Epidemiology and Anatomic Distribution of Colorectal Cancer in South Africa

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DECLARATION

I, …AKREM AMER……, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university. I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

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1. Literature review

Epidemiology of colorectal cancer

Incidence and mortality

More than one million individuals worldwide will develop colorectal cancer (CRC), which accounts for more than 9% of all new cancers annually (1). CRC is the third most common cancer in males and the second most common cancer in females worldwide (2). The majority of CRC is categorized as adenocarcinoma (90%), with the remaining 10% including adeno squamous, squamous cell , neuroendocrine, spindle cell and undifferentiated carcinomas (3). The incidence varies geographically, with a 10-fold difference between regions. Notably, 55% of the cases occur in high income countries (HICs) (2). Australia, New Zealand, Europe, and Northern America have the highest incidence rates of CRC. On the other hand, Africa, South-Central America, and South-Central Asia have lower incidence rates (4) . For both sexes, the crude incidence of CRC in Sub-Saharan Africa (SSA) was reported to be 4.04 per 100,000 population (5). However, the mortality rate in HICs has noticeably declined (6,7), while it has not in low- and middle-income countries (LMICs)(2). The 5-year survival rate was 8.3% in Uganda (8) and 17.4% in Zimbabwe (9), compared with 59% in England and Wales.(10) A low incidence of CRC in South Africa (SA) has been reported, although it has increased over the past decade. In 1989, CRC was the 10th most common cancer diagnosed in males and females (11). Currently, CRC is the fourth most common cancer among both women and men in SA. In 2014, as reported by National Cancer Registry, the gross incidence rate was 7.34 per 100,000 per year for men and 5.80 per 100,000 per year for women (12).

Risk factors

Historically, genetic and environmental factors influence the epidemiology of CRC. Age is a known risk factor for CRC. Most often, CRC presents in individuals over the age of 50 years (13). Furthermore, gender and race impacts CRC incidence with women and people of colour having a lower incidence than men and white people respectively (14), although this may be confounded by access to care.

CRC incidence increases with economic development. CRC incidence rates have increased in economically transitioning countries, whereas rates have stabilized or decreased in economically developed countries. This increase in economically transitioning countries may reflect the adoption of the Western lifestyles and behaviours, for example, low-fibre diet, animal fat, red meat, and alcohol consumption, and sedentary lifestyle are be risk factors (15,16). On the other hand, fruit and vegetable consumption, nonsteroidal anti-inflammatory drugs (NSAIDs), hormone replacement therapy, and physical activity are protective factors (15–17).

Alcohol consumption is a contributing factor to colon carcinogenesis. When comparing moderate alcohol consumption (2-3 units per day) and higher alcohol consumption with light alcohol consumption, risk for CRC increases by 20% and 50% respectively (18). Seitz & Mueller found that when alcohol enters the colon, it is microbially metabolized as acetaldehyde. This in turn damages the folate, which is responsible for DNA synthesis and the repair of cells, which increases the risk of developing mucosal dysplasia (19). Furthermore, cigarette smoking has been found to increase the risk of developing colorectal adenomas by two to three fold. This is because the gastrointestinal tract and circulatory

system spreads the cigarette carcinogens to the colorectal mucosa, increasing the risk of inflammation, mutagenesis, and carcinogenesis (20).

Up to 20% of individuals with CRC have other family members who have been impacted by this illness. (21).The explanations for the increased risk are not well explained but are possibly due to hereditary genes, shared environmental factors, or a mixture of both (21). However, most CRCs are sporadic, as three-quarters of patients have a negative family history (22, 23). Hereditary colorectal cancers related to familial adenomatous polyposis (FAP) and hereditary colorectal cancer (HNPCC) account for 10% of CRC. People with these genetic mutations will have an 80% lifetime risk. Indeed, those affected by a hereditary CRC form a specific sub-group of the patient population, representing 5–10% of all patients. HNPCC is the most prevalent (24).

Anatomic distribution of colorectal cancer

Historically, two-thirds of CRC cases are found in the left colon (descending colon and sigmoid colon), and rectum and one-third in the right colon (cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure,) (25, 26). However, there are recent epidemiological studies in HICs that report a trend of a right shift of CRC (27–29).

It is still unclear whether this right colonic shift occurred due to environmental and genetic factors or a change in screening protocols. Flexible sigmoidoscopy can detect left colonic and rectal lesions while right colonic lesions can only be found during a colonoscopy, which requires more advanced practitioner training as well as bowel preparation (30,31). For example, flexible sigmoidoscopy can be conducted by a general practitioner and only

requires a rectal enema, whereas a colonoscopy is usually done by a gastroenterologist or surgeon and requires oral bowel preparation. Increased use of colonoscopy may be a reason for the increase in right lesions detected. However, different distributions of colorectal tumours between the right, left colon and rectum might be due to environmental risk factors such as diet and lifestyle, different frequencies of hereditary colorectal neoplasms (which are characterized by increased frequency in the right colon). In addition, it has been suggested that the different embryological origins of the right and left colon provide distinct molecular patterns, which results in variable susceptibility to CRC (32).

In HICs, right colon tumour incidence has increased while left colon and rectum incidence has decreased (33). Migration of individuals from LMICs to HICs countries has changed the epidemiology of the anatomical distribution. As migrants are exposed to the environmental factors, they are at risk of developing CRC (34, 35). Notably, these migrants tend to develop CRC in the left colon (34–36) .There is an association between tumour location and dietary factors, as it has been observed that a high intake of fat increases the risk of right colonic lesions while a high intake of protein increases the incidence of left colonic and rectal lesions (37,38).

There are variations in anatomic distribution by gender in many HICs. For example, New Zealand has a difference in anatomic distribution incidence by gender. Men tended to have rectal cancer, while women had more right colonic lesions (39). Anatomic distribution is also associated with age. In the US, right colonic lesions (proximal to the splenic flexure) increased with age (40,41). However, a longitudinal study done in the United Kingdom between 1993 and 2002, including 763 patients with adenocarcinoma, showed no evidence of a shift towards the right colon when considering age and gender at the time of the diagnosis

(42).

In the United States of America (US), older individuals, particularly whites and African Americans, have been shown to experience the highest CRC burden especially right colonic lesions (43). In the US, there has been a shift in incidence towards right colonic lesions; this may be explained by increased screening using colonoscopy to examine the entire colon, including the right area, and with population ageing (43).

Japan has shown a similar trend as in the US, with rising right incidence compared with rectal cancer (44). Additionally, a recent cohort study compared the prevalence, shape, and location of colorectal neoplasia between South Korean and American patients. Among South Korean patients, there were adenomas and advanced tumours in the left colon and rectum, but a lower risk of right colonic neoplasia compared with American patients (45).

In South-East Asia, specifically Malaysia, tumours were mainly located in the left colonic and rectum side. There were no variations in anatomical location between races, sexes and age groups (46). In Africa, the data on the anatomical distribution of CRC are not well investigated. Some countries have carried out a small number of studies; however, due to the limited resources and screening programs available, these studies are limited (5) . Rectal cancer is still a predominant distribution of colorectal cancer in SSA, accounting for 46%, followed by the cecum at 17% (5). Nigeria, with the highest population in Africa, has experienced an increase in the incidence of CRC in both urban and rural areas. In a review between 1991-2000 by the Jos University Teaching Hospital, it was reported that CRC was located predominantly in the rectum (57%), followed by the colon (32%) and the cecum (8%) (47). In 2013, data in rural Nigeria showed that the subsites of CRC were predominantly in the right side, mainly in the cecum (36%) and the hepatic flexure (21%), followed by the

rectum (24%) (48). However, the right colonic shift of CRC was not observed in Sudan, as 83% of CRC patients had lesions in the rectosigmoid region and only a minority had right colonic tumours (49).

In South Africa, there are few studies reporting the prevalence and incidence or anatomic distribution of CRC. In the Northern Cape, it was reported that the right colon was the dominant location for CRC among people younger than 50 years old. This was caused mainly by inherited diseases, such as HNPCC also known as Lynch syndrome and the microsatellite instability tumour gene (MSI) (50).

Conclusion

In South Africa, a developing country, CRC has started to become a major challenge for patients and surgeons as it is the third most common cancer in women and the fourth most common cancer in men (12). The right colonic shift in CRC has occurred in some African countries (48). However, there is not sufficient data about the incidence, age group, and anatomical distribution of CRC in South Africa. This study reports the incidence, age group, and anatomical distribution of CRC between 2006 to 2010. The results of this study may have implications for screening, surveillance methods, or management plans.

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2. Publication- Ready manuscript

Epidemiology and Anatomic Distribution of Colorectal Cancer in South Africa

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Abbreviations:
CRC: Colorectal cancer, SSA: Sub-Saharan Africa, CRC-AD: Colorectal adenocarcinoma:, HIC: High income countries, FAP: Familial Adenomatous Polyposis, HNPCC: Hereditary non polyposis colorectal cancer, MSI: Microsatellite instability tumour, SANCR: South African National Cancer Registry, SEER: The Surveillance, Epidemiology, and End Results, IARC: International Agency for Research on Cancer, US: United States of America.

Abstract

Background: Colorectal cancer (CRC) is the 5th most common cancer in sub- Saharan Africa (SSA) and the 3rd most common cancer in Southern Africa. CRC characteristics in SSA, including anatomic distribution, are not well described.

Objective: To describe patient characteristics and anatomic location of colorectal adenocarcinoma (CRC-AC) in South Africa.

Design: This was a retrospective study of CRC using the South African National Cancer Registry from 2006-2011.

Main Outcome Measures: Patient age, gender, racial/ethnic group, province, histology type, and tumour location.

Results: 6146 patients were included in the analysis. Among patients with adenocarcinomas, the median age of presentation was 60 (interquartile range, 49-70) years. 1372 (25%) of patients were < 50 years and 2870 (52%) were male. There were 5498 (89%) cases of adenocarcinoma (AC). 1277 (26%) CRC-AC were right colonic lesions, 1214 (25%) were left colonic lesions, and 2404 (49%) lesions were located in the rectum. Patients ≥ 50 years at presentation (OR=1.29. p<0.001) and from Limpopo province (OR=1.46, p=0.029) were more likely to have left colonic and rectal adenocarcinoma on multivariate analysis. Patients who were black (OR=1.67, p<0.001), had right colonic lesions (OR=1.25, p=0.007), and were from Mpumalanga (OR=1.67, p=0.007), Limpopo (OR=1.60, p=0.002), or Northwest (OR=1.76, p=0.001), were significantly associated with early onset adenocarcinoma.

Conclusion: CRC-AC in South Africa presents at an earlier age than in HICs, such as the US. Early-onset CRC is higher in black South Africans who live in Mpumalanga, Limpopo, and Northwest in comparison with other provinces. The majority of colorectal cancer were left-sided and rectal; thus screening flexible sigmoidoscopy should be considered. Further studies on the age-specific incidence and the genetics and epigenetics of CRC-AC in South Africa are needed.

Background

Colorectal cancer (CRC) is the 5th most common cancer in sub-Saharan Africa (SSA) and the 3rd most common cancer in Southern Africa (1). Adenocarcinoma (AC) accounts for the vast majority of cases (2,3). The incidence of CRC in SSA is lower than in high-income countries (HICs) (4).This may be due to variations in genetic factors and environmental factors such as nutrition, obesity and rates of exercise (5,6). Additionally, differences in life expectancy and access to diagnostics and screening between SSA and HICs may influence the variation seen between regions. For example, South Africa and the United States of America (US) have a 16 year difference in life expectancy (7). Given that colorectal cancer often develops over the age of 50 years (8), South Africa's lower life expectancy and limited access to screening programs may impact incidence rates. Furthermore, gender and race impacts CRC incidence with women and people of colour having a lower incidence than men and white people respectively (9), although this may be confounded by access to care. While CRC incidence is lower in SSA than HICs, more than two-thirds of people with CRC in low- and medium- human development index (HDI) countries die compared with approximately half in high HDI. (10–12).

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, right colon (or ascending), hepatic flexure, and transverse colon. Left colonic lesions are located on the splenic flexure, left (or descending) and the sigmoid colon. Rectal lesions are located in the rectosigmoid or rectum (13–16). 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 (17). In SSA, results have been varied. Preliminary results in South Africa from one

urban centre has reported that left colonic and rectal adenocarcinoma in two- thirds of patients, which included 43% of rectal lesions (18). In Nigeria, 60% of CRC were located in the rectum (4) and in Tanzania, 60% of lesions were in the left colon (19) .

Different tumour locations in the colon are likely to have a different pathogenesis (20). 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) (21). The second is hypermethylation of the MMR gene which is a sporadic pathway associated with serrated polyps and older patients (22). Left colon cancers are usually caused by chromosomal instability of oncogenes or tumour suppressor genes and can be sporadic or hereditary (23).

The anatomic distribution of CRC has implications for screening and treatment. Currently, there is debate on the best screening method for CRC. 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 South Africa, an upper-middle income country, screening colonoscopy is not readily available in the public (government) sector, which provides health care to the majority of the population(24). Left colonic and rectal adenocarcinoma are the most common, compared with right colonic lesions (18). Flexible sigmoidoscopy, which is used to detect left colonic and rectal adenocarcinoma, could potentially be used as a screening tool, particularly because the procedure does not require sedation and can be performed by non-specialists.

Anatomic distribution can also vary based on age and race. Understanding the racial/ethnic disparities in the anatomic distribution would also have implications for early diagnosis and

treatment. In the US, the median age at presentation is 70 years (25). However, African Americans are being diagnosed with CRC at a younger age (< 50 years old), but with lower survival than whites (26,27). Therefore, earlier screening is recommended starting at the age of 40 years (28). CRC in SSA presents at a younger median age than in the US. There are also racial/ethnic differences, with black Africans presenting at a younger age than whites (18)(29–32). Furthermore, although left colonic and rectal adenocarcinoma are more common in SSA (33), among patients with right colonic lesions, a report from Zimbabwe showed that blacks had a high proportion of right lesions compared with whites especially in younger patients (29). In a regional South African study, blacks <50 years of age with CRC presented with a higher proportion of right colonic lesions and microsatellite instability compared with white patients (16).

There have not been any nationwide studies on the anatomic distribution of colorectal cancer in South Africa. The main objective of this study was to describe the anatomic distribution of CRC adenocarcinoma in South Africa using the South African National Cancer Registry (SANCR). The secondary objectives were to describe associations with early-onset cancer and left colonic lesions.

Methods

Study design and period

The SANCR was established in 1986 and collects all pathology-diagnosed cancers in the South African population (histology, cytology, and bone marrow aspirate and trephines) (34).

This was a retrospective study of all pathology-confirmed CRC reported to the SANCR from 2006-2011. During the study period, the SANCR only captured public (government) sector specimens.

Study population

All patients who had CRC confirmed tumour specimens submitted to SANCR were included. Patients with CRC but whose pathology specimens were not submitted to SANCR were excluded. In addition, patients without pathology reports on primary CRC (i.e. metastatic disease) were excluded.

Data analysis

A dataset from the SANCR for all CRC specimens for the study period were obtained. The SANCR database was established in 1986 and through 2011, included all pathology proven cancers from the public sector. The SANCR Methodology follows 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 (35). Following international practice,

CRC cancers were classified by anatomical site/topography using the International Classification of Diseases – Oncology, Version 3 (ICD-O-3) (36). Cases of confirmed CRC as coded by the SANCR coders (ICD 0 classification C18.0 to C20.9) were selected by the SANCR to be included in this study. Full pathology reports were anonymized then shared with the authors. Variables from SANCR included age, gender, province, race, ICD.10 code, and the full pathology report were extracted.

For this study, entries codes as ICD10 18.0-18.9 were extracted. The full pathology reports were read by one of several authors to confirm the anatomic location of the lesion (right, left, or rectum, unknown/other, non-primary) and the type of CRC (adenocarcinoma, carcinoid, lymphoma, squamous cell carcinoma, other). Patients who had multiple biopsies were included only once. Non-primary specimens were excluded. Patients with an unknown anatomic location were excluded from the analysis for location. Similar to previous studies, (15,16,37,38). Lesions in the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure were defined as right colonic lesions. Lesions in the descending colon, and sigmoid were defined as left colonic lesions. Lesions in the rectosigmoid and rectum were defined as rectal lesions. All patients were initially classified by tumour type, however, the analysis on associations with the location of the tumour was only done on CRC adenocarcinomas (AC). 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 anonymized, and the master data list is held by the SANCR. Ethics approval was given by the University of Cape Town Human Ethics Committee.

Results

There were 6246 patients with CRC; 100 had non-primary specimens, leaving 6146 patients for analysis. Table 1 illustrates the patient characteristics, histologic type, and anatomic location of the cancers. There were 5498 (89%) cases of AC. Among cases of AC, the median age of presentation was 60 (interquartile range (IQR), 49-70) years. It was found that 1372 (25%) patients were <50 years and 2870 (52%) were male. There were 4895 cases of known

anatomic location and 1277 (26%) of CRC-AC were right whilst 1214 (25%) were left and 2404 (49%) were located in the rectum. Anatomic location by age group are shown in Table 2. In patients <50 years of age, 26% of all adenocarcinomas were right-sided compared with 22% in patients ≥50 years (p=0.006).

Associations with Left Colonic and Rectal Adenocarcinoma

Patients ≥50 years of age at presentation (OR=1.29, p<0.001), and from the Limpopo province (OR=1.46, p=0.029) were more likely to have left colonic and rectal adenocarcinoma on multivariate analysis (see Table 3).

Associations with Early Onset Colorectal Adenocarcinoma

Patients who were black (OR=1.67, p<0.001), had right colonic lesions (OR=1.25, p=0.007) or were from Mpumalanga (OR=1.67, p=0.007), Limpopo (OR=1.60, p=0.002), or the Northwest (OR=1.76, p=0.001) provinces were more likely to be <50 years of age at presentation on multivariate analysis (see Table 4). Patients who were white were less likely to develop early onset cancer than other race groups (OR= 0.55, p<0.0001) in the multivariate analysis.

Discussion

This is the first study of CRC in South Africa using the national cancer registry data. The majority of CRC were adenocarcinomas. The median age of presentation was 60 years compared with 67 years in the US (39). One-quarter of patients were under 50 years of age. This may be influenced by South Africa's relatively lower life expectancy, genetic variation, and cultural/ environmental factors. More research is needed to understand why patients are presenting at a relatively younger age in South Africa.

Inherited cancers such as HNPCC are known to affect large cohorts of families in South Africa. In the Northern Cape, families with 13 different germline mismatch repair gene mutations have been identified with over 1500 at-risk individuals (40)(41). The specific mutation is unknown, therefore, these higher risk individuals undergo screening colonoscopy annually (36). However, in our study, a multivariate analysis revealed the Northern Cape province was not significantly associated with early-onset adenocarcinoma. It is possible that inherited cancers such as HNPCC are also prevalent in these provinces, but more epidemiologic and genetic studies are needed. In our study, 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 (16)(42). In contrast, this study revealed white patients were less likely to develop early onset adenocarcinoma than other population groups. Less global data on black people and CRC are available compared to data on white people. More research is need around risk factors for early onset adenocarcinoma including understanding tumour biology and social determinants. In our study right colonic lesions were associated with early onset adenocarcinoma. In other studies, right sided colonic lesions have been associated with hereditary CRC such as HNPCC (43,44), but this study did not distinguish between sporadic and hereditary cases.

The difference in incidence rates between right, left, and rectal colonic lesions may be influenced by accessibility of diagnostic tools. Left colonic and rectal adenocarcinoma are often diagnosed with a flexible sigmoidoscopy, which doesn't require sedation and can be done by a general practitioner compared with right colonic lesions which require the use of a colonoscopy. However, given the fact that left colonic and rectal adenocarcinoma accounted for nearly three-quarters of CRC-AC and were associated with older age in our study, flexible

sigmoidoscopy would detect the majority of colonic and rectal lesions in South Africa and should be considered as part of public health screening, especially in persons older than 50 years.

This study has 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 does not capture stage at presentation or outcomes such as mortality (45,46). Single institutions databases such as Groote Schuur Hospital have prospective databases with stage and survival data, but a South African national registry that captures these variables is needed as well. Furthermore, data from the private sector were not available. Sixteen percent of South Africans have private health insurance, especially among white South Africans (47). Without data from the private sector, the results of the study cannot be generalized to be representative of the whole of South Africa.

In conclusion, CRC-AC in South Africa presents at an earlier age than in HICs, such as the US. There are disparities with early-onset CRC. Early-onset CRC is higher in black South Africans who live in Mpumalanga, Limpopo, and Northwest in comparison with other provinces. The majority of CRC were left colonic and rectal tumours and screening flexible sigmoidoscopy should be considered. Further studies on the age-specific incidence and the genetics and epigenetics of CRC-AC in South Africa are needed.

Tables and Figures

Table 1: Demographic and Histological Characteristics of Colorectal Cancer in South Africa (2006-2011)

Characteristics	All Colorectal Cancers	Adenocarcinomas
	N (%)	N (%)
Total Number	6146 (100)	5498 (100)
Gender		
Male	3182 (51.8)	2870 (52.2)
Race		
Black	2680 (43.6)	2359 (42.9)
Mixed Race	1233 (20.1)	1130 (20.5)
White	1834 (29.8)	1650 (30.0)
Indian/Asian	134 (2.2)	120 (2.2)
Missing	265 (4.3)	237 (4.3)
Age Group		
<20	33 (0.5)	25 (0.4)
20–29	206 (3.3)	181 (3.3)
30–39	435 (7.1)	369 (6.7)
40–49	908 (14.8)	797 (14.5)
50–59	1373 (22.3)	1224 (22.3)
60–69	1520 (24.7)	1386 (25.2)
70–79	1134 (18.4)	1015 (18.5)
≥80	415 (6.7)	385 (7.0)
Missing	122 (2.0)	116 (2.1)
Provinces		
Eastern Cape	766 (12.5)	725 (13.2)
Northern Cape	158 (2.6)	148 (2.7)
Western Cape	2121 (34.5)	1977 (36.0)
Free State	429 (7.0)	376 (6.8)
Gauteng	1935 (31.5)	1595 (29.0)
Mpumalanga	162 (2.6)	146 (2.7)
Limpopo	295 (4.8)	278 (5.1)
Kwa-Zulu Natal	65 (1.1)	59 (1.1)
Northwest	215 (3.5)	194 (3.5)
Year of Diagnosis		
2006	835 (13.6)	744 (13.5)
2007	969 (15.8)	873 (15.9)
2008	958 (15.6)	853 (15.5)
2009	1106 (18.0)	993 (18.1)
2010	1092 (17.8)	974 (17.7)
2011	1186 (19.3)	1061 (19.3)
Histologic types		
Adenocarcinomas	5498 (89.5)	5498 (100)
Squamous cell carcinoma	91 (1.9)	
Carcinoid	3 (0.05)	
Other/Unknown	554 (9.0)	
Colon cancer site	n=5413[a]	n=4895[b]
Right	1479 (27.3)	1277 (26.1)
Left	1302 (24.0)	1214 (24.8)
Rectum	2632 (48.6)	2404 (49.1)

[a]733 cases with unknown anatomic location were excluded. [b]603 cases with unknown anatomic location were excluded

Table 2: 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				

Table 3: Associations with Left Colonic and Rectal Adenocarcinoma in South Africa (2006-2011)

	Univariate analysis			Multivariate analysis		
	OR	95% Cl	P value	OR	95% Cl	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						
Blacks	1.03	(0.90-1.17)	0.675			
Mixed Race	0.91	(0.79-1.07)	0.276			
Whites	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			
Provinces						
Eastern Cape	1.19	(0.98-1.45)	**0.068**	1.16	(0.95-1.43)	0.150
Northern Cape	0.88	(0.59-1.30)	0.520			
Western Cape	0.87	(0.76-0.99)	**0.036**	0.91	(0.79-1.04)	0.180
Free State	0.89	(0.70-1.14)	0.363			
Gauteng	1.02	(0.88-1.18)	0.729			
Mpumalanga	1.03	(0.69-1.55)	0.853			
Limpopo	1.42	(1.02-1.98)	**0.035**	1.46	(1.04-2.05)	**0.029**
Kwa-Zulu Natal	0.88	(0.46-1.60)	0.626			
Northwest	1.15	(0.80-1.67)	0.438			

OR, odds ratio; CI, confidence interval

Table 4: Associations with Early 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			
Provinces						
Eastern Cape	0.83	(0.69-1.00)	**0.054**	1.27	(1.06-1.51)	0.167
Northern Cape	1.41	(0.99-2.01)	**0.054**	1.61	(1.07-2.43)	0.065
Western Cape	0.78	(0.69-0.88)	**<0.001**	1.17	(0.98-1.41)	0.081
Free State	0.99	(0.77-1.26)	0.918			
Gauteng	0.97	(0.84-1.11)	0.630			
Mpumalanga	2.09	(1.49-2.92)	**<0.001**	1.67	(1.16-2.46)	**0.007**
Limpopo	1.80	(1.40-2.32)	**<0.001**	1.60	(1.19-2.14)	**0.002**
Kwa-Zulu Natal	0.85	(0.46-1.58)	0.603			
Northwest	1.78	(1.32-2.39)	**<0.001**	1.76	(1.25-2.48)	**0.001**
OR, odds ratio; CI, confidence interval						

Figure 1: Distribution of all Colorectal cancer and Adenocarcinoma of by Age Group in South Africa (2006-2011)

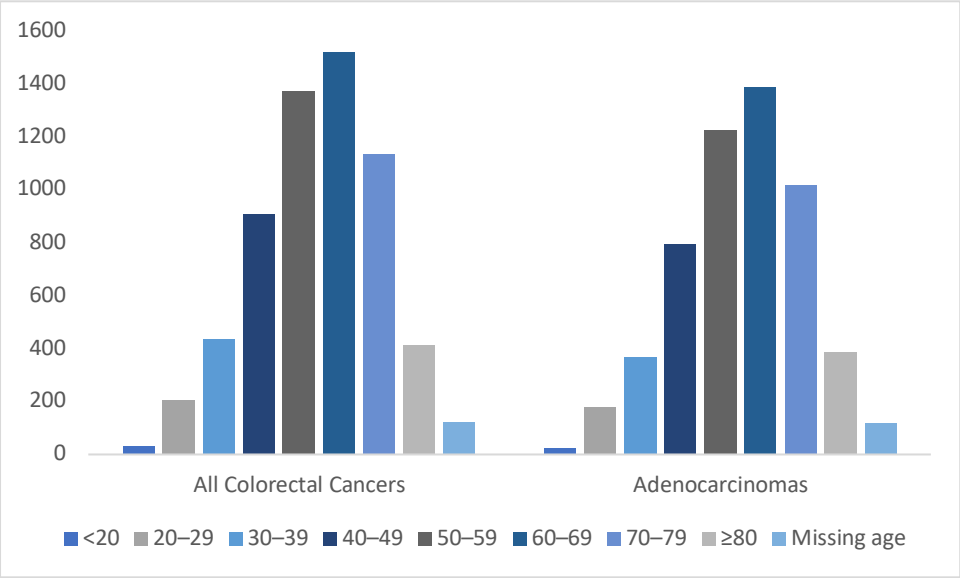
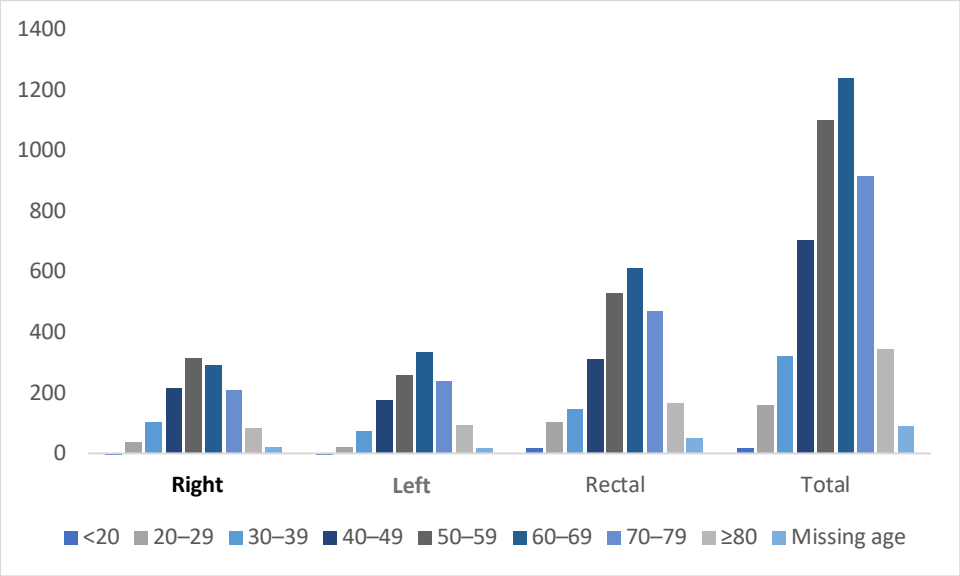


Figure 2: Anatomic Distribution of Colorectal Adenocarcinoma by Age Group in South Africa (2006-2011)



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