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Survival of patients with colorectal cancer in a Cancer Center

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ABSTRACT – **Background** – Hospital-based studies recently have shown increases in colorectal cancer survival, and better survival for women, young people, and patients diagnosed at an early disease stage. **Objective** – To describe the overall survival and analyze the prognostic factors of patients treated for colorectal cancer at an oncology center. **Methods** – The analysis included patients diagnosed with colon and rectal adenocarcinoma between 2000 and 2013 and identified in the Hospital Cancer Registry at A.C.Camargo Cancer Center. Overall 5-year survival was estimated using the Kaplan-Meier method, and prognostic factors were evaluated in a Cox regression model. Hazard ratios (HR) are reported with 95% confidence intervals (CI). **Results** – Of 2,279 colorectal cancer cases analyzed, 58.4% were in the colon. The 5-year overall survival rate for colorectal cancer patients was 63.5% (65.6% and 60.6% for colonic and rectal malignancies, respectively). The risk of death was elevated for patients in the 50–74-year (HR=1.24, 95%CI =1.02–1.51) and ≥75-year (HR=3.02, 95%CI =2.42–3.78) age groups, for patients with rectal cancer (HR=1.37, 95%CI =1.11–1.69) and for those whose treatment was started >60 days after diagnosis (HR=1.22, 95%CI =1.04–1.43). The risk decreased for patients diagnosed in recent time periods (2005–2009 HR=0.76, 95%CI =0.63–0.91; 2010–2013 HR=0.69, 95%CI =0.57–0.83). **Conclusion** – Better survival of patients with colorectal cancer improves with early stage and started treatment within 60 days of diagnosis. Age over 70 years old was an independent factor predictive of a poor prognosis. The overall survival increased to all patients treated in the period 2000–2004 to 2010–2013.

HEADINGS – Survival analysis. Colorectal neoplasms. Registries. Prognosis.

INTRODUCTION

In 2018, colorectal cancer (CRC) was the third most common cancer among men and the second most among women worldwide. It is the fourth cause of death from cancer among men and the second among women[1]. In Brazil, the estimates for 2018 show that CRC was the third most common cancer in men (17,380 cases; 8.7%) and the second in women (18,980 cases; 9.4%)[2].

Cancer incidence and mortality rate have been related to the human development of the countries. CRC incidence and mortality rates have been increasing in low- and middle-income countries, while it is stable or decreasing in highly developed countries[3]. Within Brazil, mortality rates and trends have been found to differ across federal units, after adjusting for socioeconomic conditions[4-5].

In terms of relative population survival, data from 296 registers show high variability in relative survival among patients with colon cancer. Israel, South Korea, and Australia have survival rates over 70%. The survival rate from six population-based cancer registries of Brazilian have been stable in fifteen years period (44.5% for 2000–2004, 50.6% for 2005–2009, and 48.3% for 2010–2014). For rectal cancer, relative survival has been more variable across world regions (294 registers), with only Korea and Australia having rates above 70%. In Brazil, the relative survival was 37.7% for 2000–2004, 45.7% for 2005–2009, and 42.4% for 2010–2014[6]. Hospital-based studies recently have shown increases in survival, and better survival for women, young people, and patients diagnosed at an early disease stage[7-10].

The survival data for patients treated at specialized cancer centers serves as an indicator of how a patient comes to be treated. Very few studies have use data from Brazilian hospital cancer registries to evaluate CRC survival. Thus, the objective this study was to describe the profile of patients treated for CRC at an oncology center and to analyze their survival.

METHODS

We included patients with CRC during the period of 2000 to 2013 who were treated at A.C.Camargo Cancer Center (ACCCC) with follow-up through December 31, 2018: invasive adenocarcinomas (M81403, 82013, 82103, 82113, 82203, 82613, 82623, 82633, 84413, 84703, 84803, 84813, 84903, 85103, 85603); colon cancer (ICD-O3 C18-19); and rectal cancer (ICD-O3 C20). We obtained the cases from the ACCCC's Hospital Cancer Registry. The ACCCC's Research Ethics Committee approved the project (n. 2462/17) on May 12, 2017.

Analyses were performed based on patient age group (≤49, 50–74, and ≥75 years of age), gender (male and female), period of

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diagnosis (2000–2004, 2005–2009, and 2010–2013), site (left colon, right colon, unspecified, and rectal), clinical stage (I, II, III, and IV); delay to start treatment from the date of diagnosis in days (≤60 days and ≥61 days)[11]; type of treatment for the colon (surgery, surgery + chemotherapy, other combination, or none for the colon; surgery; surgery + chemotherapy, radiation therapy + chemotherapy; surgery + chemotherapy, + radiotherapy, other combination, or none for the rectal). Absolute and relative frequencies were calculated. Patients groups were compared with chi-squared tests.

Overall Survival (OS) was calculated as the difference between the date of diagnosis and the date of death (from any cause) or the date of the most recent information in the medical records. Survival curves were estimated by the Kaplan-Meier estimator, and 60-month probabilities were presented according to independent variables. Survival curves were compared with the log-rank test. Hazard ratios (HR) and associated 95% confidence intervals (95%CI) were estimated with a Cox regression model. The assumption of proportional hazards was assessed based on the so-called Schoenfeld residuals and the Grambsch and Therneau global test. There was one independent variable that did not satisfy the proportional hazards assumption (clinical stage) and thus the stratified Cox model by clinical stage was fitted. There was evidence that covariates had a constant effect over time in all cases. The significance level was fixed at 5% for all tests and the analyses performed in Stata SE 15.

RESULTS

Between 2000 and 2013, 2,279 patients with CRC were treated at the ACCCC. The majority of these patients were male (51.3%); 50–74 years old (62.5%), with colon cancer (58.4%), clinical stage III/IV (52.8%), and started treatment within 60 days of diagnosis (70.4%) (all $P<0.05$) (TABLE 1). Among colon cancer patients, 43.2% had surgery alone and 40.8% had surgery and chemotherapy. Among rectal cancer patients, 41.5% had surgery, chemotherapy, and radiation therapy, and 20.7% had surgery alone (TABLE 2).

We observed a 5-year OS rate of 63.5% (FIGURE 1.A), without difference between men and women. Survival was higher in patients younger than 49 years old (70.0%) and worse in those over 75 years old, 43.8% ($P<0.001$). OS was better for the most recent period (2010–2013, 66.4%) than for prior time periods ($P<0.012$, FIGURE 1.C). Patients younger than 49 years old with stage I or II colon cancer had an OS of 100%, while rectal cancer for stage I was 89.8% and 88.0% for stage II (TABLE 3). In the adjusted model stratified by clinical stage, mortality risk increased with increasing age (50–74 years HR=1.24; and ≥75 years HR=3.02) and was high for those diagnosed with rectal cancer (HR=1.37) and for those who started treatment more than 60 days after diagnosis (HR=1.22). Mortality risk was lowest for the two most recent time periods (2005–2009, HR=0.76; and 2010–2013, HR=0.69) (TABLE 4).

TABLE 1. Characteristics of patients diagnosed with colorectal cancer and treated at A.C.Camargo Cancer Center, between 2000 and 2013.

Characteristic	Colon N=1,332 n (%)	Rectal N=947 n (%)	Total N=2,279 n (%)	*P*
Gender				
Male	642 (48.2)	528 (55.8)	1,170 (51.3)	<0.001
Female	690 (51.8)	419 (44.2)	1,109 (48.7)	
Age group (years)				
≤49	245 (18.4)	204 (21.5)	449 (19.7)	
50–74	842 (63.2)	582 (61.5)	1,424 (62.5)	0.160
≥75	245 (18.4)	161 (17.0)	406 (17.8)	
Period of diagnosis				
2000–2004	233 (17.5)	202 (21.3)	435 (19.1)	
2005–2009	413 (31.0)	355 (37.5)	768 (33.7)	<0.001
2010–2013	686 (51.5)	390 (41.2)	1,076 (47.2)	
Site				
Right colon	-	-	377 (16.5)	
Left colon	-	-	819 (35.9)	
Colon (non-specified)	-	-	136 (6.0)	-
Rectal	-	-	947 (41.6)	
Clinical stage				
I	264 (19.8)	163 (17.2)	427 (18.7)	
II	318 (23.9)	216 (22.8)	534 (23.4)	
III	318 (23.9)	313 (33.1)	631 (27.7)	<0.001
IV	380 (28.5)	192 (20.3)	572 (25.1)	
No data	52 (3.9)	63 (6.6)	115 (5.1)	
Delay to start treatment				
≤60 days	1,003 (78.5)	546 (59.1)	1.549 (70.4)	<0.001
≥61 days	274 (21.5)	378 (40.9)	652 (29.6)	

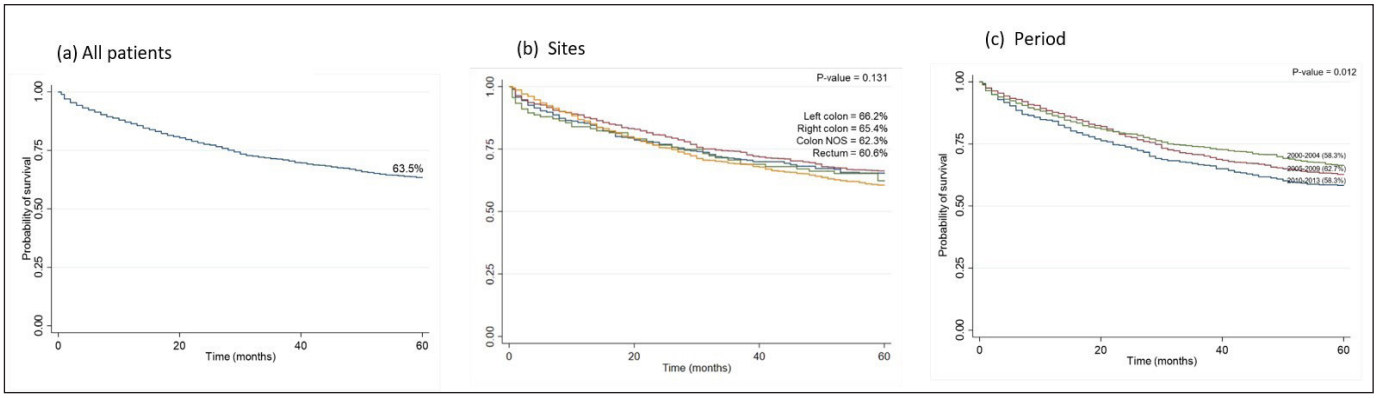

FIGURE 1. Kaplan-Meier 5-year overall survival rates for patients with colorectal cancer from 2000 to 2013.

TABLE 2. Treatments to colorectal cancer patients, by clinical stage, at A.C.Camargo Cancer Center, between 2000 and 2013.

Treatment	I	II	III	IV	Total
Colon					
Surgery	247 (93.6)	202 (63.5)	59 (18.6)	45 (11.8)	575 (43.2)
Surgery + CT	12 (4.6)	103 (32.4)	230 (72.3)	197 (51.8)	544 (40.8)
CT	0 (0)	1 (0.3)	8 (2.5)	73 (19.2)	84 (6.3)
Other(s)	4 (1.5)	8 (2.5)	20 (6.3)	37 (9.7)	71 (5.3)
None	1 (0.3)	4 (1.3)	1 (0.3)	28 (7.5)	58 (4.4)
All treatment groups	264 (100.0)	318 (100.0)	318 (100.0)	380 (100.0)	1.332 (100.0)
Rectal					
Surgery	99 (60.7)	41 (19.0)	31 (9.9)	15 (7.8)	196 (20.7)
Surgery + CT	1 (0.6)	24 (11.1)	70 (22.4)	49 (25.5)	147 (15.5)
Radiotherapy + CT	3 (1.8)	19 (8.8)	22 (7.0)	36 (18.8)	88 (9.3)
Surgery + RT + CT	48 (29.5)	114 (52.8)	178 (56.9)	40 (20.8)	393 (41.5)
CT	0 (0)	1 (0.5)	2 (0.6)	34 (17.7)	37 (3.9)
Other(s)	11 (6.8)	15 (6.9)	10 (3.2)	9 (4.7)	64 (6.8)
None	1 (0.6)	2 (0.9)	0 (0)	9 (4.7)	22 (2.3)
All treatment groups	163 (100.0)	216 (100.0)	313 (100.0)	192 (100.0)	947 (100.0)

CT: chemotherapy; RT: radiotherapy.

TABLE 3. Overall Survival for patients with colorectal cancer, according to characteristics and site, at A.C.Camargo Cancer Center between 2000 and 2013.

Characteristic	Colon			Rectal			All		
	Deaths/total	5-year OS	*P*	Deaths/total	5-year OS	*P*	Deaths/total	5-year OS	*P*
Gender									
Male	206/642	65.9	0.919	198/528	61.1	0.587	404/1,170	63.7	0.802
Female	226/690	65.3		362/419	59.9		390/1,109	63.2	
Age group (years)									
≤49	60/245	73.5	<0.001	67/204	66.0	<0.001	127/449	70.0	<0.001
50–74	246/842	69.1		204/582	63.9		450/1,424	66.9	
≥75	126/245	45.3		91/161	41.7		217/406	43.8	
Period of diagnosis									
2000–2004	92/233	60.4	0.109	89/202	55.9	0.153	181/435	58.3	0.012
2005–2009	144/413	65.0		141/355	60.1		285/768	62.7	
2010–2013	196/686	67.9		132/390	63.8		328/1,076	66.4	
Clinical staging by age group									
≤49 years									
I	0/43	100.0	<0.001	3/32	89.8	<0.001	3/75	95.4	<0.001
II	0/52	100.0		5/45	88.0		5/97	94.3	
III	10/63	82.6		18/72	73.8		28/135	77.8	
IV	47/80	37.8		35/43	16.8		82/123	30.3	
50-74 years									
I	11/170	92.7	<0.001	12/100	87.4	<0.001	23/270	90.7	<0.001
II	18/196	90.4		27/125	77.6		45/321	85.4	
III	38/207	80.6		60/206	70.1		98/413	75.3	
IV	162/241	28.0		94/121	20.3		256/362	25.3	
≥75 years									
I	17/51	64.2	<0.001	8/31	70.3	<0.001	25/82	66.5	<0.001
II	24/70	64.3		21/46	54.2		45/116	60.0	
III	24/48	43.6		19/35	43.9		43/83	43.4	
IV	47/59	17.5		26/28	7.1		73/87	14.1	
Starting treatment									
≤60 days	289/1,003	69.3	0.151	200/546	62.1	0.676	489/1,549	66.7	0.058
≥61 days	92/274	64.2		144/378	60.8		236/652	62.2	
Total	432/1,332	65.6		362/947	60.6		794/2,279	63.5	

OS: overall survival.

TABLE 4. Prognostic factors associated with colorectal cancer, by site (A.C.Camargo Cancer Center, 2000–2013).

Characteristic	Colon		Rectal		All	
	HR (95%CI)	HRa* (95%CI)	HR (95%CI)	HRa* (95%CI)	HR (95%CI)	HRa* (95%CI)
Gender						
Male	Reference	Reference	Reference	Reference	Reference	Reference
Female	1.01 (0.84; 1.22)	0.98 (0.81; 1.18)	1.06 (0.86; 1.30)	1.17 (0.95; 1.45)	1.02 (0.89; 1.17)	1.06 (0.92; 1.22)
Age group (yrs)						
≤49	Reference	Reference	Reference	Reference	Reference	Reference
50–74	1.24 (0.94; 1.65)	1.48 (1.11; 1.96)	1.09 (0.82; 1.43)	1.03 (0.78; 1.36)	1.15 (0.95; 1.40)	1.24 (1.02; 1.51)
≥75	2.85 (2.10; 3.88)	3.67 (2.69; 5.01)	2.27 (1.65; 3.11)	2.47 (1.80; 3.41)	2.54 (2.04; 3.16)	3.02 (2.42; 3.78)
Period of diagnosis						
2000–2004	Reference	Reference	Reference	Reference	Reference	Reference
2005–2009	0.87 (0.67; 1.12)	0.64 (0.49; 0.83)	0.83 (0.64; 1.08)	0.85 (0.65; 1.11)	0.85 (0.71; 1.03)	0.76 (0.63; 0.91)
2010–2013	0.77 (0.60; 0.99)	0.60 (0.47; 0.77)	0.77 (0.59; 1.01)	0.76 (0.58; 1.00)	0.76 (0.64; 0.91)	0.69 (0.57; 0.83)
Site						
Right colon	-	-	-	-	Reference	Reference
Left colon	-	-	-	-	0.94 (0.76; 1.17)	1.04 (0.84; 1.29)
Colon, NOS	-	-	-	-	1.10 (0.79; 1.55)	1.10 (0.79; 1.55)
Rectal	-	-	-	-	1.13 (0.92; 1.39)	1.37 (1.11; 1.69)
Starting treatment						
≤60 days	Reference	Reference	Reference	Reference	Reference	Reference
≥61 days	1.19 (0.94; 1.50)	1.19 (0.94; 1.51)	1.05 (0.84; 1.30)	1.22 (0.99; 1.53)	1.16 (0.99; 1.36)	1.22 (1.04; 1.43)

* Stratified by clinical stage; test of proportional-hazard assumption: colon (P=0.156); rectal (P=0.329); all (P=0.149).

Patients whose cancer was in the colon had a 5-year OS of 65.6%, (P<0.001). Subgroups of colon cancer patients with higher OS rates included patients who were ≤49 years old (73.5%) (TABLE 3). Mortality risk increased with increasing age (50–74 years HR=1.24; and ≥75 years HR=2.85). Mortality risk decreased for the most recent time periods (2005-2009 HR=0.87; and 2010–2013 HR=0.77) (TABLE 4).

Patients with rectal cancer had a 5-year OS rate of 60.6% (FIGURE 1.B). Again, subgroups of rectal cancer patients with higher OS rates included patients who were ≤49 years old (66.0%) (P<0.001) (TABLE 3). Mortality risk was increased among patients aged 75 and over (HR=2.47) (TABLE 4).

The best survival rates were observed among the subgroup of young patients with early stage (I–II) colon cancer, whose 5-year OS achieved 100%. The worst survival rates were observed among the subgroup of elderly patients with metastatic rectal cancer, whose 5-year OS were 7.1%.

DISCUSSION

The 5-year OS rate obtained for our CRC patient cohort (63.5%) was similar to those found in hospital-based studies in Iran (58.5% for 2005–2010)[12], Australia (63.0% for 2005–2010)[13], and Taiwan (68.7% for 2007–2013)[14], but notably higher than rates reported in China (range, 28.4–41.7% in the period of 2002–2014)[15]. We did not identify differences based on sex, even after adjusting for other characteristics[12-13]. Some studies have suggested that survival may be lower for men, due to differences in access to health services[7,16].

Survival decreased with increasing age, as previously described[7,12,16]. More than 80% of the patients were 50 years old or older. Increased age is a predictive factor for death in cancer patients[10,17] and has been associated with a higher risk of comorbidities, which reduce patient survival[18,19]. In a study in Japan, 20% of 792 patients had a Charlson Comorbidity Index (CCI) higher than or equal to 1, with a 1.20 increment of risk of overall mortality for each CCI point[10]. Meanwhile, in a Danish study of patients 70 years old or older, a 1.41 increase in the risk of overall mortality per CCI increment was observed[8]. These data reinforce the importance of the multidisciplinary team in treatment decision, as oncologic diagnosis is not the only risk.

We identified an improvement in survival in recent time periods. Similar results have previously been described[7,13,16]. Improved survival over time may be related to the implementation of treatment guidelines and new technologies to treat CRC.

OS was five percentage points higher for colon cancer patients (65.6%) than for rectal cancer patients (60.6%), consistent with prior studies reporting a poorer prognosis for rectal cancer than colon cancer[6,12-13,20]. In addition, our findings suggest that this lower of survival may be associated with the percentage of patients who began treatment more than 60 days after diagnosis (21.5% for colon cancer versus 40.9% for rectal cancer). As the treatment of rectal cancer is more complex than colon cancer, involving more exams for staging as well as the need of multimodality treatment, maybe these patients are more susceptible for delaying the start of treatment.

We did not identify any differences based on laterality of colon cancer (right vs left colon), contrasting with prior studies reporting lower survival rates for cancers located in the right colon[16,21,22]. In comparing survival rates across colon sites, we did not find differences in a combined analysis of patients with stage I, II, or III. However, we did identify a difference according to stage, in the right colon having a better prognosis when diagnosed at stage II (HR=0.92, 95%CI =0.87–0.97) than at stage III (HR=1.12, 95%CI =1.06–1.18)[16].

In terms of the type of treatment patients with stage I or II received only surgery, whereas patients with stage III or IV colon cancer received surgery combined with chemotherapy. For patients with rectal cancer stage II or III the treatment was surgery combined with both radiotherapy and chemotherapy. These findings were similar to those of other studies[13,23-25]. Advanced age may be an independent predictor to preclude adjuvant therapies[26].

Starting treatment more than 60 days after diagnosis was a predictor of poorer survival, which shows the need for implementing policies that enable universal access to early treatment[11].

Given than survival rates are better among patients in an early clinical stage, the CRC patient treated at the ACCCC had advanced-stage cancer (colorectal, 52-53%) underscores a need for the implementation of CRC screening programs[27-29]. It is notable that survival rates of patients with CRC showed an improvement over time. However, early stage remains critical and to ensuring that treatment starts as soon as possible following diagnosis.

Authors' contribution

Aguiar Junior S and Curado MP contributed to conception and design; Oliveira MM contributed to analysis, interpretation the data and drafted the manuscript; Silva DRM extracted the data and drafted the manuscript; Aguiar Junior S, Mello CAL, Calsavara VF critically reviewed the manuscript; Curado MP discussed, critically reviewed the manuscript and supervised the research. All authors approved the final version of the manuscript to be published.

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RESUMO – **Contexto** – Estudos hospitalares recentes têm demonstrado aumento da sobrevida do câncer colorretal e melhor sobrevida para mulheres, jovens e pacientes diagnosticados em estágio precoce da doença. **Objetivo** – Descrever a sobrevida global e analisar os fatores prognósticos de pacientes tratados para câncer colorretal em um centro de oncologia. **Métodos** – Foram incluídos pacientes com diagnóstico de adenocarcinoma de cólon e reto entre 2000 e 2013, identificados no Registro Hospitalar de Câncer do A.C.Camargo Cancer Center. A sobrevida global aos 5 anos foi estimada pelo método de Kaplan-Meier e os fatores prognósticos foram avaliados pelo modelo de Cox. As razões de risco (HR) são relatadas com intervalos de confiança (IC) de 95%. **Resultados** – Dos 2.279 casos de câncer colorretal analisados, 58,4% eram de cólon. A taxa de sobrevida global aos 5 anos para pacientes com câncer colorretal foi de 63,5% (65,6% e 60,6% para câncer de cólon e retal, respectivamente). O risco de óbito foi elevado para pacientes na faixa etária de 50–74 anos (HR=1,24; IC95% =1,02–1,51) e ≥75 anos (HR=3,02; IC95% =2,42–3,78), para pacientes com câncer retal (HR=1,37; IC95% =1,11–1,69) e para aqueles cujo tratamento foi iniciado >60 dias após o diagnóstico (HR=1,22; IC95% =1,04–1,43). O risco diminuiu para pacientes diagnosticados em períodos recentes (2005–2009 HR=0,76; IC95% =0,63–0,91; 2010–2013 HR=0,69; IC95% =0,57–0,83). **Conclusão** – A sobrevida dos pacientes com câncer colorretal é maior naqueles em estágio inicial e com início do tratamento antes dos 60 dias.. Idade acima de 70 anos foi fator independente preditivo de mau prognóstico. A sobrevida global aumentou para todos os pacientes tratados no período de 2000–2004 a 2010–2013.

DESCRITORES – Análise de sobrevida. Neoplasias colorretais. Sistema de registros. Prognóstico.

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