COMPARISON OF COLORECTAL CANCER FEATURES DURING THREE PERIODS IN HOSPITAL CANCER REGISTRY

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SUMMARY – The aim of the study was to analyze the possible effects of the 1991-1995 war in Croatia on the localization, age and sex distribution and stage of colon cancer. Three periods were analyzed: distant prewar (1982-1983), immediate prewar (1989-1990) and postwar (1998-2000) periods. Patient data were obtained from the computer based colorectal cancer registry established at the Department of Pathology. There was a statistically significant increase in the number of cases with right-sided colon involvement during the postwar period (p<0.01). A shift from the 60-69 to 70-79 age group was observed during the postwar period. There was no statistically significant difference in age and sex distribution of tumors. Concerning TNM staging, patients presented in more advanced stages in the postwar period (p<0.01). A similar difference was also recorded by comparing Dukes' stages during the three periods of observation (p<0.01). Results of the study pointed to an increasing prevalence of right-sided colon carcinoma. Towards the end of the overall period of observation, patients tended to present in more advanced stages of the disease. These changes could have probably be, at least in part, attributed to the impact of war.

Key words: *Colon, pathology; Colonic neoplasms, epidemiology; Rectal neoplasms, epidemiology; Rectal, pathology; War; Croatia*

Introduction

Colorectal carcinoma is one of the most prevalent tumors in the western world, accounting for about 150,000 new cases and causing more than 60,000 deaths *per* year only in the US[1]. It is only second to lung carcinoma in the overall prevalence and death incidence. Colorectal carcinoma shows strong correlation with industrial development of the area. The highest incidence rates are found in western Europe, North America, Australia and New Zealand, intermediary rates in eastern Europe, while lowest incidence is recorded in Africa, Asia and South America[2].

However, there have been some interesting trends in the past few decades related to the changing anatomical location of colon carcinoma presentation. An increase in the incidence of right-sided colonic cancer and a decrease in the incidence of rectosigmoid cancer have been observed[3]. As far as Croatia is concerned, colorectal carcinoma is the second most common tumor in females, immediately after breast carcinoma, with an overall incidence of 30.1/100,000 (1988-1991)[4]. In males, colorectal carcinoma is the fourth among the five most common tumors, with an overall incidence of 31.1/100,000 (1988-1991)[4]. However, in the year 1998, the overall incidence substantially increased to 40.1/100,000 and 52.9/100,000 in females and males, respectively[5].

The war in Croatia raged from 1991 till 1995. Although our population belongs to the eastern European group according to the incidence of colorectal carcinoma, great socioeconomic changes induced by the war probably modified the pathologic features of the disease. Therefore we designed, in continuation of our previous studies[6,7], a study aimed at analyzing the possible impact of war on the colorectal carcinoma features. Three periods were investigated: distant prewar (1982-1983), immediate prewar (1989-1990), and postwar (1998-2000) periods.

Patients and Methods

A total of 1367 patients with colorectal cancer were analyzed. For the purpose of this study, the patients were divided into three groups according to the year of primary tumor diagnosis within either of the three time periods relative to the war in Croatia (1991-1995): distant prewar (1982-1983), immediate prewar (1989-1990), and postwar (1998-2000) periods. Patient data were obtained from the computer based colorectal cancer registry established at the Ljudevit Jurak University Department of Pathology, Sestre milosrdnice University Hospital, Zagreb. The database contains personal data on each patient (personal identification number, date of birth, age at diagnosis, and sex), pathologic diagnosis, and macroscopic and microscopic findings. The following parameters were analyzed for each individual patient: anatomical site (localization) of large bowel cancer, age and sex distribution, and anatomical spread of the disease (stage). The site of pathologic lesion, spread through the intestinal wall, presence of lymph node, and distant organ metastases were determined according to macroscopic description of the specimen in the pathologic report. For the purpose of the study, large bowel was divided into four segments: cecum and ascending colon, hepatic flexure with transverse colon, splenic flexure with descending colon, and rectosigmoid colon (sigmoid colon, rectosigmoid junction and rectum). For tumor staging, all biopsy findings from immediate prewar period (1989-1990) and postwar period (1998-2000) were revised, and Dukes' and TNM classification was determined whenever possible[8]. The 1932 Dukes' classification of colorectal cancer was used[9]. Biopsy findings from distant prewar period (1982-1983) had already been classified according to original Dukes' classification from the year 1958[10], and were not reclassified because the computer base did not contain data on these patients.

Statistical analysis was performed by use of the SPSS (Statistical Package for Social Sciences) program on an IBM PC/AT computer. The frequencies observed were tested by χ^2-test at the level of significance of p<0.01.

Results

A total of 1367 patients were analyzed across three different periods of time according to the war in Croatia. The patients were divided into three groups according to the age at primary tumor diagnosis within either of the three time periods observed: distant prewar (1982-1983), immediate prewar (1989-1990), and postwar (1998-2000) periods. Rectosigmoid cancer was the most common localization of large bowel cancer in all the three periods (Table 1), however, the prevalence of cancer in the rectosigmoid region significantly decreased during the overall period of observation, i.e. from 93.8% in the 1982-1983 period to 68.9% in the 1998-2000 period (p<0.01). In contrast, the prevalence of ascending colon cancer increased from 3.1% in the 1982-1983 period to 13.3% in the 1998-2000 period (p<0.01) (Fig. 1).

Age distribution of colorectal cancer could be analyzed in a total of 1297 cases (Table 2). A minor male predominance was recorded in all the three periods of observation, with the F/M ratio of 1/1.8, 1/1.1 and 1/1.4 in distant prewar, immediate prewar and postwar period, respectively (Table 3). The 60-69 age group was most commonly involved in distant prewar (1982-1983) and immediate prewar (1989-1990) period (30.6% *vs.* 33.5%). However, during the postwar period (1998-2000), the 70-79 age group was found to be most commonly affected (34.9%), followed by the 60-69 age group (31.8%). In all three periods, more than 80% of cases were diagnosed between the age of 50-80 (Fig. 2). Sex distribution showed no statistically significant differences in any of the periods of observation.

Pathologic TNM staging of colorectal carcinoma during two different periods of time (immediate prewar and postwar periods) is shown in Fig. 3. For the immediate prewar period (1989-1990), TNM stage could be determined in 189 cases. The most common tumor stage was T3N0MX (30.2%), followed by T2N0MX (28.0%). In the postwar period (1998-2000), T3N0MX and T2N0MX were most common stages again (26.5% and 18.6%, respectively), recorded in 456 determinable cases. Comparison of the prewar and postwar periods revealed the rate of tumor diagnosis at an advanced stage to sig-

Table 1. Anatomical localization of colorectal cancer according to study periods

| Localization | Time period | | | | | |
| | 1982-1983 | | 1989-1990 | | 1998-2000 | |
	n	%	n	%	n	%
Ascending colon	10	3.1	26	9.1	101	13.3
Transverse colon	5	1.6	18	6.3	21	2.8
Descending colon	4	1.2	11	3.9	115	15.1
Rectosigmoid colon	302	93.8	230	80.7	524	68.9
Total	321	100.0	285	100.0	761	100.0
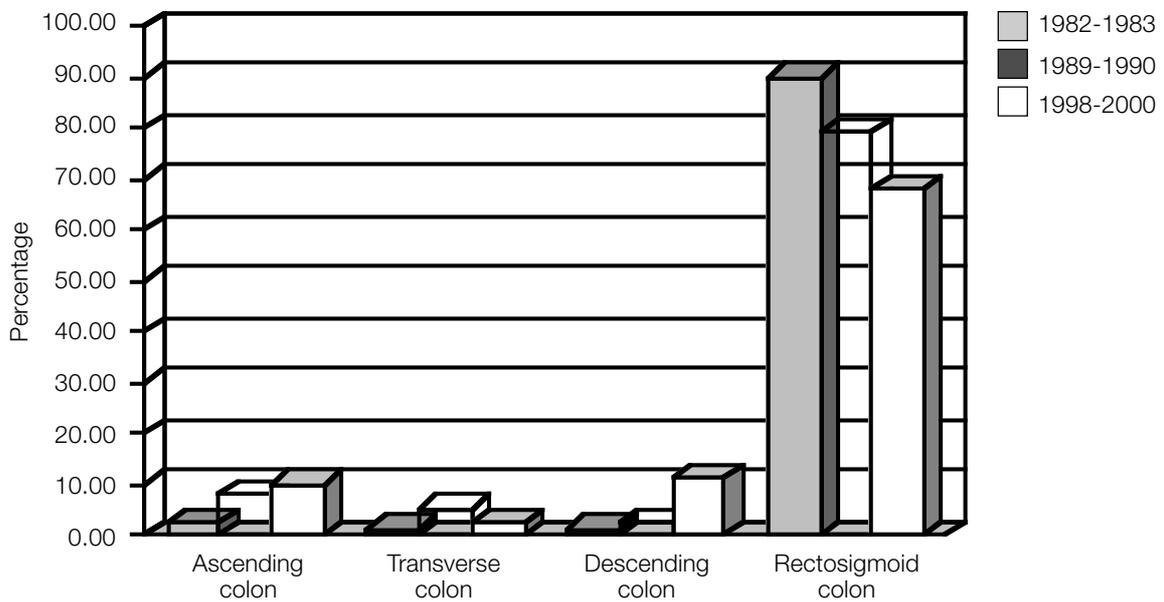
Fig. 1. Localization of colorectal cancer

Table 2. Age and sex distribution of colorectal cancer according to study periods

| Age group (yrs) | Study period | | | | | | | | |
| | 1982-1983 | | | 1989-1990 | | | 1998-2000 | | |
	M	F	Total	M	F	Total	M	F	Total
0.-9	0	0	0	0	0	0	0	0	0
10-19	0	1	1	0	0	0	0	0	0
20-29	1	3	4	2	0	2	1	0	1
30-39	1	6	7	1	5	6	11	8	19
40-49	19	13	32	8	10	18	23	17	40
50-59	35	41	76	37	24	61	74	44	118
60-69	51	44	95	52	52	104	134	88	222
70-79	52	27	79	28	31	59	137	107	244
80-89	9	6	15	11	8	19	25	23	48
90-99	0	1	1	0	1	1	3	4	7
Total	168	142	310	139	131	270	408	291	699

Table 3. Female to male (F/M) ratio according to study periods

	Study period		
	1982-1983	1989-1990	1998-2000
F	142	131	291
M	168	139	408
F/M	1/1.18	1/1.06	1/1.4

determined in a total of 195 patients. The most common stage was Dukes B (34.9%, n=68), followed by Dukes A (34.4%, n=67) and Dukes C (26.2%, n=51). In the post-war years, a total of 509 cases were examined. The most common stage was Dukes C (40.5%, n=206), and comparison with the prewar period yielded a statistically significant difference (p<0.01).

Table 4. Dukes' classification of colorectal cancer according to sex

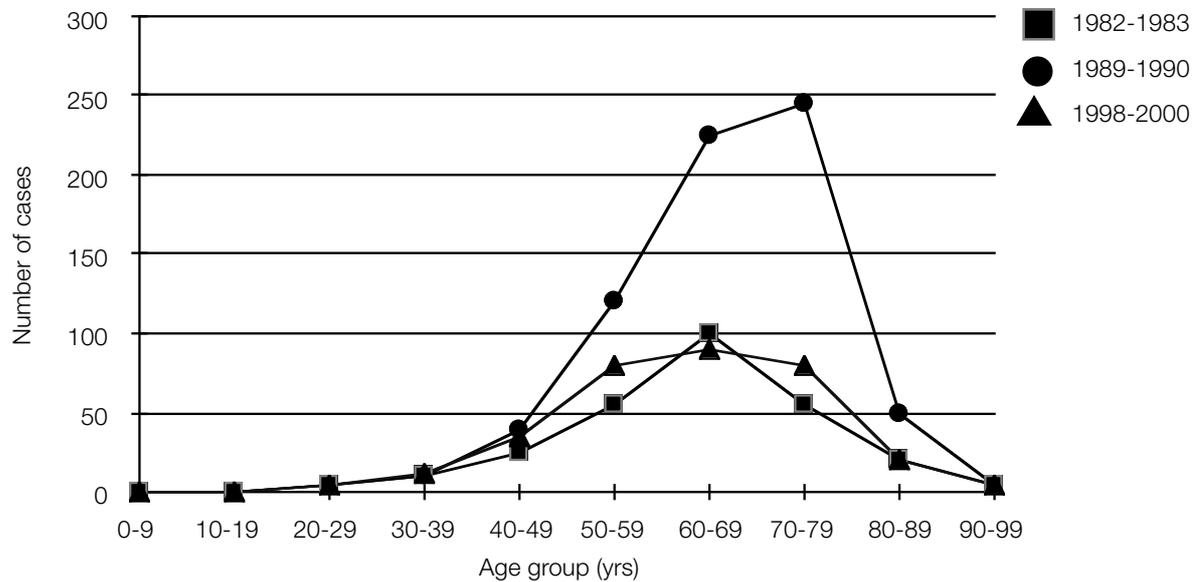| Dukes' stage	1990-1990						1998-2000					
	Male		Female		Total		Male		Female		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
A	36	18.46	31	15.89	67	34.35	84	16.50	55	10.81	139	27.31
B	31	15.89	37	18.97	68	34.87	87	17.09	54	10.61	141	27.70
AC	6	3.07	3	1.54	9	4.61	18	3.54	5	0.98	23	4.52
C	32	16.41	19	9.74	51	26.15	111	21.81	95	18.66	206	40.47
Total	105		90		195		300		209		509	

Fig. 2. Age distribution of colorectal cancer

nificantly increase with time. So, stage T3N2MX accounted for 16.4% of the tumors diagnosed in the post-war years *versus* only 3.2% in the prewar years (p<0.01).

Dukes' classification of colorectal cancer is shown in Table 4 and Fig. 4. In the prewar period, Dukes' stage was

Discussion and Conclusion

The study included 1367 patients with the diagnosis of colorectal carcinoma. The source of data was the Department computer based colorectal cancer registry. The
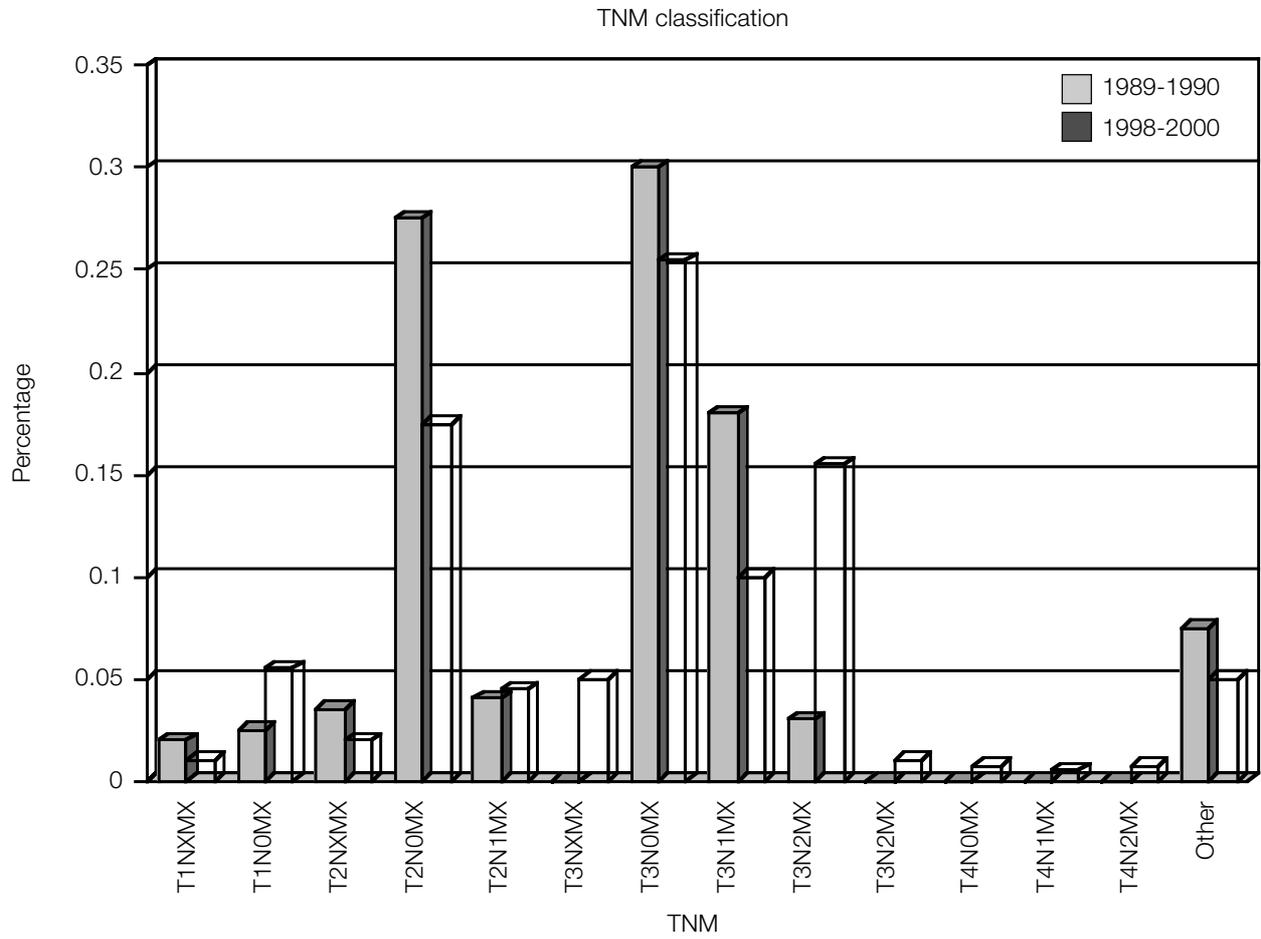
TNM classification
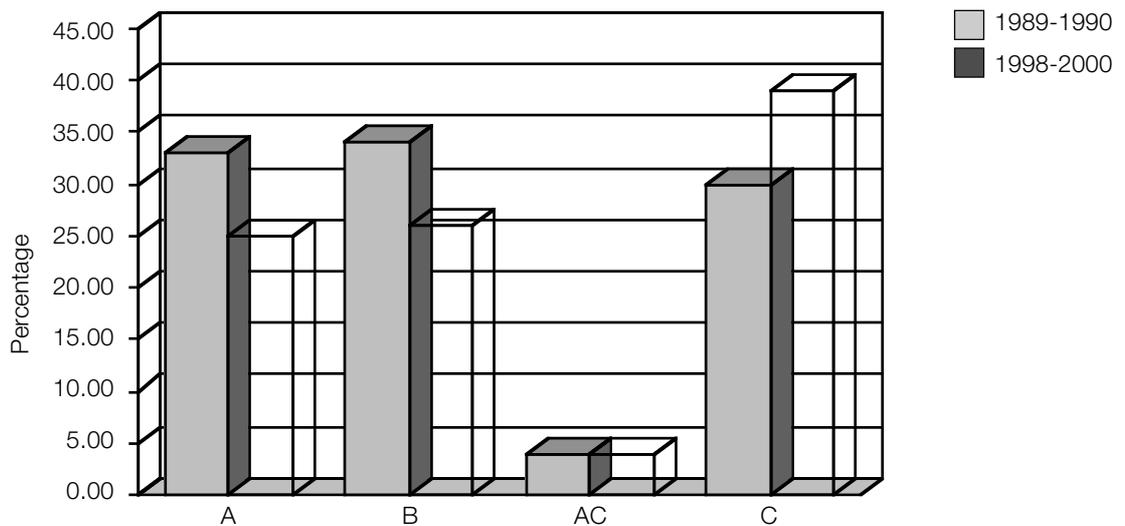

Fig. 3. TNM staging of colorectal cancer

Fig. 4. Dukes' classification of colorectal cancer

aim was to compare some colorectal cancer features (localization, age and sex distribution, and anatomical spread of the disease) during three different time periods (distant prewar, immediate prewar, and postwar periods), in order to assess the possible impact of war in Croatia (1991-1995) on these disease parameters. We also tried to compare the changes observed with similar colorectal cancer features reported worldwide[1-4]. Concerning localization of primary large bowel cancer, the rectosigmoid region was found to predominate in our population, as it was involved in a vast majority of cases. Comparison of distant prewar period, when 93.8% of cases were detected in the rectosigmoid region, with the other two periods revealed a decreasing tendency in the immediate prewar and postwar periods (80.7% and 68.9%, respectively). In contrast, the number of cases diagnosed in the region of ascending colon and cecum increased from distant prewar (3.1%) through immediate prewar (9.1%) to postwar (13.3%) period. These results confirmed the global trend reported elsewhere, according to which the localization of colorectal carcinoma has been shifting rightwards, proximally to the intestine[11,12]. These modifications could partly be due to advances in the field of diagnostic tools over the last few decades, helping clinicians in population screening for adenomatous colon lesions now considered precursors of colon cancer. This especially holds for distal large bowel (rectosigmoid region), which has become more easily accessible by these techniques than the right side of the colon. Meticulous investigations of the mechanism of molecular progression of colorectal cancer have revealed a direct polyp − adenoma − carcinoma sequence[13,14].

Age distribution showed no significant sex difference, and confirmed that colorectal cancer is primarily a disease of elderly population. In both distant and immediate prewar periods, the majority of cases were diagnosed in the 60-69 age group, with a shift to the 70-79 age group during the postwar period, which might be explained by the impact of the 1991-1995 war in Croatia. The war caused deterioration of socioeconomic conditions, which may have resulted in delayed (according to both age and stage of disease) presentation of patients with colorectal cancer.

The results on sex distribution and M/F ratio showed a slight male predominance in all three study periods, which did not reach statistical significance and was consistent with literature data[1,2,4].

Anatomical spread of the disease was assessed by use of two classification systems, TNM staging and Dukes' classification. Two time periods were compared, i.e. immediate prewar and postwar period. In postwar period, patients with large bowel cancer more commonly presented in an advanced stage of the disease than in the prewar period. In postwar period, there were 40.5% of Dukes' C stage as compared with 26.2% in prewar period. TNM classification showed T3N0MX tumor stage to be most common in both study periods, followed by T2N0MX. In postwar period, there were significantly more cases diagnosed at advanced T2N0MX stage than in prewar period (16.4% *vs.* 3.2%), which could be ascribed to the effects of war on the health care system.

In conclusion, the study pointed to significant modifications in the localization of primary bowel cancer, with a shift from the rectosigmoid region towards the right colon. Also, the patients appeared to present at a more advanced stage of disease and at an older age, which could probably be explained by poor socioeconomic conditions in Croatia due to the war. However, additional epidemiologic studies over a longer time span are needed to see whether or not these changes are of a continuous nature. Also, reasonable steps to better understand this pathologic entity would be genetic and molecular analysis of the population, along with evaluation of dietary habits and comparison with neighboring countries.

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Sažetak

USPOREDBA OBILJEŽJA KARCINOMA DEBELOG CRIJEVA U TRIMA RAZDOBLJIMA PREMA BOLNIČKOM REGISTRU ZA RAK

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Cilj istraživanja bila je analiza mogućih učinaka agresije na Hrvatsku tijekom razdoblja od 1991. do 1995. godine na lokalizaciju, spol i dob bolesnika te stadij karcinoma debelog crijeva. Analizirana su tri razdoblja: prijeratno (1982. - 1983.), neposredno prijeratno (1989. - 1990.) i poslijeratno (1998. - 2000.). Podaci o bolesnicima dobiveni su iz Registra kolorektalnog karcinoma koji je uspostavljen pri Zavodu za patologiju. Utvrđen je statistički značajan porast učestalosti raka u desnostranom debelom crijevu u poslijeratnom razdoblju (p<0,01). Ustanovljen je pomak učestalosti raka debelog crijeva iz dobne skupine od 60-69 godina u prijeratnom razdoblju na dobnu skupinu od 70-79 godina u poslijeratnom razdoblju. Nije bilo statistički značajne razlike u spolnoj distribuciji karcinoma debelog crijeva. Glede stadija TNM, utvrđeno je da se u poslijeratnom razdoblju statistički značajno veći broj bolesnika javlja u uznapredovalijim stadijima bolesti (p<0,01). Slična je razlika nađena i prema Dukesovoj klasifikaciji (p<0,01). Zaključeno je kako postoji povećanje broja slučajeva karcinoma desne strane debelog crijeva. U poslijeratnom razdoblju bolesnici se češće javljaju u uznapredovalom stadiju bolesti. Smatramo da se navedene pojave mogu barem djelomice pripisati učincima rata.

Ključne riječi: *Kolon, patologija; Neoplazme kolona, epidemiologija; Neoplazme rektuma, epidemiologija; Rektum, patologija; Rat; Hrvatska*