

ORIGINAL PAPERS

Increasing incidence of colorectal cancer in the province of Salamanca. Comparison of two periods: 2004-2006 and 2010-2012

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ABSTRACT

Objectives: To compare incidence, mortality and epidemiological characteristics of patients diagnosed with colorectal cancer (CRC) in the province of Salamanca over two different periods: 2010-2012 and 2004-2006.

Methods: Retrospective observational study. We include all diagnosed cases of CRC according to histopathological criteria from 01/01/2004 to 31/12/2006 and from 01/01/2010 to 31/12/2012. The studied variables were sex, age, date of diagnosis and tumor location. Cumulative incidence and specific incidence in different age groups were measured and compared between the two periods. The age rates were adjusted to the standard world population so that the results could be compared with those of other populations.

Results: We detected 38% more cases of CRC in the 2010-2012 period than in 2004-2006. Variables distribution (sex, age at diagnosis and location) was similar in both groups. More than twice as many colonoscopies were performed in 2010-2012 than in 2004-2006. Population mortality due to CRC also increased, although much less importantly than the incidence of this condition.

Conclusions: There has been a clear increase in CRC incidence in the province of Salamanca from 2004-2006 to 2010-2012 which is not related to the ageing of the population. The remarkable increase in colonoscopies may have been an important factor for the increased detection.

Key words: Colorectal cancer. Epidemiology. Incidence.

INTRODUCTION

The growing trend of incidence, morbidity and mortality for colorectal cancer (CRC) has turned this pathology into a first-order health problem. In developed countries, and when both sexes are taken into account, it ranks in the fourth place of incidence (12.2%), with very similar figures to the other three causes (breast, lung and prostate cancer), and it occupies the second place regarding cancer-related mortality (11.6%). In men, it is the third most common can-

cer (12.4%) and the second one regarding cancer-related mortality (11%). In women it is the second most common cancer (12%) and the third one regarding cancer-related mortality (12.3%) (1). If we take into account the progressive ageing of the population, the differences between populations within the same country and the increased risk of suffering from CRC in the population which emigrates from a country with low incidence to areas with a higher incidence, we can posit that CRC is particularly sensitive to variations in environmental and socioeconomic factors. However, it is still not possible to determine which factors are responsible for this fact, and it is not possible to put forward a set of individual or collective interventions for primary prevention, with the exception of the recommendation to have a healthy lifestyle and diet (2).

Given the high incidence, morbidity and mortality associated to CRC, it is justified to carry out epidemiological studies in order to determine the need for early diagnosis plans for each geographical area, because it is the best and most cost-effective strategy to alleviate this first-rate health problem. Also, the main international scientific societies recommend colonoscopies under the slightest clinical suspicion, as well as the implementation of early detection programs (3,4). In Spain, in the year 2009, population screening for CRC was established as a target (5), based on fecal occult blood test (FOB) every two years, and followed by a colonoscopy in positive cases, which had to be offered to all men and women between 50 and 69 years old. This strategy was finally implemented in 2014 (6) and it has been applied since November 2013 in Castile and Leon. Until that moment, only opportunistic screening was performed.

The excellent cost-effectiveness relation of the different options of CRC screening in Spain is already known (7-9), as well as the fact that an increased participation

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and spreading of these programmes improve the results obtained (10).

We have information on patients diagnosed with CRC over the last 15 years (11), and our objective is to compare incidence, mortality and epidemiological and clinical characteristics of patients with CRC diagnosed in our province in 2010-2012 and in the period 2004-2006.

METHODS

Observational, descriptive, retrospective and epidemiological study. Study population includes those people of the province of Salamanca who have been diagnosed with cancer of colon or rectum under histopathological criteria from January 1st 2010 to December 31st 2012. Patients with colon tumors with histology of squamous cell carcinoma (derived from an anorectal junction), carcinoid tumors, lymphomas, melanomas, stromal tumors, sarcomas and metastases from other types of tumor as well as recurrence of anastomosis were excluded. The data from the general population and mortality of Salamanca were obtained from the population census of years 2010, 2011 and 2012 - Spanish National Institute of Statistics (INE) (13). All CRC cases in the province have been included, because all possible data sources were consulted, both in public and private medicine: Digestive Endoscopies Unit, Pathological Anatomy Department and Clinical Documentation Department of the University Hospital of Salamanca databases, apart from those of the Digestive Endoscopies Unit of the Santísima Trinidad Hospital of Salamanca (including cases from both private practices and mutual health insurance schemes). In all these databases, a comprehensive search was carried out regarding both periods included in our study. The Clinical Documentation Department database provided all the diagnoses of hospital discharges according to the CIE-10 classification, and these data were complemented with the results obtained from the search in the remaining databases in which the following search codes were used: adenocarcinoma, neoplasm, cancer, rectum, colon. Finally, the clinical history of each case was revised individually in order to eliminate duplicates. Variables studied were sex, age, date of diagnosis and tumor location, as well as data regarding mortality in both periods. We calculated cumulative incidence (defined as the number of incidental cases per year divided by the total study population at the beginning of that year), specific incidence divided into age groups (the population was divided into a group of people younger than 20, then every 5 years, plus a group of people over 84, as well as into larger age groups) and incidence adjusted by age to the standard world population through a direct method. The reference world population used to adjust age rates was the standard world population proposed by Segi in 1954 and corrected by Doll in 1966 (12), which has been used in international comparative studies on cancer. Age-adjusted incidence shows the theoretical number of affected people in a predetermined population if the risks that act in the real population to cause the disease operated in the theoretical population of reference, which is generally made up of 100,000 people. Afterwards, data were compared with their equivalents from years 2004, 2005 and 2006 in the province of Salamanca, which had already been analyzed by the same Digestive Diseases Department of Salamanca (11). The demographics of Salamanca remained constant in both periods, with a mean total population of 352,169 people

in the 2004-2006 period and 352,389 people in 2010-2012 (13). Statistical analysis was performed using SPSS software for Windows v. 22.0. In the descriptive analysis of the population, categorical variables are presented as total number and frequencies. The Chi-square test was used for the comparison of qualitative variables, odds ratio (OR) used as a measure of association and Student's t-test was used for quantitative variables, with statistical significance set at $p < 0.05$.

RESULTS

Cumulative incidence and age-adjusted incidence using world population

We collected 1,065 CRC cases diagnosed in the province of Salamanca in the years 2010, 2011 and 2012, with a mean of 355 cases per year, compared with 771 CRC cases diagnosed in the years 2004, 2005 and 2006, which correspond to a mean of approximately 257 cases per year (11). Consequently, 38.1% more CRC cases were detected in the 2010-2012 period than in 2004-2006. In both periods Salamanca's population has remained virtually the same, both in absolute values and in age groups, and mortality rates for CRC have increased by 16.2% (474 cases in the 2004-2006 period and 551 cases in the 2010-2012 period) (13). We may highlight that in the province of Salamanca more than twice as many colonoscopies were performed in the 2010-2012 period ($n = 15,816$) than in the 2004-2006 period ($n = 7,111$).

The men/women ratio for all the cases over three years in 2010-2012 was 1.61, similar to 1.64 in the previous period (Table I).

The mean cumulative incidence of CRC in 2010-2012 in the province of Salamanca for both sexes was 100.74 cases per 100,000 people per year, and the incidence was 1.68 times higher in men than in women (126.88 and 75.35/100,000 inhabitants, respectively). The mean cumulative incidence of CRC in 2004-2006 in the province of Salamanca for both sexes was approximately 73 cases per 100,000 inhabitants per year approximately, and it was 1.77 times higher in men than in women (94 and 53 cases/100,000 inhabitants/year, respectively) (11).

The mean incidence, age-adjusted to the world population for both sexes in the province of Salamanca in the period 2010-2012, was 36.98 CRC cases per 100,000 inhabitants per year (34.65 in the year 2010, 38.49 in 2011 and 37.82 in 2012).

CRC and age groups

Mean age is 72.71 years, compared with 73.01 years from the previous period (11). In the period 2010-2012, age distribution was similar for both sexes, although there is a trend towards a higher age for women. The mean age of women was 73.45 years, and in men it was 72.22 years, and these differences were not statistically significant ($p = 0.09$; 95% CI: -2.6 to 0.20).

Table I. Absolute frequency values (and cumulative incidence per 100,000 inhabitants and per year) for different locations

Location	Year 2010			Year 2011			Year 2012			
	M n (CI)	W n (CI)	T n (CI)	M n (CI)	W n (CI)	T n (CI)	M n (CI)	W n (CI)	T n (CI)	
Total	141 (39.86)	104 (29.40)	265 (69.26)	147 (41.64)	96 (27.18)	243 (68.82)	162 (46.20)	92 (26.27)	254 (72.44)	
Colon	Right	63 (17.81)	46 (13)	109 (30.81)	56 (15.86)	42 (11.89)	98 (27.75)	68 (19.39)	40 (11.41)	108 (30.80)
	Left	78 (22.05)	58 (16.40)	136 (38.45)	91 (25.78)	54 (15.29)	145 (41.07)	94 (26.81)	52 (14.83)	146 (41.64)
Rectum	65 (18.38)	35 (9.89)	100 (28.28)	69 (19.54)	44 (12.46)	113 (32.00)	72 (20.53)	38 (10.83)	110 (31.36)	

M: Men; W: Women; T: Total for both sexes; n: Absolute frequency; CI: Cumulative incidence per 100,000 inhabitants per year.

Ninety-nine percent of the cases were diagnosed after the age of 40 (98.6% of men and 99.5% of women); 96.2%, after the age of 50 (97.0% men and 94.9% women); 87.1%, from the age of 60 (87.5% men and 86.5% women); and 65.0%, from the age of 70 (63.0% men and 66.6% women). The absolute number of CRC cases increased progressively with age and it reached its peak in men at 75-79 years (like in the previous study) and slightly later in women, in the group of 80-84 years (in the previous study, the peak value for women was found in the group over 85 years old) (11) (Fig. 1).

CRC location

According to tumor location, over the three years of the study it has been observed that 30.3% of the tumors appeared on the rectum (previously 32.2%) and 69.3% of them appeared on the colon (previously 62.8%). In the group of colon tumors, 40.1% were located in the left colon, and 76% in the sigmoid section (previously 84%), 12% were in the descending colon (previously 13%) and 12% in the splenic flexure (previously 3%). Regarding CRC, 29.2% were found in the right colon (previously 22.9%), 14.7% of which were located in the transverse colon (previously 20.0%), 19.2% in the hepatic flexure (previously 5.0%), 37.7% in the ascending colon

(previously 38.0%) and 29.5% in the cecum (previously 37.0%) (11).

When comparing gender according to tumor location in the rectum or the colon, no statistically significant differences were observed ($p = 0.31$; OR = 1.14 [95% CI: 0.87-1.50]). However, mean age of patients with a diagnosis of CRC located in the rectum is lower (71.47 years) than that of patients in which the tumor was located in the colon (73.26 years) and this difference is statistically significant ($p = 0.021$; 95% CI: -3.30 to -0.27). When CRC cases were divided into right (from the cecum to the transverse colon, both included) and left locations (from the splenic flexure to the rectum, both included), no statistically significant differences were observed regarding sex ($p = 0.30$; OR = 1.15 [95% CI: 0.88-1.50]) or age ($p = 0.38$; 95% CI: -2.2 to 0.85). We can state that being a man is associated to a higher risk of CRC in absolute terms (in any of its locations). Regarding CRC location and sex, the following results were observed for men and women, respectively: mean cumulative incidence of the rectum, 19.48 and 11.06 cases per 100,000 inhabitants; left colon, 24.88 and 15.50 cases per 100,000 inhabitants; and right colon, 17.68 and 12.1 cases per 100,000 inhabitants (Table I).

We finally include mortality data from the two periods, as extracted from the INE: 474 cases (262 men and 212 women; ratio: 1.23) in 2004-2006 and 551 cases in 2010-2012 (307 men and 244 women; ratio: 1.26) (13).

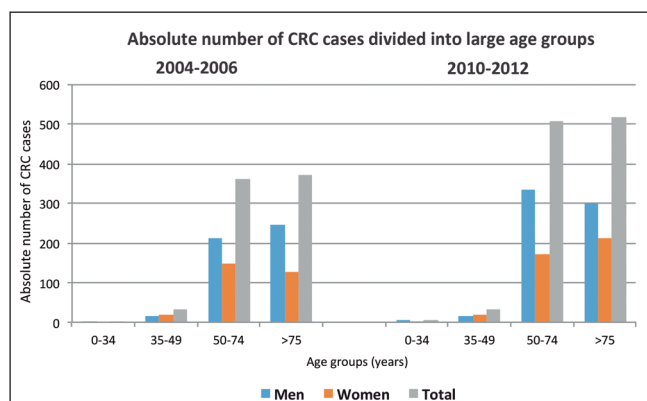


Fig. 1. Absolute number of cases of colorectal cancer (CRC) divided into large age groups in both periods.

DISCUSSION

CRC incidence in our country may be considered to be high for both sexes when compared with the world population: in Spain, 43.9 new cases/100,000 inhabitants/year are diagnosed in men, and 24.2 in women, compared with 20.6 and 14.3 cases/100,000 inhabitants/year in the world population, respectively (rates adjusted for standard world population). However, if Spain is compared with the European Union and other developed countries, it is in a similar situation (in the European Union 39.5 new cases/100,000 inhabitants/year are diagnosed in men and 24.4 in women, and 36.3 and 23.6 cases are diagnosed in the population of other developed countries, respectively) (1). Therefore, we can observe that the highest incidence rates are found

in developed countries, whereas the lowest rates belong to underdeveloped countries. In Salamanca, in the period 2010-2012, we have detected an incidence rate of 100.74 cases/100,000 inhabitants/year in both sexes (in the period 2004-2006 it was 73 cases/100,000 inhabitants/year). If that rate is adjusted for the standard world population, the average result in the years 2010, 2011 and 2012 is 36.98 CRC cases/100,000 inhabitants/year, which makes it possible to assert that the incidence in Salamanca is higher than that of Spain, the European Union and the developed countries, in which the rate is 33.1, 31.3, and 29.2 cases/100,000 inhabitants/year, respectively (1). If we compare the world-population-adjusted incidence rates of Salamanca with the most recent data from the rest of provinces in Spain (14), we can observe that Salamanca is the second Spanish province with the highest incidence of CRC (36.98 cases/100,000 inhabitants/year), right after Tarragona, with 38.85 CRC cases/100,000 inhabitants/year, and followed closely by Girona and the Basque Country, with 36.85 and 36.35 cases/100,000 inhabitants/year, respectively (1).

Variables as sex, age at diagnosis, and location were similar in both study groups (2004-2006 and 2010-2012). The men/women incidence ratio was 1.61 in the period 2010-2012 and 1.64 in the period 2004-2006. However, this same men/women ratio is slightly lower regarding mortality in both periods (1.26 in 2010-2012 and 1.23 in 2004-2006).

The study on 2004-2006 showed that, in our population, being male was associated to a higher incidence of cancer on the left colon while being female was associated to a higher incidence of proximal cancer (right colon) (11). The study on 2010-2012 did not reveal any association, because sex was not associated to a higher incidence in any of the three locations (right colon, left colon and rectum). However, we can state that mean age at diagnosis of rectal carcinoma is two years lower than the age at diagnosis of colon cancer, and that this difference is statistically significant.

Based on these findings, we may conclude that there is a clear increase in the incidence (38.1%) and, to a lesser extent, of mortality (16.2%) of CRC in the province of Salamanca which is not related to ageing, because the population remains stable in absolute terms and when considering age groups and it was virtually identical in both periods.

The remarkable rise in the number of colonoscopies (more than twice as many as in the previous period) may have been an important factor for the increased detection rates.

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