Increased Incidence of Colorectal Cancer in the Split-Dalmatia County: Epidemiological Study

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Aim. To investigate the incidence of colorectal cancer in the Split-Dalmatia County in the 1981-1998 period, and compare it with the incidence in the Republic of Croatia.

Methods. The data were obtained using case records and registries of all hospitals and Public Health Institute in the County and the Croatian Cancer Registry. Age-standardized incidence per 100,000 was calculated from the number of patients with colorectal cancer and the number of inhabitants.

Results. There were 2,454 new cases of colorectal cancer (1,383 men and 1,071 women) in the Split-Dalmatia County in 1981-1998. Colon cancer was diagnosed in 55% of the cases. Age-standardized incidence rates for colorectal carcinoma per 100,000 population were 11.4 (men 14.8, women 9.0) in 1981, and 63.5 (men 93.1, women 42.5) in 1998. The total incidence increased from 16.1 (colon cancer 7.9, rectal cancer 8.2) in 1981-1985 period to 52.8 (colon cancer 30.5, rectal cancer 22.3) in 1994-1998 period, or approximately 3.3 times. The colorectal cancer incidence rate in the Split-Dalmatia County increased from 16.2 in 1985 to 46.4 in 1995, and in whole Croatia from 32.4 in 1985 to 37.8 in 1995.

Conclusion. There was a great increase in the reported incidence of colorectal cancer in the Split-Dalmatia County in the 1981-1998 period. The relative increase of incidence in colorectal cancer was much greater in the Split-Dalmatia County than in Croatia as a whole. These changes call for preventive and screening measures for colorectal carcinoma.

Key words: colon; colorectal neoplasms; Croatia; digestive system diseases; gastrointestinal neoplasms; incidence; rectum

Colorectal cancer is one of the most common in the European Community, with estimated 169,400 new cases in 12 countries in 1990 (1). The cause of this cancer is not known, but diet and psychosocial status seem to have an important role in its etiology (2-11). In Europe, population-based data for colorectal cancer show that over the last 20 years the colorectal cancer mortality has been steadily declining, while its incidence has been increasing (12-14). This may be explained by significant improvements in early detection and therapy of this cancer (15-17). Many studies showed that the incidence rates of the colorectal cancer are lower in the southern countries of European Community (ie, Italy, Spain, and Greece) then in the nothern (1,13,14,18,19). Moreover, the incidence of this cancer differs between southern and northern regions within a country. For example, colorectal cancer is the major cause of death, with 12% of all deaths due to cancer in Italy, but the incidence is lower in southern regions (13,20). An increase in the age-standardized incidence of colorectal cancer by about 50% for women and 140% for men was reported for some southern Italian regions in 1970-1990, and these figures were higher than in northern regions (13).

There is a lack of similar data for countries in transition, where changes in the diet and especially psychosocial stress to the population are much more pronounced than in other European countries. In addition to the burdens of a transitional country, Croatia has also experienced a war (1991-1995), which was preceded by the economical and social crisis in the mid to late 1980’s. The only study published on the colorectal cancer incidence in Croatia reported an increase of colorectal carcinoma incidence from 13.6 in 1965 to 26 in 1982 (21).

The aim of the present study was to analyze the recent trend in the incidence of colorectal carcinoma in Split-Dalmatia County and compare it to the incidence in
Croatia as a whole. Since the County is situated in the southern part of Croatia, which is a typical Mediterranean region by its geographic and dietary characteristics, we expected the incidence to be lower there, by analogy to neighboring Italy. But to our surprise, the incidence of colon cancer in the County showed a sharp increase over the last 10 years and surpassed the incidence in the whole Croatia.

Patients and Methods

We studied 2,454 case records of colorectal carcinoma (1,383 men and 1,071 women) diagnosed in the Split-Dalmatia County between 1981 and 1998. The data were obtained from patient charts from two hospitals and all other medical institutions in the county, oncology lists of the Public Health Institute of the County, and the Croatian National Cancer Registry (22). In each hospital, forms with the patient charts data were obtained from the Public Health Institute for this period were not available. In the overlapping period, from 1987 to 1998, our local data showed similar trends as the Croatian Cancer Registry data. We presented only the latter for the consistency reasons. Those data included sex, number of patients with colorectal cancer for all towns (and municipalities) in the country, and site of lesion (colon or rectum only).

For comparison between the Split-Dalmatia County and Croatia as a whole, we used age-standardized incidence rates from the Croatian Cancer Registry.

Patients with secondary and relapse carcinoma and those residing in other counties were excluded from the data collected locally. Thus, the refugees from other regions of Croatia or neighboring Bosnia and Herzegovina were excluded. Furthermore, we checked for double registries, using name, sex, date of birth, and address. The study considered all cases of colorectal cancer as defined in the International Classification of Disease-9 (ICD-9, ICD code 153 for colon, and 154 for rectal cancer) (18,23).

The yearly incidence was obtained with regard to the year when the cancer was first diagnosed. Age-standardized incidence per 100,000 population was calculated from the number of patients with colorectal cancer and the number of inhabitants according to the last two censuses, in 1981 and 1991 (24,25), with interpolation (assuming the linear yearly increase) for all years. The incidence was also presented as a 3-year moving average to avoid year-to-year oscillations. The standardized incidence was obtained by direct standardization method according to European reference population (18).

According to the 1991 census, Split-Dalmatia County had 474,019 inhabitants (233,195 men and 240,824 women). Croatia as a whole had a population of 4,784,265 (2,318,623 men and 2,465,642 women), which means that the population of the Split-Dalmatia County made about 10% of the Croatian population.

The primary tumor sites of the cancer lesions studied from the patient charts and hospital records in 1987-1998 were grouped into the proximal colon (cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure), distal colon (descending colon, sigma), overlapping site, and rectum cancers (rectosigmoid junction and rectum) (23).

Table I. Annual changes in the colorectal carcinoma incidence in the Split-Dalmatia County in the 1981-1998 period

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| a | Per 100,000. | b | Age-standardized incidence per European population. | c | Ratio of crude incidence. |

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Results

In the 1981-1998 period, there were 2,454 patients with colorectal cancer (1,383 men and 1,071 women) in the Split-Dalmatia County. Colon carcinoma was diagnosed in 1,353 patients (717 men and 636 women), and rectal carcinoma in 1,101 patients (666 men and 435 women). The age-standardized incidence (Table 1) of colon carcinoma increased from 5.5 per 100,000 (5.9 for men vs 5.2 for women) in 1981 to 9.6 (10.5 vs 9.0) in 1989, and to 36.7 per 100,000 (50.5 vs. 27.4) in 1998. The incidence of rectal carcinoma increased from 5.9 per 100,000 (8.9 for men vs 5.2 for women) in 1981 to 8.0 per 100,000 (13.1 vs 4.0) in 1989, and to 26.8 (42.6 vs 15.1) in 1998.

There was a relatively greater increase in the incidence of colon carcinoma than rectal carcinoma. In men, this increase was 756% for colon carcinoma and 379% for rectal carcinoma, whereas in women, it was 427% and 227%, respectively. In both sexes and for both locations, there was a steeper slope on the curve starting approximately in the late 1980s and early 1990s. The 3-year moving average of crude incidence rates per 100,000 increased in all age groups, most sharply in the age group of >65 years (Figs. 1 and 2 for men, Figs. 3 and 4 for women). In this age group, the relative increase for colon carcinoma from 1982 until 1997 was 690% for men and 203% for women. For rectal carcinoma, the increase was 199% and 268%, respectively. In both sexes and for both locations, there was a steeper slope on the curve starting approximately in the late 1980s and early 1990s (Figs. 1-4).

The age-standardized incidence rates of colorectal cancer in the Split-Dalmatia County in 1985 were lower than in Croatia as a whole for both sexes (Table 2). In 1990, the incidence rates were greater in Croatia than in the Split-Dalmatia County for all groups, except for the rectal cancer in men. In 1995, the incidence rates in the Split-Dalmatia County were greater than in Croatia as a whole for all groups analyzed (Table 2).

With regard to the site of carcinoma, for the 1987-1996 period (Table 3), 91% of patients had a known carcinoma site. Rectal carcinoma was diagnosed in 45%, and colon carcinoma in 55%, out of which 48.6% had proximal colon carcinoma, and 51.4% had distal colon carcinoma.

Discussion

This study showed a great increase in the incidence of colorectal cancer in the Split-Dalmatia County from 1981 to 1998. In the 1985-1995 period, this increase was greater than in the Republic of Croatia as a whole. In 1985, the incidence of both colon carcinoma and rectal carcinoma was greater in the Republic of Croatia as a whole than in the Split-Dalmatia County for both sexes (Table 2). However, there was a complete reversal in 1995 and the incidence became higher in the Split-Dalmatia County for both colon carcinoma and rectal carcinoma, and for both sexes as well. Considering the location of the colorectal cancer, there was a relatively greater increase in the incidence of colon carcinoma than rectal carcinoma for both men and women in the Split-Dalmatia County.

One can argue that the increase in the incidence in colorectal cancer could be at least partially caused by the

Table 2. The incidence rates of colorectal cancer in the population of Split-Dalmatia County (SDC) and the Republic of Croatia as a whole

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<td>Colon</td>
<td>men</td>
<td>7.1±1.10</td>
<td>15.4±1.01</td>
<td>18.4±1.70</td>
<td>19.6±1.02</td>
<td>31.4±2.20</td>
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<td>women</td>
<td>6.8±0.98</td>
<td>13.0±0.74</td>
<td>11.5±1.36</td>
<td>13.3±0.69</td>
<td>17.4±1.64</td>
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<td>23.9±1.23</td>
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<td>6.1±1.05</td>
<td>14.6±0.77</td>
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<td>18.3±0.67</td>
<td>15.0±1.53</td>
<td>16.5±0.58</td>
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<td>18.9±0.63</td>
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A The age-standardized rates (per European population) are shown as means ±SEM.

Table 3. Distribution (No. of cases, %) of colorectal carcinoma according to the colon site in the population of Split-Dalmatia County, 1987-1996

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<th>Cecum</th>
<th>Ascending colon</th>
<th>Hepatic flexure</th>
<th>Transverse colon</th>
<th>Splenic flexure</th>
<th>Descending colon</th>
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<td>3 (1.5)</td>
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<td>1992-1996</td>
<td>9 (1.8)</td>
<td>65 (12.9)</td>
<td>14 (2.8)</td>
<td>23 (4.6)</td>
<td>8 (1.6)</td>
<td>30 (5.9)</td>
<td>97 (19.2)</td>
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<td>45 (6.4)</td>
<td>140 (19.9)</td>
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<td>84 (11.9)</td>
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Total 25 (2.0) 183 (14.5) 25 (2.0) 64 (5.1) 26 (2.1) 74 (5.9) 267 (21.2) 30 (2.4) 158 (12.5) 409 (32.4) 1261 (100.0)
progress in diagnostic methods in the later part of the observed period. However, the improvement in diagnostic techniques in the Split-Dalmatia County hospitals was limited due to war-related problems and economical crisis and did not happen until the end of war in 1995. Another explanation for the observed change could be underreporting of cases to the Croatian Cancer Registry in the early 1980’s. If the numbers were more correct toward the end of observed period due to improved reporting, it could have led to a false conclusion on increasing incidence of colorectal cancer. However, we collected data locally from the hospitals and from the Public Health Institute of the Split-Dalmatia County, and they also showed steady increase in the incidence rates from 1987 until 1998, with a similar trend as for the Croatian Cancer Registry data.

Rates of colon cancer vary by race and ethnic status. The highest rates were seen among Caucasians of northern European origin in both their native countries and areas to which they have migrated, whereas lower rates were seen among Caucasians of southern European background (2). However, in the areas with lower rates, rates of colon cancer tend to rise with migration and westernization (2). Also, there is a significant difference between the north and the south within a same country in Europe, but it seems to narrow over time, as described earlier (13). Results of our study are in agreement with this observation. For example, in southern Italian regions, the incidence rates in 1990 were in the range from 18.9 to 32.6 for men and from 17.4 to 24.1 for women (13), with respective rates of 45.1 and 30.0 for Italy as a whole (18). Comparison of our data with the data of other European countries showed that our incidence rates and incidence rates in European countries differed more in the beginning of the studied period (1980s) than toward the end (1990s). On the island of Majorca, the incidence rates of colorectal cancer in the 1982-1986 were 23.1 and 15.0, for men and women, respectively (6). In the province of Soria in Spain, the incidence rates for men increased from 13.1 in the 1981-1985 period to 27.6 in the 1986-1990 period and for women from 9.8 to 19.2 in respective periods (26). In Spain as a whole in 1990, these rates were 41.5 for men and 28.2 for women (18). In 1990, the estimated age-standardized (European population) incidence rates

Figure 1. Changes in the colon cancer incidence by age groups in the male population of the Split-Dalmatia County in the 1981-1998 period, shown as a 3-year moving average. Rhomb, 24-44 years; square, 45-64 years; and triangle, over 65 years.

Figure 2. Changes in the rectal cancer incidence by age groups in the male population of the Split-Dalmatia County in the 1981-1998 period, shown as a 3-year moving average. Rhomb, 24-44 years; square, 45-64 years; and triangle, over 65 years.

Figure 3. Changes in the colon cancer incidence by age groups in the female population of the Split-Dalmatia County in the 1981-1998 period, shown as a 3-year moving average. Rhomb, 24-44 years; square, 45-64 years; and triangle, over 65 years.

Figure 4. Changes in the rectal cancer incidence by age groups in the female population of the Split-Dalmatia County in the 1981-1998 period, shown as a 3-year moving average. Rhomb, 24-44 years; square, 45-64 years; and triangle, over 65 years.
of the colorectal cancer in European Union countries were in the range between 16.6 and 64.7, depending on the sex. The lowest rates were in Greece (20.6 for men and 16.6 for women), and the highest were around 63 for men in Austria, Germany, and Luxembourg, and around 45 for women in Denmark and Germany (18). In France, the incidence of colorectal cancer rose from 48.2 to 79.6 for men and from 32.5 to 48.8 for women in the 1985-1995 period (27). In Japan, where the incidence rate is traditionally lower, there was an increase in the incidence rates of colorectal cancer of 217% from 1974 until 1991 (10.4 vs 33), with a relatively greater increase in the incidence of colon carcinoma than rectal carcinoma for both men and women (28).

Among the factors influencing the etiology of colorectal cancer – diet, physical activity, smoking, and psychosocial stress – several could have contributed to the observed change in Croatia.

The role for a diet change has been described in different cultures and different world regions (1-6). For example, during the 1955-1975 period, fat intake in Japan has increased by 10% and total energy intake by 25% (29). Many studies emphasized the possible protective characteristics of the Mediterranean diet (5,6,30,31). However, diet characteristics in the Mediterranean have also changed in recent years, with decreased intake of fruits and vegetables, and increased intake of milk, meat, and animal protein (32). Current data suggest that consuming a Western style diet (high in meat, refined grains, and sugar; and low in vegetables and fiber) may contribute to risk of colon cancer (33).

The increase in the incidence of colorectal cancer in the Split-Dalmatia County could be at least partly explained by a similar change in the diet. There are no studies available on the diet characteristics of this population. One can assume that there is a trend in a diet change similar to the one in Italian southern regions, where the North-South difference narrowed over time (13,20). Considering Croatia as a country in transition, going through serious changes that reflect on the lifestyle and diet characteristics of its population, this may be even more pronounced.

Physical activity, energy balance, and maintaining an appropriate body weight have been associated with a reduced risk of colon cancer (33). Overweight has long been recognized as a risk factor for hormone-related and other cancers and this is confirmed not only by case-control studies but by large cohort studies as well (34). Cancer of the large bowel is the most commonly investigated factor (33). In the period of 1991-1995, Croatia experienced a brutal war and was burdened with refugees from the neighboring Bosnia and Herzegovina (BH) and the occupied parts of Croatia. Split-Dalmatia County was especially burdened with the refugees from BH.

In consideration of such high increase in the incidence of colorectal carcinoma in Split-Dalmatia County, as shown in this study, the emphasis should be put on prevention and early detection of colorectal carcinoma, since the prognosis of colorectal cancer has gradually improved with advances in fecal occult blood tests, increasingly widespread use of mass screening, improvements in diagnostic techniques, and advances in surgical treatment (15,17,23,44). This prevention should also include assessment and follow-up of the war-induced psychosocial stress on man and should seriously consider the diet and lifestyle changes in the population of this Mediterranean region of the Republic of Croatia. Early detection conducted through screening for colorectal carcinoma should be of major interest in the field of public health.

Smoking cigarettes has been consistently associated with adenomatous polyps. However, only a few studies have reported associations between smoking cigarettes or using other forms of tobacco and colon cancer (37). In two large prospective studies on women and men, a statistically significant association between cigarette smoking and increased risk of colorectal cancer was found, but only after more than 35 years of smoking (38). In the study on women in U.S., the risk for both the colon and the rectum cancer significantly increased with the number of cigarettes smoked per day, longer duration of smoking, and earlier age at initiation. Among former smokers, risk for both colon and rectal cancer remained elevated (39). However, one large cohort study in Sweden did not indicate any excess risk of colon cancer in males who were long-term heavy smokers and provided only weak support for an association with rectal cancer. The reasons for the discrepancies in comparison with recent U.S. data have yet to be identified (38). Epidemiological studies in Croatia showed increase in the prevalence of smoking in 1991-1995 (40).

Except for diet and lifestyle changes, Croatia went through psychosocial stress, war, and the change of political system (40-42), which could be very important in the etiology of colorectal cancer. There is a strong relationship of stressful life events with the risk of colorectal cancer (43). In the period of 1991-1995, Croatia experienced a brutal war and was burdened with refugees from the neighboring Bosnia and Herzegovina (BH) and the occupied parts of Croatia. Split-Dalmatia County was especially burdened with the refugees from BH.

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