases were found in other tissues or organs. Isolated local recurrence was defined as cancer detected in the pelvis only. Distant metastases were defined as tumor recurrence outside the pelvis and included metastases of the liver, lungs, bones or brain.

Data concerning death was acquired from the Slovenian cancer register, and the cause verified for cancer specificity for each deceased patient[20].

Survival was calculated using the Kaplan-Meier method and compared using the log-rank test. All analyses were performed using statistical SPSS software for Windows 10.0.

Results

Between 1996 and 2005 we operated on 628 patients with rectal cancer. The number of patients operated on fluctuated.

According to our criteria, we included 406 patients in study, which represented 66 percent of all those operated on. There were slightly more men (215) than women (191). The median age of the patients was 66, 9 years (range 29–93). All patients were divided in two groups. There were 172 patients who were operated on between year 1996 and 2000 and 234 patients operated on between 2001 and 2005. The percentage of eligible patients is higher in second group of patients (Table 1).

We can see clearly in Table 2 that in the second time interval there was a significant fall in number of mutilating operations such as abdominoperineal excisions (APE), and rise of sphincter preserving low anterior resections (LAR).

It is obvious that in first period between 1996 and 2000 (group 1) there were a lot of abdominoperineal excisions performed on. The number of those operations than decreases on account of low anterior resection operations. The difference is especially obvious at cancers located at middle third of rectum (Table 3). While in first period nearly half of patients with rectal cancer between 7 and 12 centimeters ended with stoma, in second period this rate falls to only 10 percent.

TABLE 1
NUMBER OF ALL PATIENTS OPERATED ON FOR RECTAL CANCER PER YEAR AND PERCENTAGE OF STUDY ELIGIBLE PATIENTS PER YEAR AND TIME PERIOD

Year	Number of all patients	Number of patients eligible for study	Percent of eligible patients (%)
1996	43	27	62.79
1997	54	36	66.67
1998	78	46	58.97
1999	52	31	59.62
2000	62	32	51.61
1st interval together	289	172	59.52
2001	73	51	69.86
2002	58	35	60.34
2003	84	58	69.05
2004	60	45	75.00
2005	64	45	70.31
2nd interval together	339	234	69.03

TABLE 2
NUMBER AND PERCENTAGE OF OPERATIONS ACCORDING TO GROUPS

	Group 1 (1996–2000)	Group 2 (2001–2005)
Low anterior resection	75 (44%)	153 (66%)
Abdominoperineal excision	88 (51%)	62 (26%)
Low anterior resection with stoma	5 (3%)	10 (4%)
Other	4 (2%)	9 (4%)

TABLE 3
TYPE OF OPERATION ACCORDING TO GROUP AND DISTANCE OF THE TUMOR FROM ANOCUTANEAL VERGE

Location of tumor	0–7 cm		7–12 cm		12–15 cm	
	Group 1	Group2	Group1	Group2	Group1	Group2
	N=63	N=98	N=63	N=78	N=46	N=58
Technique						
LAR	1 (1.6 %)	33 (34%)	31 (49%)	66 (85%)	43	54
APE	58 (92%)	53 (54 %)	30 (48%)	8 (10%)	0	0

The rate of local recurrence (LR) was 9.11% for all patients in study. In first group there were 22 local recurrences or 12.8% and in second group 15 patients with LR (6.4%). There was significant difference between both groups ($p<0.005$).

Patients in group 2 had better 5-year cancer specific survival –69% and patients in group 1 only 59% ($p<0.005$).

Discussion and Conclusion

In the recent 20 years, improvements have been reached in the outcomes of colorectal surgery with the better diagnostic and staging methods, advances in surgical techniques as well as adjuvant therapy[20,21].

According to our results, there was a significant increase in the number of radical operations. In second period the rate of curative resections was 10 percent higher than five years before. We believe that this is the result of better preoperative staging, better operative technique and of course result of positive effect of preoperative chemoradiotherapy. Many tumors, first valued as non resectable could have been resected after downsizing and downgrading effect of oncological therapy.

The results of our study have shown a significant trend over the ten year period towards the better prognosis for patients with rectal cancer.

It is difficult to ascribe improvements demonstrated in our study to one single factor. More likely they have resulted from a number of changes[22]. One of them is surely a shift in operating mode from abdominoperineal excision towards low anterior resection.

Many studies stated that local recurrence and survival rates after anterior resection have improved to the higher degree as that seen with abdominoperineal excision of the rectum and anus[23,24]. The difference in outcome may be explained by a combination of the anatomic and surgical difficulties associated with standard APE surgery.

Our results show that in short period we manage to diminish the share of APE for nearly 40 percent for patients with rectal cancer in the middle third of rectum and this could be an important factor in overall improvement.

Another issue, closely related to operative management, is introduction of total mesorectal excision, a technique which improved the local recurrence control and survival all over the world[25].

In recent years neoadjuvant therapy made a huge step forward. Nowadays all of our patients with stage 3 and some with stage 2 rectal cancers receive neoadjuvant therapy which became standard in treatment of rectal cancer. Together with adjuvant treatment it is indispensable in rectal cancer treatment.

The improvements in survival and local recurrence control may also reflect better quality staging and histological review. More accurate staging through the detection of metastases or nodal disease could create a noticeable improvement in results. Pathologists now have a standardized reporting procedure and improved staging can select out poor prognostic patients, leading to apparent stage migration.

In conclusion we can stress that we have observed a significant improvements in rates of recurrence and in total survival after rectal cancer operations and we can say that our results are improving but there is still much work to do to be able to compare us with the world's leading centers for rectal cancer surgery.

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LIJEČENJE RAKA REKTUMA I STOPA PREŽIVLJAVANJA – USPOREDBA DVA VREMENSKA INTERVALA OD PET GODINA

S A Ž E T A K

U posljednja je dva desetljeća učinjen velik napredak u liječenju raka rektuma. Cilj našeg istraživanja bio je usporediti dva vremenska intervala s obzirom na metode liječenja i rezultate radikalne rektalne operacije. U studiju je bilo uključeno 407 pacijenata kojima je odstranjen rektalni tumor, a koji su preživjeli prvi mjesec nakon operacije. Pacijenti su podijeljeni u dvije skupine s obzirom na vrijeme operacije. U jednoj skupini bili su pacijenti operirani između 1996. i 2000. godine, a u drugoj pacijenti operirani između 2001. i 2005. godine. Usporedili smo dobivene rezultate s posebnim osvrtom na tip operacije i poziciju tumora, ponovno lokalno pojavljivanje tumora i stopu preživljavanja. Uočene su značajne razlike između dvije skupine. U drugoj je skupini bilo više pacijenata kod kojih je operacijom spašen sfinkter, kod kojih ima manje slučaja ponovnog lokalnog pojavljivanja tumora i koji imaju višu stopu preživljavanja. Iz naših rezultata možemo zaključiti da je vidljiv znatan napredak u stopi preživljavanja pacijenata koji boluju od raka rektuma, no još uvijek nas čeka mnogo posla dok se ne budemo mogli uspoređivati s najboljim svjetskim centrima za operativne zahvate vezane uz rak rektuma.