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Epidemiology and anatomic distribution of colorectal cancer in South Africa

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Background: Colorectal cancer (CRC) is the fifth most common cancer in sub-Saharan Africa (SSA) and the third most common in South Africa (SA). CRC characteristics in SSA are not well described. The aim is to describe patient characteristics and anatomic location of colorectal adenocarcinoma (CRC-AC) in SA.
Methods: A retrospective analysis of the histology specimens of CRC in SA through utilisation of the South African National Cancer Registry from 2006 to 2011.
Results: Six thousand one hundred and forty-six patients with colorectal malignancies were identified of which 5 498 (89%) had CRC-AC. The median age at presentation was 60 (interquartile range, 49–70) years. One thousand three hundred and seventy-two (25%) were < 50 years and 2 870 (52%) were male. Right colonic tumours were found in 1 277 (26%), 1 214 (25%) were left colonic lesions, and 2 404 (49%) lesions were located in the rectum. Patients ≥ 50 years at presentation (OR = 1.29, 95% CI = 1.11–1.50, $p < 0.001$) were more likely to have left colonic and rectal adenocarcinoma. Patients < 50 years at presentation were more likely to be black (OR = 1.67, 95% CI = 1.39–2.02, $p < 0.001$) and have right-sided tumours (OR = 1.25, 95% CI = 1.06–1.46, $p < 0.007$).
Conclusion: CRC-AC in SA presents at an earlier age than in HICs, such as the United States of America. The majority of CRC were left-sided and rectal; thus, screening with faecal immunochemical testing and flexible sigmoidoscopy should be considered. Further studies on the age-specific incidence and the genetics and epigenetics and socioeconomic determinants of CRC-AC in SA are needed.
Keywords: colorectal cancer, colorectal adenocarcinoma, patient characteristics, anatomic location

Introduction

Colorectal cancer (CRC) is the 5th most common cancer in sub-Saharan Africa (SSA) and the 3rd most common cancer in South Africa (SA).[1] Adenocarcinoma (AC) accounts for the vast majority of cases.[2,3] SA is an upper-middle-income country with high human development index (HDI). The incidence of CRC in SA is lower than in high-income countries (HICs).[4] This may be due to variations in genetic and environmental factors such as nutrition, obesity and activity.[5,6] Additionally, differences in life expectancy and access to screening, diagnostics and treatment between SA and HIC countries may influence the variation between regions. For example, SA and the United States of America (US) have a 16-year difference in life expectancy.[7] Given that CRC often develops over the age of 50 years, SA's lower life expectancy and limited access to screening programmes may impact incidence rates.[8,9] While the incidence of CRC is lower in SA than HICs, more than two-thirds of people with CRC in low- to middle-income countries die from the disease, compared with approximately half in HIC countries.[10]

CRC is distributed throughout the colon and rectum and can be classified into right colonic, left colonic, and rectal lesions. Right colonic lesions are found in the cecum, ascending colon, hepatic flexure, and transverse colon. Left colonic lesions are located in the splenic flexure, descending colon and the sigmoid colon. Rectal lesions are located in the rectosigmoid or rectum.[11,12] In the US, the majority of lesions were historically found in the rectum and the left colon, however, a right colonic shift, especially in older patients, has been noted.[13] In SSA, results have been varied. Preliminary results from an urban centre in SA reported left colonic and rectal AC in two-thirds of patients, which included 43% of rectal lesions.[5] In Nigeria, 60% of CRCs were located in the rectum[2] and in Tanzania, 60% of lesions were in the left colon.[14]

Colonic tumours in different locations are likely to have different pathogeneses.[15] Two CRC pathways involving mismatch repair (MMR) genes preferentially affect the right colon. The first is microsatellite instability (MSI) from

MMR mutations and is associated with younger patients and hereditary non-polyposis colon cancer (HNPCC). The second is hypermethylation of the MMR gene, which is a sporadic pathway associated with serrated polyps and older patients.[16] Left colon cancers are usually caused by chromosomal instability of oncogenes or tumour suppressor genes and can be sporadic or hereditary.[12]

The anatomical distribution of CRC or "sidedness" has been researched extensively to help predict prognosis and treatment. Previous studies demonstrated that right-sided colon cancers are more likely to occur in older patients, women, present with more advanced disease, and to have mucinous histology.[17] For earlier stage colon cancer (stages I and II), right-sided cancers have been shown to have a better prognosis, but worse for more advanced stages (stages III and IV).[13,18]

Location may also be important to guide screening modalities. While colonoscopy has been the gold standard in the US, it has risks and usually requires a specialist (surgeon or gastroenterologist) to perform the procedure. In SA, screening colonoscopy is not readily available.[19] Flexible sigmoidoscopy, which is used to detect left colonic and rectal AC, in conjunction with stool-based tests like faecal immunochemistry testing (FIT), could potentially be used as a screening tool, particularly because the procedure does not require sedation and could be performed by trained non-specialists.

Data on the distribution of CRC in SSA is limited. Only 23 of the 47 countries in SSA have registries, and these registries often only include data from individual centres, urban areas or regions.[20] There have not been any nationwide studies on the anatomic distribution of CRC in SA. The main objective of this study was to describe the anatomical distribution of colorectal adenocarcinoma (CRC-AC) in SA using the South African National Cancer Registry (SANCR) data.

Methodology

Study design and period

The SANCR was established in 1986 and collects data on all pathology-diagnosed cancers in the South African population (histology, cytology, and bone marrow aspirate and trephines).[21] This was a retrospective study of all pathology-confirmed CRC reported to the SANCR from 2006 to 2011.

Study population

All patients who had CRC confirmed pathology reports submitted to SANCR were included. Patients with CRC but whose pathology reports were not submitted to SANCR were excluded. In addition, patients' pathology reports on non-primary CRC (i.e. metastatic disease) only were excluded.

SA has a two-tiered, unequal healthcare system. Eighty-six per cent of the population utilise the state-funded public health system. Despite this, approximately 50% of the total health expenditure is allocated to the public health system. The private healthcare system is mainly utilised by insured individuals. Patients accessing public health services are, therefore more likely to be from the lower income class. During the study period, only specimens from public healthcare laboratories were captured. From 2011 onwards, the SANCR included specimens from private laboratories. Because of the potential heterogeneity, this study only included data until 2011, therefore only public sector specimens.

Data analysis

The SANCR methodology is based on the recommendations by the International Agency for Research on Cancer (IARC). Pathology reports were received in electronic or hard copy format, from which appropriate data items, namely demographics and tumour information, were abstracted. A hot-deck imputation method was used to allocate population groups to cases without this information. CRC cancers were classified by anatomical site/topography using the International Classification of Diseases – Oncology, Version 3 (ICD-O-3).[22] Cases of confirmed CRC as coded by the SANCR coders (ICD-O-3 classification C18.0 to C20) were included. Full pathology reports were anonymised then shared with the authors. Variables extracted included age, gender, province, race, ICD-O-3 code, and the full pathology report.

For this study, entries codes as ICD-O-3 C18.0-18.9 and C20 were extracted. This included biopsy and resection specimens. Patients who had biopsy then resection were included only once. Patients who had multiple biopsies were included only once. The full pathology reports were read by one of the authors to confirm the anatomic location of the lesion (right, left, or rectum, unknown/other, non-primary) and the type of CRC (AC, carcinoid, lymphoma, squamous cell carcinoma, other). Non-primary specimens were excluded. Patients with an unknown anatomic location were excluded from the analysis for location, similar to the methodology in previous studies.[10,23,24] Lesions in the caecum, ascending colon, hepatic flexure and transverse colon were defined as right colonic lesions. Lesions in the splenic flexure, descending colon, and sigmoid were defined as left colonic lesions. Lesions in the rectosigmoid and rectum were defined as rectal lesions. Patients < 50 years of age at presentation were defined as early-onset cancer. Data were analysed using Stata 15 (College Park, Texas USA). Univariate and multivariate analysis was performed to determine associations with location. Variables with a p-value ≤ 0.10 were included in the multivariate analysis. All data were anonymised, and the master data list is held by the SANCR. Ethical approval was given by the University of Cape Town Human Ethics Committee.

Results

There were 6 246 patients with CRC; 100 had non-primary specimens and were excluded; therefore 6 146 patients were analysed. Table I illustrates patient demographics and anatomic location of the ACs. There were 5 498 (89%) cases of AC. Among cases of AC, the median age of presentation was 60 (interquartile range (IQR), 49–70) years. Forty-nine per cent were black, 30% white, 20.6% mixed race and 6.5% Indian. One thousand three hundred and seventy-two (25%) patients were < 50 years and 2 870 (52%) were male. Of the 4 895 cases with known anatomic location, 1 277 (26%) were right, 1 214 (25%) were left and 2 404 (49%) were located in the rectum. Anatomic location by age group is shown in Table II. In patients < 50 years of age, 26% of ACs were right-sided compared with 22% in patients ≥ 50 years (p = 0.006).

On multivariate analysis patients ≥ 50 years of age at presentation were more likely to have left colonic and rectal

Table I: Demographic and histological characteristics of colorectal cancer in South Africa (2006–2011)

Variable	Adenocarcinomas								
	n	Per cent by race							
		Black		White		Mixed		Indian	
Total number	5498	40.9 %		30%		20.6%		6.5%	
		n	%	*n*	%	*n*	%	*n*	%
Male gender	2870	1202	42	884	31	719	25	65	2
Age group									
< 20	25	19	76	6	24	0	0	0	0
20–29	181	128	71	23	13	28	15.4	2	1
30–39	369	208	56	67	18	86	23.3	8	2
40–49	797	431	54	150	19	207	25.9	9	1
50–59	1224	549	45	326	27	312	25.4	37	3
60–69	1386	492	35	487	35	377	27.2	30	2
70–79	1015	338	33	396	39	259	25.2	22	2
≥ 80	385	132	34	173	45	75	19.4	5	1
Missing	116	62	53	24	20	23	19.8	7	6
Year of diagnosis									
2006	744	293	39	238	31.9	196	26.3	17	2
2007	873	347	39.7	257	29.4	253	28.9	16	2
2008	853	341	39.9	276	32.3	228	26.7	8	1
2009	993	453	45	269	27	244	34.5	22	2
2010	974	433	44.4	304	31.2	210	21.5	27	3
2011	1061	492	46.3	308	29	231	21.7	30	3
Colon cancer site	*n* = 4895[a]								
Right	1277	530	41.5	383	29.9	341	27	23	2
Left	1214	502	41.3	374	30.8	316	26	22	2
Rectum	2404	1024	42.5	728	30	588	24	64	3

[a] 603 cases with unknown anatomic location were excluded

Table II: Anatomic distribution of colorectal adenocarcinoma by age group in South Africa (2006–2011)

	Right	Left	Rectal	Total[a]
Age group	*n* (%)	*n* (%)	*n* (%)	*n* (%)
< 20	2 (10.5)	2 (10.5)	15 (78.9)	19(100)
20–29	38 (23.8)	20 (12.5)	102 (63.8)	160 (100)
30–39	102 (31.8)	73 (22.7)	146 (45.5)	321 (100)
40–49	215 (30.6)	175 (24.9)	312 (44.4)	702 (100)
50–59	313 (28.4)	258 (23.4)	530 (48.1)	1101 (100)
60–69	293 (23.6)	336 (27.0)	612 (49.3)	1241(100
70–79	208 (22.7)	237 (25.9)	471 (51.4)	916 (100)
≥ 80	83 (24.0)	95 (27.5)	167 (48.4)	345 (100)
Missing age	23 (25.6)	18 (20.0)	49 (54.4)	90 (100)

[a] 603 cases with unknown anatomic location were excluded

AC (OR = 1.29, 95% CI = 1.11–1.50, $p < 0.001$) (Table III). Patients who were black (OR = 1.67, 95% CI = 1.39–2.02, $p < 0.001$), and of younger age (< 50 years) (OR = 1.25, 95% CI = 1.06–1.14, $p = 0.007$) were more likely to present with right colonic lesions, with white patients less likely to have early age of onset cancer in comparison to other race groups (OR = 0.55, 95% CI = 0.45–0.67, $p < 0.0001$)(Table IV).

Discussion

This is the first study of CRC in SA using the national cancer registry data. The majority of CRCs were ACs. The median age of presentation was 60 years compared with 67 years reported in the US.[6] One-quarter of patients were under 50 years of age.

Black South Africans were more likely to present with early-onset cancer than other population groups. This is consistent with studies from other SSA countries as well as the US.[5,6] In contrast, this study revealed white patients were less likely to develop early age of onset AC than other population groups.

Access to colonoscopy in SA is limited. There is no population screening programme for CRC. Left colonic and rectal AC could be diagnosed with a flexible sigmoidoscopy, which does not require sedation and can be done by a general practitioner compared with right colonic lesions which require the use of a colonoscopy. As nearly three-quarters of CRC-AC were located in the left colon and rectum and were associated with older age in our study, flexible sigmoidoscopy could detect the majority of colonic and rectal lesions in SA and could be considered as part of public health screening, especially in persons older than 50 years.

This study has several limitations. Unlike other national registries such as Surveillance, Epidemiology, and End Results (SEER) in the US and the Sweden Cancer Register, the SANCR is only based on registered pathologic specimens and does not capture stage at presentation, treatment or outcomes such as mortality. Data from the private sector, accounting for approximately 15% of the population, were

Table III: Associations with left colonic and rectal adenocarcinoma in South Africa (2006–2011)

	Univariate analysis			Multivariate analysis		
	OR	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Age group						
≥ 50 years	1.27	(1.10–1.47)	**0.001**	1.29	(1.11–1.50)	**< 0.001**
Gender						
Male	0.92	(0.81–1.05)	0.225			
Race						
Black	1.03	(0.90–1.17)	0.675			
Mixed race	0.91	(0.79–1.07)	0.276			
White	1.02	(0.89–1.17)	0.755			
Indians/Asian	1.33	(0.83–2.11)	0.232			
Missing	0.94	(0.68–1.28)	0.682			
Year of diagnosis						
2006	1.10	(0.91–1.34)	0.314			
2007	0.99	(0.83–1.18)	0.945			
2008	0.91	(0.77–1.09)	0.335			
2009	1.06	(0.88–1.22)	0.680			
2010	1.07	(0.91–1.27)	0.413			
2011	0.91	(0.78–1.07)	0.269			

OR – Odds ratio, CI – Confidence interval

Table IV: Associations with early age of onset adenocarcinoma in South Africa (2006–2011)

	Univariate analysis			Multivariate analysis		
	OR	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Gender						
Male	0.92	(0.81–1.03)	0.156			
Race						
Black	2.17	(1.92–2.46)	**< 0.001**	1.67	(1.39–2.02)	**< 0.001**
Mixed Race	0.91	(0.78–1.06)	0.218			
White	0.42	(0.36–0.49)	**< 0.001**	0.55	(0.45–0.67)	**< 0.001**
Indian/Asian	0.56	(0.34–0.92)	0.021	0.66	(0.38–1.13)	0.125
Missing	0.90	(0.66–1.23)	0.525			
Colon cancer site						
Right	1.27	(1.10–1.47)	0.001	1.25	(1.06–1.46)	0.007
Left	0.84	(0.72–0.98)	0.031	0.91	(0.76–1.07)	0.240
Rectum	0.91	(0.80–1.06)	0.118			
Year of diagnosis						
2006	1.04	(0.80–1.06)	0.693			
2007	0.96	(0.76–1.2)	0.713			
2008	1.02	(0.81–1.28)	0.866			
2009	0.94	(0.76–1.18)	0.611			
2010	1.01	(0.81–1.25)	0.951			
2011	0.91	(0.73–1.13)	0.385			

OR – Odds ratio, CI – Confidence interval

not available during this period. Patients utilising the public health service in SA are more likely to be uninsured, and therefore from the lower income group. Racial distribution was included, but socioeconomic status was not included in the dataset. Without data from the private sector, the results of the study cannot be generalised to be representative of the whole of SA.

In conclusion, CRC-AC in SA presents at an earlier age than in HICs, such as the US. The majority of lesions were left-sided and rectal; thus, screening modalities like FIT and flexible sigmoidoscopy should be considered. Further studies on the age-specific incidence, and the genetics and epigenetics and socioeconomic determinants of CRC-AC in SA are needed.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

Ethical approval was obtained from the University of Cape Town Faculty of Health Science Human Research Ethics Committee (Ref: 692/2016).

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