1130-0108/2012/104/11/572-577
Revista Española de Enfermedades Digestivas
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Rev Esp Enferm Dig (Madrid)
Vol. 104. N.° 11, pp. 572-577, 2012

ORIGINAL PAPERS

Colorectal cancer survival: Results from a hospital-based cancer registry

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ABSTRACT

Introduction: colorectal cancer is one of the most common malignancies in developed countries. Data on specific and 10-year survival are scarce. This study analyzes overall and disease-specific survival for patients with colorectal cancer and assesses the value of clinical factors on disease-specific survival.

Methods: a retrospective cohort study of newly diagnosed invasive colorectal cancer cases diagnosed from 1992 to 2007 were identified through the Hospital del Mar Cancer Registry. Five- and 10-year survival functions were estimated using Kaplan-Meier method. Cox proportional hazard models were used to assess prognostic factors.

Results: a total of 2,080 patients with colorectal cancer were identified. The median age at diagnosis was 72 years and 58.5% were men. By the end of the follow-up period (December 2008), 1,225 patients had died and 68.4% of deaths were due to colorectal cancer. The 5- and 10-year cancer-specific survival rates were 55.5% (95%CI 53.9-57.9%) and 48.5% (95%CI 45.6-51.3%), respectively. The 5-year specific survival rate improved in the last period (2003-2007) (60.4%, 95%CI 55.4-65.0) compared with 1992-1997 (53.4%; 95%CI 49.2-57.4) and 1998-2002 (52.0%; 95%CI 47.8-56.2). Various factors were independently associated with excess CRC mortality: male sex (HR 1.21), age at diagnosis > 75 years (HR 1.97), rectal location (HR 1.33), more advanced stages (stage IV: HR 18.54), poorly differentiated/undifferentiated tumors (HR 1.80), and admission through the emergency department (HR 1.52).

Conclusions: cancer-specific survival improved from 1992 to 2007. This improvement could be due to more effective treatment, since changes in stage distribution or age at diagnosis were not observed during the study period. Overall survival rates should notably improve with the implementation of a population-based colorectal cancer screening program in Spain.

Key words: Colorectal neoplasms. Survival analysis. Prognosis. Hospitals. Registries.

INTRODUCTION

Colorectal cancer (CRC) is one of the most common cancers in developed countries. Incidence rates are high in Europe and, within Europe, are particularly high in Catalonia. CRC was the most common cancer from 1998 to 2002 and its incidence is estimated to have an upward trend in the present decade (1). The prognosis of CRC is relatively good in terms of survival, which varies markedly across European countries (2). In Europe and Catalonia (3), survival in CRC patients has increased. In Catalonia (3), the 5-year relative survival rate was 42.7% (95%CI 38-48) in 1985-1989 and 52.9% (95% IC 49-57) in 1995-1999. Several publications have observed an independent prognostic effect of factors such as age at diagnosis (4), sex (4,5), stage at diagnosis (6), histological grade (4), anatomical location (4,5), type of treatment received (7), degree of co-morbidity (8), and type of hospital admission (9).

Population-based cancer registries have been the information source for many of the above-mentioned studies and are an essential tool to characterize this malignancy. However, the information on tumor features provided by these registries is sometimes limited and data on the 10-year survival rate are scarce. In contrast, hospital-based cancer registries complement this information, usually providing more detailed data, which allows specific mortality to be estimated and/or the prognostic value of clinical variables to be investigated.

The Cancer Registry of Hospital del Mar (Barcelona) is one of the best established hospital-based cancer registries in Spain, with comprehensive clinical data and extensive follow-up (9). The aim of this study was to calculate the

Received: 13-04-2012
Accepted: 30-10-2012

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Agüero F, Murta-Nascimento C, Gallén M, Andreu-García M, Pera M, Hernández C, Burón A, Macià F. Colorectal cancer survival: results from a hospital-based cancer registry. Rev Esp Enferm Dig 2012;104:572-577.

5- and 10-year survival rates for patients with newly diagnosed CRC and to assess the prognostic value of clinical factors.

METHODS

Data source

This study was based on the information collected by the Cancer Registry of Hospital del Mar. This public general teaching hospital serves a population of approximately 300,000 inhabitants living in two of the 10 municipal districts of Barcelona (Catalonia, Spain). The cancer registry approach has been described in detail elsewhere (9). Briefly, this registry collects data on all cancer cases diagnosed and/or treated at Hospital del Mar. In this database, cancers are coded according to the International Classification of Diseases for Oncology, 1st edition (ICD-O-1). The follow-up information is updated automatically at each patient visit or if patients are admitted to the hospital. Information on the date and cause of death are obtained annually through a record linkage procedure between the hospital registry and the Catalonian Mortality Registry.

Patients with newly diagnosed invasive cancer of the colon (ICD-O-1 T-153) and rectum (ICD-O-1 T-154) diagnosed between January 1, 1992 and December 31, 2007 were included in this analysis. Tumors that penetrated into the submucosa or beyond were considered invasive cancer.

Tumors of the anal canal (154.2) and anus unspecified (154.3) were excluded. Patients were also excluded if their tumor was diagnosed at autopsy (n = 11). We further restricted the analysis to adenocarcinomas (ICD-O-1 M-8140/3), mucinous adenocarcinomas (ICD-O-1 M-8480/3) and signet ring cell carcinoma (ICD-O-1 M-8490/3).

The beginning of follow-up was the date of histopathological diagnosis. The events of interest were death due to any cause (overall survival) and death due to CRC (cause-specific survival). Patients alive at the end of the follow-up (December 31, 2008), those lost to follow-up, and those who died of causes other than CRC cancer were censored either at the last contact or at death.

Study variables

The demographic variables examined included age at diagnosis, categorized in three groups (0-49, 50-75 and > 75 years), sex, and year of diagnosis, grouped in three periods (1992-1997, 1998-2002 and 2003-2007). Tumor characteristics included anatomical site (right colon: from cecum to transverse; left colon: from the splenic flexure to sigmoid colon; colon *NOS* –not otherwise specified–; and rectum). Patients with synchronous tumors were classified according to the lesion at the most advanced stage. The stage grouping at presentation was classified according to the version of the pathological tumor-node-metastasis (TNM) classification that was used in the year of diagnosis. For patients offered neoadjuvant therapy and those who did not undergo surgery, staging was based on the TNM clinical classification. Finally, patients were classified according to the type of hospital admission (elective or emergency).

Statistical analysis

The 5- and 10-year overall and specific survival rates were estimated using the Kaplan-Meier method. Survival curves were estimated using the Kaplan-Meier product limit method and the differences between the categories of each variable were assessed using the log-rank test. The relationship between specific survival time and covariates of interest (age, sex, stage, anatomical site, period of diagnosis, histological grade and type of hospital admission) was assessed by Cox regression models. To calculate overall and CRC-specific survival, Stata statistical software (version 8.0) was used.

This study was performed in accordance with the ethical standards of the Declaration of Helsinki and complied with the legal regulations on data confidentiality (*Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal*). It was also approved by the Ethics Committee of Parc de Salut Mar.

RESULTS

We identified 2,080 newly diagnosed invasive CRC cases diagnosed between 1992-2007. Table I shows the characteristics of the study cohort. The median age at diagnosis was 72 years (interquartile range 64-79 years) and 58.5% were male. The CRC sites were as follows: right colon 25.0%, left colon 36.1%, colon *NOS* 5.9%, and rectum 33.0%. Almost half of the cases were diagnosed in stage I or II (47.8%). The most common histological type was adenocarcinoma (93.7%), followed by mucinous adenocarcinoma (5.7%) and signet ring cell carcinoma (0.6%). The percentage of patients aged 75 or more at diagnosis increased over time. We observed a decline in patients with tumors located in the rectum and in those admitted through the emergency department. Colon cancer, as well as rectal cancer treatment, changed over time (i.e. the use of radiotherapy plus chemotherapy followed by surgery for rectal cancer increased from 1.2% in the first period to 37.5% in the last period) (data not shown). Adjuvant chemotherapy was administrated to 62.3% of patients with colon cancer and to 31.5% of those with rectum cancer.

By the end of follow-up, 1,225 patients had died: 838 deaths (68.4%) were due specifically to colorectal neoplasm and 12 (0.6%) were due to unknown causes. Around 84% of surviving patients had been visited at some time during 2008.

The 5- and 10-year overall survival rates for the entire cohort were 44.0% (95%CI 41.6-46.3) and 28.8% (95%CI 26.2-31.4), respectively (Table II). CRC-specific survival

Table I. Distribution of colorectal cancer cases by period of diagnosis, n (%)

Characteristic	*Total*	*%*	*Period of diagnosis*					
			1992-1997		*1998-2002*		*2003-2007*	
Number of cases		2,080	633	(30.4)	636	(30.6)	811	(39.0)
Sex								
Female	863	(41.5)	267	(42.2)	279	(43.9)	317	(39.1)
Male	1217	(58.5)	366	(57.8)	357	(56.1)	494	(60.9)
Age at diagnosis (years)								
< 50	109	(5.2)	29	(4.6)	39	(6.1)	41	(5.1)
50-75	1,199	(57.6)	408	(64.5)	339	(53.3)	452	(55.7)
> 75	772	(37.1)	196	(31.0)	258	(40.6)	318	(39.2)
Site								
Right colon	521	(25.0)	124	(19.6)	167	(26.3)	230	(28.4)
Left colon	750	(36.1)	188	(29.7)	238	(37.4)	324	(39.9)
Colon, *NOS*	122	(5.9)	68	(10.7)	32	(5.0)	22	(2.7)
Rectum	687	(33.0)	253	(40.0)	199	(31.3)	235	(29.0)
Stage grouping at diagnosis								
I	321	(15.4)	106	(16.7)	81	(12.7)	134	(16.5)
II	674	(32.4)	216	(34.1)	222	(34.9)	236	(29.1)
III	581	(27.9)	167	(26.4)	165	(25.9)	249	(30.7)
IV	426	(20.5)	122	(19.3)	134	(21.1)	170	(21.0)
Unknown	78	(3.8)	22	(3.5)	34	(5.3)	22	(2.7)
Histological grade								
I	104	(5.0)	26	(4.1)	26	(4.10)	52	(6.4)
II	1,691	(81.3)	535	(84.5)	528	(83.0)	628	(77.4)
III/IV	167	(8.0)	30	(4.7)	50	(7.9)	87	(10.7)
Unknown or not evaluated	118	(5.7)	42	(6.6)	32	(5.0)	44	(5.4)
Type of hospital admission								
Elective	1,047	(50.3)	262	(41.4)	300	(47.2)	485	(59.8)
Emergency	1,033	(49.7)	371	(58.6)	336	(52.8)	326	(40.2)

Colon, NOS = colon, not otherwise specified.

rates were higher: 55.5% (95%CI 53.0-57.9) at 5-years and 48.5% (95%CI 45.6-51.3) at 10-years. The median cancer-specific survival was 7.7 years (95%CI 6.38-12.01 years) (Fig. 1). The 5-year specific survival rate showed an absolute increase of 7 points between the first period (1992-1997) and the third (2003-2007). However, the survival rate was slightly lower in the second period (1998-2002) (Table II). The lowest 5-year CRC-specific survival was observed among males (54.0%), patients aged > 75 years (48.4%), tumors located in the rectum (54.7%), stage IV tumors (5.5%), poorly differentiated/undifferentiated tumors (31.8%) and patients admitted through the emergency department (46.1%).

Multivariate analysis showed that the factors leading to a less favorable prognosis were diagnosis in 1992-1997 (HR 1.43; 95%CI 1.20-1.70), male sex (HR 1.21; 95%CI 1.05-1.39), age > 75 years (HR 1.97; 95%CI 1.41-2.75), neoplasms located in the rectum (HR 1.33; 95%CI 1.10-1.61), stage IV tumors (HR 18.54; 95%CI 13.28-25.89), poorly differentiated/undifferentiated tumors (HR 1.80; 95%CI 1.17-2.77), and admission through the emergency department (HR 1.52; 95%CI 1.32-1.75) (data not shown).

DISCUSSION

Five- and 10-year CRC-specific survival rates were 55.5 and 48.5%, respectively. Various CRC characteristics changed over the study period and 5-year survival improved in the last period. Moreover, various factors independently associated with excess risk of death were identified.

The results show that both the 5-year overall and CRC-specific survival were similar to those described by previous studies. Galceran et al. (3) reported that the overall and rel-

Table II. Five- and 10-year overall and colorectal cancer-specific survival[1]

Characteristic	*Overall survival (95%CI)*				*Specific survival (95%CI)*			
	5-year		*10-year*		*5-year*		*10-year*	
Overall	44.0	41.6-46.3	28.8	26.2-31.4	55.5	53.9-57.9	48.5	45.6-51.3
Period of diagnosis								
2003-2007	48.6	43.5-53.5	-		60.4	55.4-65.0	-	
1998-2002	39.8	35.9-43.6	27.8	23.9-31.8	52.0	47.8-56.2	47.9	43.5-52.2
1992-1997	42.7	38.8-46.6	27.4	23.9-31.0	53.4	49.2-57.4	45.7	41.3-49.9
Sex								
Female	47.4	43.8-51.0	34.8	30.7-38.9	57.4	53.6-61.0	52.3	48.1-56.4
Male	41.4	38.3-44.5	24.4	21.2-27.8	54.0	50.6-57.1	45.4	41.5-49.2
Age at diagnosis (years)								
< 50	58.5	47.6-67.9	55.2	44.0-65.0	61.6	50.8-70.7	58.1	46.8-67.8
50-75	51.2	48.0-54.2	36.0	32.5-39.4	59.3	56.1-62.4	51.6	48.0-55.1
> 75	30.3	26.7-34.0	12.8	9.5-16.7	48.4	44.2-52.6	41.7	35.9-47.3
Site								
Right colon	45.7	41.0-50.4	33.0	27.9-38.3	59.1	54.1-63.7	54.9	49.5-60.0
Left colon	44.8	40.8-48.8	29.3	24.9-33.9	55.8	51.6-59.8	49.8	44.5-54.2
Colon NOS	32.9	24.2-41.8	20.2	12.8-28.8	43.0	33.2-52.4	36.4	26.4-46.5
Rectum	43.7	39.6-47.7	27.2	22.9-31.6	54.7	50.3-58.9	45.6	40.5-50.4
Stage grouping at diagnosis								
I	71.2	65.3-76.2	48.4	40.5-55.9	87.9	83.1-91.4	80.7	73.1-86.4
II	56.4	52.2-60.4	39.1	34.4-43.8	71.0	66.9-74.7	63.8	58.9-68.3
III	45.0	40.3-49.5	25.0	20.1-30.3	55.9	50.9-60.6	44.0	37.9-49.9
IV	4.5	2.5-7.4	-		5.5	3.1-9.0	-	
Unknown	20.9	12.2-31.1	-		36.6	23.8-49.4	-	
Histological grade								
I	48.1	37.2-58.3	34.6	22.7-46.8	68.8	57.1-77.9	68.8	57.1-77.9
II	46.3	43.6-48.9	29.8	26.9-32.7	58.8	55.0-60.4	49.7	46.4-52.8
III/IV	24.9	17.0-33.6	-		31.8	22.8-41.2	-	
Unknown	32.0	23.5-40.9	23.5	14.9-33.4	42.7	32.7-51.4	40.5	30.9-50.0
Type of hospital admission								
Elective	53.1	49.6-56.5	34.8	30.6-38.3	64.9	61.1-67.9	55.0	50.6-69.2
Emergency	35.0	31.9-38.1	22.9	19.9-26.1	46.1	42.6-49.5	41.5	37.7-45.2

[1]Results expressed in percentages. Colon, NOS = colon, not otherwise specified.

ative survival rates in Catalonia in 1995-1999 were 43.8 and 52.1%, respectively. According to Chirlaque et al. (10), the 5-year relative survival rate for CCR in Spain (considering seven Spanish geographical areas) during the same period was 52%. The highest 5-year relative survival rates for colon cancer during the period 1995-1999 were observed in the population-based cancer registries of Murcia (59.6%, 95%CI 56.5-62.6) and Girona (57.9%, 95%CI 54.3-61.4) while the lowest rates were in Albacete 51.5% (95%CI 45.6-57.0) and Granada (50.5%, 95%CI 46.6-54.4). Regarding rectum cancer, the highest 5-year relative survival rates were 54.4% (95%CI 50.5-58.2) in Murcia and 53.3% (95%CI 48.4-57.9) in Navarre. Contrarily, the lowest 5-year relative survival rates for rectum cancer were 45.9% (95%CI 40.6-51.0) in Granada and 43.6% (95%CI 36.8-50.2) in Albacete (10).

In Europe during the period 1997-1999, 5-year relative survival rate was 58.8% in Northern countries (Finland, Iceland, Norway and Sweden), 50.5% in United Kingdom and 57.4% in central countries (Germany, Austria, Switzerland, France and Netherland) (2).

Studies reporting 10-year survival rates are scarce. Verdecchia et al. (11) found a difference of less than 5 points when comparing 5- and 10-year relative survival rates. This

finding indicates that deaths occur primarily within 5 years of diagnosis. Our study found a similar difference (7 points) and the 10-year relative survival rates (46% in the first period and 48% in the second) were higher than those observed by Mitry et al. (12,13) in England and Wales (35%-40% in 1991-1995). The modest improvement in survival over the study period is consistent with the results of other studies performed in Catalonia (3) and other European countries (2,12,13). This phenomenon has been attributed to improvements in diagnosis and treatment in more recent periods (3,12,13). We observed that the proportion of cancers in stages I-II slightly declined from the first period (50.8%) to the last (45.6%). Therefore, earlier cancer detection could not be considered as the main reason for the improved survival in our setting. This result was expected, as population-based CRC screening program only started recently (2009) in Catalonia and during the study period screening

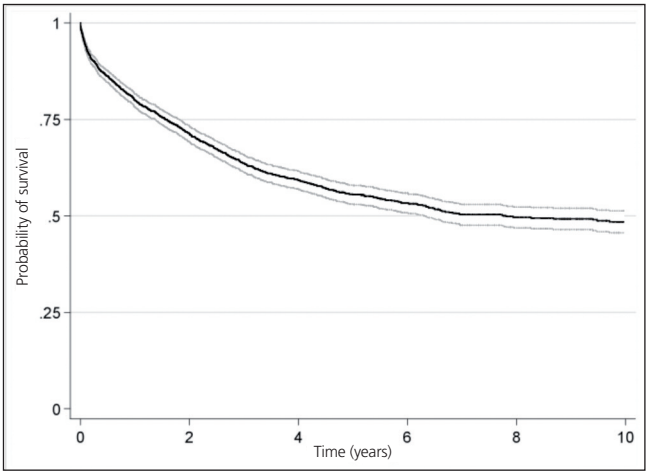

Fig. 1. Kaplan-Meier curve for colorectal cancer-specific survival.

Table III. Crude and adjusted hazard ratios (HR) for colorectal cancer-specific mortality

Characteristic	*Total*	*Events*	*Univariate*		*Multivariate**	
			HR	*95%CI*	*HR*	*95%CI*
Period of diagnosis						
2003-2007	811	240	1.00	ref.	1.00	ref.
1998-2002	636	285	1.29	1.09-1.54	1.26	1.06-1.50
1992-1997	633	313	1.29	1.09-1.53	1.43	1.20-1.70
Sex						
Female	863	336	1.00	ref.	1.00	ref.
Male	1,217	502	1.13	0.98-1.30	1.21	1.05-1.39
Age at diagnosis (years)						
<50	109	39	1.00	ref.	1.00	ref.
50-75	1,199	460	1.06	0.76-1.47	1.05	0.75-1.45
>75	772	339	1.66	1.20-2.33	1.97	1.41-2.75
Site						
Right colon	521	189	1.00	ref.	1.00	ref.
Left colon	750	297	1.07	0.89-1.28	1.15	0.95-1.39
Colon NOS	122	66	1.75	1.33-2.33	1.71	1.28-2.29
Rectum	687	286	1.09	0.90-1.31	1.33	1.10-1.61
Stage grouping at diagnosis						
I	321	41	1.00	ref.	1.00	ref.
II	674	184	2.38	1.70-3.33	2.17	1.54-3.05
III	581	225	3.87	2.77-5.40	3.77	2.70-5.28
IV	426	348	18.63	13.41-25.89	18.54	13.28-25.89
Unknown	78	40	8.94	5.78-13.83	7.37	4.75-11.45
Histological grade						
I	104	27	1.00	ref.	1.00	ref.
II	1,691	651	1.48	1.00-2.17	1.12	0.76-1.64
III/IV	167	95	3.52	2.29-5.40	1.80	1.17-2.77
Unknown or not evaluated	118	65	3.00	1.92-4.71	1.90	1.20-2.99
Type of hospital admission						
Elective	1,047	337	1.00	ref.	1.00	ref.
Emergency	1,033	501	1.81	1.57-2.08	1.52	1.32-1.75

*Adjusted by sex, age group, stage at diagnosis, period of diagnosis, histological grade and type of hospital admission. Colon, NOS = colon, not otherwise specified.

was purely opportunistic. The improved survival could have been influenced by changes in treatment patterns (i.e. an increasing proportion of colon cancer cases were treated with surgery followed by chemotherapy while cases of rectal cancer were treated by the combination of radiotherapy, chemotherapy and surgery).

In agreement with other studies (4,5), survival rates were statistically significantly higher in women. This association has been attributed to many underlying factors, such as access to care, sex-specific co-morbidites, treatment disparities and hormonal status. Like previous studies (4,6), our data also showed that survival was poorer in the elderly than in younger patients.

As an inherent consequence of the methods used to calculate overall and cancer-specific survival rates, our results also show a gradient in the difference between the two methods: the older the age group, the greater the difference in the results of the two methods.

The CONCORD study observed that in most countries, survival was better in patients with colon cancers than in those with rectal cancers (5). In Spain (10), the 5-year relative survival rates for colon cancer of seven population-based cancer registries were higher than those for rectum cancer.

The association found between an excess risk of death and some clinical factors is consistent with the results of previous studies. Advanced stage at diagnosis (6), undifferentiated/poorly differentiated tumors (4), and admission through the emergency department (9) are factors that are well known and described in the literature.

To our knowledge, this is one of the largest studies ever performed in Spain that estimates CRC-specific survival and provides direct evidence that clinical characteristics are major determinants of survival. Other advantages are the long follow-up and the low percentage of cases with an unknown cause of death. However, this study has some limitations. First, the information source was a single institution and thus the cohort studied cannot be considered as representative of all CRC patients in Barcelona. However, referral selection bias is unlikely to have occurred, as our center is well coordinated with its catchment area. Secondly, our registry lacks data on some factors, such as patients' medical co-morbidities and socioeconomic status, which have been associated with survival (8).

In conclusion, the overall and specific survival rates of patients with CRC improved from 1992 to 2007. The most important factors associated with mortality were older age and advanced stage at diagnosis. As no changes in stage distribution or age of diagnosis were observed during this period, the improvement in survival rate can be attributed to more effective treatment. The main challenge for the future is to detect cases in earlier stages with the introduction of the population-based CRC screening program in Spain. Further studies will be needed to determine the impact of these programs.

ACKNOWLEDGMENTS

We are grateful to Àngels Hospital, Mercè-Piracés and Ramon Clèries. This work was supported by a grant from the Fondo de Investigación Sanitaria, ISCIII, Spain (FIS-FEDER PI07/90861) CIBER Epidemiología y Salud Pública (CIBERESP), and FEDER RTICC (RD06/0020/0109), Spain.

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