Descriptive epidemiological study of South African colorectal cancer patients at a Johannesburg Hospital Academic institution

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Key words
colorectal cancer, descriptive epidemiology, race, South Africa.

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Abstract

Background and Aim: Epidemiological studies of colorectal cancer (CRC) in South Africa (SA) have been poorly characterized. Black and white SA population groups have demonstrated distinct CRC clinical presentations, suggesting that black SA patients follow a different carcinogenic pathway than their white counterparts. Thus, the aim of this study was to identify unique demographic and histopathological features associated with black SA patients to facilitate earlier diagnosis and to improve disease management.

Methods: This preliminary descriptive epidemiological study included 665 retrospective CRC cases diagnosed between the period 2011 and 2015 at the Charlotte Maxeke Johannesburg Academic Hospital. Demographic and histopathological features in black versus other race groups (ORG) were compared, and Student’s t-test, Chi-square, and Fischer’s exact tests were used for statistical analysis.

Results: Statistical analysis demonstrated that patients with left-sided tumors of invasive adenocarcinoma were predominantly black and male. These patients were considerably younger when compared to ORG (median 56 vs 62 years, respectively), P < 0.0001. However, no significant propensity for other histological features was illustrated. Polyps were mostly tubular adenomas (51%) and tubulovillous adenomas (TVAs) (44%). TVAs were mostly high-grade lesions (P < 0.0001) and associated with left-sided CRC (P = 0.0325).

Conclusion: These findings verify that black SA CRC patients have an earlier disease onset in comparison to ORG; however, no increased tendency for tumor site, precursor lesion, stage of disease, or gender was evident. Thus, a deeper molecular characterization of CRC is required to understand the underlying causes associated with earlier disease onset in black SA CRC patients.

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide and the fourth most common cause of cancer-related mortalities.1 Within South Africa (SA), it is the fourth most commonly diagnosed cancer, being the second most common among males and the fourth most common among females and the sixth leading cause of cancer mortalities in SA.1,2 Male and female ratios have remained constant (53–55% vs 45–47%, respectively).2–6 Male patients have a 1.27 estimated lifetime risk of developing CRC, and females have a lower risk of 0.75.6 CRC incidence rates within SA have progressively increased over the years, with the annual crude incidence in SA CRC male and female patients in 2014 reported as 7.34 and 5.86 per 100 000, respectively.6 CRC occurs mostly within the white (Caucasian) population group in SA patients (52–54%), followed by black (African) (26–28%), colored (mixed ancestry) (14–15%), and Asian (Indian) patients (4–7%).2–6 The pathogenesis of CRC is complex and diverse and is influenced by multiple factors, including diet, lifestyle, and genetic predispositions. It is reported that the white patient population group in SA appears to follow the classic Western trend, which presents at a later age, having an association with diet and lifestyle factors, although the molecular pathology has not been extensively investigated.7,8 Comparatively, the black SA population has a higher frequency of young (<50 years) CRC patients, possibly because of diet and lifestyle changes either due to urbanization or a familial contribution.7–9 A study by Prodehl et al. showed that 49.0% of SA CRC patients reported a family history of cancer, with CRC the most frequently diagnosed, where maternal (35%) and paternal (33%) members were the most affected, followed by maternal members (25%).10

High prevalence rates for young CRC patients, <40 years of age, have been reported globally, with the lowest rates found...
in the United States, Europe, and New Zealand (1–6%) and the highest in Asian and Middle Eastern countries (10–39%).

The current SA National Cancer Registry (NCR) statistics, spanning a 5-year period (2010–2014), show that young CRC patients, under 50 years of age, contribute an average of 18% of all CRC cases, of which approximately 7% were younger than 40 years of age. The NCR 2014 report also showed an exponential growth in CRC incidence in male patients from 2010 to 2014. A correlation between race and age was also demonstrated as the majority of young patients younger than 50 years old were black (32%) versus white patients (11%) (P < 0.0001) (NCR 2013–2014).

The burden of disease in SA has also been a challenge to assess due to underreporting of CRC cases as registries are mainly limited to small urban areas.

Thus, this descriptive epidemiological study will serve as a preliminary study to obtain a greater understanding of the development of CRC, particularly in black SA CRC patients. This will include screening demographic and histopathological data in the hope of identifying key features associated with the disease to assist with earlier detection and improvement of prognosis, particularly within this population group.

**Methods**

A retrospective laboratory information system (LIS) search was conducted on all patients who had biopsy samples or colorectal resections reported by the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) branch of the National Health Laboratory Service (NHLS)/Anatomical Pathology Division, Faculty of Health Sciences, University of the Witwatersrand. Histological reports of all patients diagnosed with colorectal adenocarcinoma between 2011 and 2015 were reviewed, and data were described with respect to age, race, gender, tumor site ([left-sided] and proximal to the splenic flexure [left-sided]), histological subtype and grade, presence and grade of precursor lesion, invasive tumor including the presence of tumor infiltrating lymphocytes (TIL), Crohn’s-like inflammatory reaction (CIR), and the tumor stage (TNM). The Ethics Committee of the University of the Witwatersrand (clearance number M120994) approved this study.

**Statistical analysis.** Statistical associations between race groups were investigated using Student’s t-test, Fisher’s exact test, and Chi Square test analysis. Non-black race patients were included in a single group, termed the “Other Race” group (White, Colored/mixed ancestry, Indian) due to small case numbers in the colored and Indian groups in comparison to the black patient group. Race was compared with age, tumor site, and morphological features as stated above. Statistical data analysis was completed using Stata Intercooled 7.0 (Stata, College Station, TX, USA) and Graphpad Prism version 7 (GraphPad Software, La Jolla, CA, USA). The results were considered statistically significant when P < 0.05* and highly significant when P < 0.001**.

**Results**

A total of 665 CRC patients were diagnosed at CMJAH between 2011 and 2015, with the majority of patients being black (391/665; 59%) (Table 1). Overall, the patients were predominantly male (366/665; 55%), and no variation of gender was seen among race groups. The median age of CRC was 59 years (inter-quartile range: 49–68). A significant association was seen between patient age and race (black vs other race group [ORG]) (median age: 56 vs 62 respectively) (P < 0.0001). Most tumors occurred in the left colon (427/621; 69%), had an invasive adenocarcinoma subtype (596/646; 92%), were low-grade (LG) (568/624; 91%), and presented as TNM stage III (180/350; 52%). The majority of CRC cases did not contain TILs (224/345; 65%) or a CIR (263/345; 76%), nor did they show lymphatic invasion (296/422; 70%). A minority of polyps was found (140/408; 34%), with tubular adenomas (TAs) being reported as the predominant subtype (72/140; 51%), followed by tubulovillous adenomas (TVAs) (61/410; 44%). TAs mostly displayed LG dysplasia (40/67; 60%); however, TVAs were mostly associated with high-grade (HG) dysplasia (49/60; 82%) (P < 0.0001). All the aforementioned pathological characteristics lacked any correlation with race. BRAF V600E mutations, however, exclusively occurred in ORG patients (5/21; 24%) (P = 0.0011).

Correlation between age groups, young versus old (≤50 vs >50 years) and CRC subtype, tumor grade, TIL, and lymphatic invasion was identified (Table 2). Signet ring cell carcinoma occurred at a higher frequency in the younger patient group (16/183; 9%) versus the older patient group (4/463; 1%) (P = 0.0030), while a mild to moderate TIL response was more commonly found in the older patient group (95/247; 38%) than in the younger group (26/98; 27%) (P = 0.0450). Lymphatic invasion was associated more with younger patients (45/120; 37%) than with the older group (81/302; 27%) (P = 0.0341), and BRAF V600E mutations were exclusively found in older patients (5/36; 24%) versus younger patients (0/40; 0%) (P = 0.0204). No significant association was found between gender and histopathological data (Table 3).

The majority of polyps were found in the left colon (81/131; 62%) and in male patients (89/140; 64%) (Tables 3 and 4). A particular association between the side of colon and grade of TVAs was noted here (P = 0.0325) as left-sided CRCs were mostly associated with HG TVAs (31/34; 91%), BRAF V600E mutations occurred exclusively in the right colon (5/34; 15%), and none were associated with left CRC tumors (0/42; 0%) (P = 0.0151).

**Discussion**

The focus of this study was to ascertain common features, particularly demographic and histopathological characteristics, associated with black patients to assist in the earlier detection and better management of the disease. Although this study demonstrated no significant differences between male and female patients, black versus ORG and younger versus older patient groups illustrated significant differences in a number of parameters.

A total of 665 CRC patients were diagnosed at CMJAH over a 5-year period, from 2011 to 2015. Patients were predominantly male and black, with a considerable proportion being young. The median age of black patients compared to ORG patients (56 vs 62 years, respectively) was significantly younger. The data confirmed local and international reports...
### Table 1 Descriptive histopathological analysis of colorectal cancer cases diagnosed at Charlotte Maxeke Johannesburg Academic Hospital between 2011 and 2015: Black versus other race groups

| Demographic data | Number of cases (%) | Black (B) | Other race groups (O) | Statistical analysis: |
|------------------|---------------------|-----------|-----------------------|-----------------------|
| **Gender**       |                     |           |                       |                       |
| Male             | 665                 | 391       | 274                   |                       |
| Female           | 299 (45)            | 175 (45)  | 124 (45)              |                       |
| **Age**          | 660                 | 389       | 271                   |                       |
| Median           | 59                  | 56***     | 62                    |                       |
| Min–Max          | 15–94               | 15–94     | 25–92                 |                       |
| Mean ± SD        | 57 ± 14             | 55 ± 15   | 62 ± 13               |                       |
| P25–P75          | 49–68               | 45–65     | 55–71                 |                       |
| 95% CI           | [56–59]             | [53–56]   | [60–64]               |                       |
| ≤50 years        | 184 (28)            | 142 (37)**| 42 (15)               | P < 0.0001***         |
| >50 years        | 476 (72)            | 247 (63)  | 229 (65)              |                       |
| **Tumor site**   | 621                 | 368       | 253                   |                       |
| Left             | 427 (69)            | 250 (68)  | 177 (70)              |                       |
| Right            | 190 (30)            | 115 (31)  | 75 (30)               |                       |
| Left and right   | 4 (1)               | 3 (1)     | 1 (0)                 |                       |
| **Tumor subtype**| 646                 | 380       | 266                   |                       |
| Invasive adenocarcinoma | 596 (92) | 349 (92) | 247 (93) |                       |
| Mucinous adenocarcinoma | 29 (5)  | 16 (4)   | 13 (5)                |                       |
| Signet ring cell adenocarcinoma | 20 (3)  | 15 (4)   | 5 (2)                 |                       |
| Neuroendocrine carcinoma | 1 (0)   | 0 (0)    | 1 (0)                 |                       |
| **Tumor grade**  | 624                 | 372       | 252                   |                       |
| LG               | 568 (91)            | 336 (90)  | 232 (92)              |                       |
| HG               | 56 (9)              | 36 (10)   | 20 (8)                |                       |
| **AJCC TNM staging** | 350     | 208       | 142                   |                       |
| I                | 46 (13)             | 26 (13)   | 20 (15)               |                       |
| II               | 109 (31)            | 59 (28)   | 50 (35)               |                       |
| III              | 180 (52)            | 114 (55)  | 66 (46)               |                       |
| IV               | 15 (4)              | 9 (4)     | 6 (4)                 |                       |
| **Tumor-infiltrating lymphocytes** | 345 | 202 | 143 | P = 0.4231 |
| None             | 224 (65)            | 135 (67)  | 89 (62)               |                       |
| Mild–moderate    | 121 (35)            | 67 (33)   | 54 (38)               |                       |
| **Crohn’s-like inflammatory response** | 345 | 202 | 143 | P = 0.3077 |
| None             | 263 (76)            | 158 (78)  | 105 (73)              |                       |
| Mild–moderate    | 82 (24)             | 44 (22)   | 38 (27)               |                       |
| **Lymphatic invasion** | 422 | 254 | 168 | P = 0.1935 |
| Absent           | 296 (70)            | 172 (68)  | 124 (74)              |                       |
| Present          | 126 (30)            | 82 (22)   | 44 (26)               |                       |
| **Polyps**       | 408                 | 234       | 174                   |                       |
| Absent           | 268 (66)            | 160 (68)  | 108 (62)              |                       |
| Present          | 140 (34)            | 74 (32)   | 66 (38)               |                       |
| **Polyp subtype**| 140                 | 75        | 65                    |                       |
| Hyperplastic polyp | 4 (3)               | 1 (1)     | 3 (5)                 |                       |
| Pseudopolyp      | 2 (1)               | 2 (3)     | 0 (0)                 |                       |
| Sessile serrated adenoma | 1 (1) | 0 (0) | 1 (1) |                       |
| TA               | 72 (51)             | 43 (57)   | 29 (45)               |                       |
| TVA              | 61 (44)             | 29 (39)   | 32 (49)               |                       |
| **TA grade**     | 67                  | 39        | 28                    | P = 0.2161            |
| LG               | 40 (60)             | 25 (65)   | 15 (54)               |                       |
| HG               | 27 (40)             | 14 (35)   | 13 (46)               |                       |
| **TVA grade**    | 60                  | 28        | 32                    |                       |
| LG               | 11 (18)             | 2 (7)     | 8 (25)                |                       |
| HG               | 49 (82)             | 25 (93)** | 24 (75)               |                       |
| **BRAF V600E**   | 76                  | 55        | 21                    | P = 0.0011***        |
| Wild-type        | 71                  | 55 (100)  | 16 (76)               |                       |
| Mutation         | 5                   | 0 (0)     | 5 (24)**              |                       |

*Statistically significant.

***Statistically highly significant.

AJCC, American Joint Committee on Cancer; CI, confidence interval; HG, high grade; LG, low grade; TA, tubular adenoma; TNM, tumor node metastases; TVA, tubulovillous adenoma.

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Table 2: Descriptive histopathological analysis of colorectal cancer cases diagnosed at Charlotte Maxeke Johannesburg Academic Hospital between 2011 and 2015: Younger (≤50 years) versus older (>50 years) patients

| Demographic data                        | Number of cases (%) | ≤50 years | >50 years | Statistical analysis: |
|-----------------------------------------|---------------------|-----------|-----------|-----------------------|
| Gender                                  | 665                 | 189       | 476       |                       |
| Male                                    | 366 (55)            | 114 (60)  | 252 (53)  |                       |
| Female                                  | 299 (45)            | 75 (40)   | 224 (47)  |                       |
| Age                                     | 660                 | 389       | 271       |                       |
| Median                                  | 59                  | 41        | 64        |                       |
| Min–Max                                 | 15–94               | 15–50     | 51–94     |                       |
| Mean ± SD                               | 57 ± 14             | 40 ± 8    | 65 ± 9    |                       |
| P25–P75                                 | 49–68               | 34–46     | 57–71     |                       |
| 95% CI                                  | [56–59]             | [39–41]   | [64–66]   |                       |
| Tumor site                              | 660                 | 179       | 442       |                       |
| Left                                    | 426 (68)            | 119 (66)  | 307 (69)  |                       |
| Right                                   | 191 (31)            | 60 (34)   | 131 (30)  |                       |
| Left and right                          | 4 (1)               | 0 (0)     | 4 (1)     |                       |
| Tumor subtype                           | 646                 | 183       | 463       |                       |
| Invasive adenocarcinoma                 | 596 (92)            | 159 (87)  | 437 (94)  |                       |
| Mucinous adenocarcinoma                 | 29 (5)              | 8 (4)     | 21 (5)    |                       |
| Signet ring cell adenocarcinoma         | 20 (3)              | 16 (9)**  | 4 (1)     |                       |
| Neuroendocrine carcinoma                | 1 (0)               | 0 (0)     | 1 (0)     |                       |
| Tumor grade                             | 624                 | 178       | 446       |                       |
| LG                                      | 566 (91)            | 152 (85)  | 416 (90)  |                       |
| HG                                      | 56 (9)              | 26 (15)** | 30 (7)    |                       |
| AJCC TNM staging                        | 350                 | 100       | 250       |                       |
| I                                       | 46 (13)             | 9 (9)     | 37 (15)   |                       |
| II                                      | 109 (31)            | 27 (27)   | 82 (23)   |                       |
| III                                     | 180 (52)            | 59 (59)   | 121 (48)  |                       |
| IV                                      | 15 (4)              | 5 (5)     | 10 (4)    |                       |
| Tumor-infiltrating lymphocytes           | 345                 | 98        | 247       |                       |
| None                                    | 224 (65)            | 72 (73)   | 152 (62)  |                       |
| Mild–moderate                           | 121 (35)            | 26 (27)   | 95 (38)*  |                       |
| Crohn’s-like inflammatory response      | 345                 | 98        | 247       |                       |
| None                                    | 263 (76)            | 80 (82)   | 183 (74)  |                       |
| Mild–moderate                           | 82 (24)             | 18 (18)   | 64 (26)   |                       |
| Lymphatic invasion                      | 422                 | 120       | 302       |                       |
| Absent                                  | 296 (70)            | 75 (63)   | 221 (73)  |                       |
| Present                                 | 126 (30)            | 46 (37)*  | 81 (27)   |                       |
| Polyps                                  | 408                 | 111       | 297       |                       |
| Absent                                  | 268 (66)            | 79 (71)   | 189 (64)  |                       |
| Present                                 | 140 (34)            | 32 (23)   | 108 (36)  |                       |
| Polyp subtype                           | 140                 | 32        | 108       |                       |
| Hyperplastic polyp                      | 4 (3)               | 0 (0)     | 4 (4)     |                       |
| Pseudopolyp                             | 2 (1)               | 1 (3)     | 1 (1)     |                       |
| Sessile serrated adenoma                | 1 (1)               | 0 (0)     | 1 (1)     |                       |
| TA                                      | 72 (51)             | 18 (56)   | 54 (50)   |                       |
| TVA                                     | 61 (44)             | 13 (41)   | 48 (44)   |                       |
| Polyp grade                             | 67                  | 18        | 49        |                       |
| TA                                      | 40 (60)             | 10 (56)   | 30 (60)   |                       |
| LG                                      | 27 (40)             | 8 (44)    | 19 (40)   |                       |
| TVA                                     | 60                  | 12        | 48        |                       |
| LG                                      | 11 (18)             | 3 (25)    | 8 (17)    |                       |
| HG                                      | 49 (82)             | 9 (75)    | 40 (83)   |                       |
| BRAF V600E                              | 76                  | 40        | 36        |                       |
| Wildtype                                | 71                  | 40 (100)  | 31 (76)   |                       |
| Mutation                                | 5                   | 0 (0)     | 5 (24)*   |                       |

*Statistically significant.
***Statistically highly significant.
AJCC, American Joint Committee on Cancer; CI, confidence interval; HG, high grade; LG, low grade; TA, tubular adenoma; TNM, tumor node metastases; TVA, tubulovillous adenoma.
Table 3 Descriptive histopathological analysis of colorectal cancer cases diagnosed at Charlotte Maxeke Johannesburg Academic Hospital between 2011 and 2015: Male versus female

| Demographic data                             | Number of cases (%) | Male     | Female    | Statistical analysis: |
|----------------------------------------------|---------------------|----------|-----------|-----------------------|
| Gender                                       | 665                 | 366 (55%)| 299 (45%)|                       |
| Age                                          | 660                 | 364      | 296       |                       |
| Median                                       | 59                  | 58       | 60        |                       |
| Min-Max                                      | 15–94               | 16–94    | 20–92     |                       |
| Mean ± SD                                    | 57 ± 14             | 56 ± 14  | 59 ± 14   |                       |
| P25-P75                                      | 49–68               | 47–67    | 51–69     |                       |
| 95% CI                                       | [56–59]             | [55–58]  | [58–61]   |                       |
| Tumor site                                   | 621                 | 344      | 277       |                       |
| Left                                         | 426 (68)            | 237 (69) | 189 (68)  |                       |
| Right                                        | 191 (31)            | 105 (31) | 86 (31)   |                       |
| Left and right                               | 4 (1)               | 2 (0)    | 2 (1)     |                       |
| Tumor subtype                                | 646                 | 183      | 463       |                       |
| Invasive adenocarcinoma                      | 596 (92)            | 437 (87)| 267 (94)  |                       |
| Mucinous adenocarcinoma                      | 29 (5)              | 21 (4)   | 14 (5)    |                       |
| Signet ring cell adenocarcinoma              | 20 (3)              | 4 (9)    | 9 (1)     |                       |
| Neuroendocrine carcinoma                     | 1 (0)               | 1 (0)    | 0 (0)     |                       |
| Tumor grade                                  | 624                 | 344      | 280       |                       |
| LG                                           | 568 (91)            | 308 (85)| 260 (93)  |                       |
| HG                                           | 56 (9)              | 36 (15)  | 20 (7)    |                       |
| AJCC TNM staging                             | 350                 | 100      | 250       |                       |
| I                                            | 46 (13)             | 9 (9)    | 37 (15)   |                       |
| II                                           | 109 (31)            | 27 (27)  | 82 (33)   |                       |
| III                                          | 180 (52)            | 59 (59)  | 121 (48)  |                       |
| IV                                           | 15 (4)              | 5 (5)    | 10 (4)    |                       |
| Tumor-infiltrating lymphocytes               | 345                 | 192      | 153       |                       |
| None                                         | 224 (65)            | 132 (69)| 92 (60)   |                       |
| Mild–moderate                                | 121 (35)            | 60 (31)  | 61 (40)   |                       |
| Crohn’s-like inflammatory response           | 345                 | 192      | 153       |                       |
| None                                         | 263 (76)            | 154 (80)| 109 (71)  |                       |
| Mild–moderate                                | 82 (24)             | 38 (20)  | 44 (29)   |                       |
| Lymphatic invasion                           | 422                 | 234      | 188       |                       |
| Absent                                       | 296 (70)            | 162 (69)| 134 (71)  |                       |
| Present                                      | 126 (30)            | 72 (31)  | 54 (29)   |                       |
| Polyps                                       | 408                 | 236      | 174       |                       |
| Absent                                       | 268 (66)            | 147 (62)| 123 (71)  |                       |
| Present                                      | 140 (34)            | 89 (38)  | 51 (29)   |                       |
| Polyp subtype                                | 140                 | 89       | 51        |                       |
| Hyperplastic polyp                           | 4 (3)               | 3 (4)    | 1 (2)     |                       |
| Pseudopolyp                                  | 2 (1)               | 2 (2)    | 0 (0)     |                       |
| Sessile serrated adenoma                     | 1 (1)               | 0 (0)    | 1 (2)     |                       |
| TA                                           | 72 (51)             | 43 (48)  | 29 (57)   |                       |
| TVA                                          | 61 (44)             | 41 (46)  | 20 (39)   |                       |
| Polyp grade                                  |                      |          |           |                       |
| TA                                           | 67                  | 36       | 28        |                       |
| LG                                           | 40 (60)             | 21 (58)  | 17 (54)   |                       |
| HG                                           | 27 (40)             | 15 (42)  | 11 (46)   |                       |
| TVA                                          | 60                  | 41       | 19        |                       |
| LG                                           | 11 (18)             | 6 (15)   | 5 (28)    |                       |
| HG                                           | 49 (82)             | 35 (85)  | 14 (72)   |                       |
| BRAF V600E                                   | 76                  | 44       | 32        |                       |
| Wildtype                                     | 71                  | 42 (95)  | 29 (91)   |                       |
| Mutation                                     | 5                   | 2 (5)    | 3 (9)     |                       |

*Statistically significant.
***Statistically highly significant.
AJCC, American Joint Committee on Cancer; CI, confidence interval; HG, high grade; LG, low grade; TA, tubular adenoma; TNM, tumor node metastases; TVA, tubulovillous adenoma.
regarding male versus female ratios (55 vs 45%, respectively),\textsuperscript{1,5} with black patients showing an earlier age of onset in comparison to the white group.\textsuperscript{7,15} In comparison, in African Americans (AA), the median age of onset in males and females were reported to be 66 and 70 years, respectively, compared to 72 and 77 in white men and women, respectively.\textsuperscript{16} In this SA cohort, the median age for male and female black patients was 55 and 56 years, respectively, versus 62 and 65 years for males and females of ORG, respectively. The median age for white male and female patients (separated from Indian and colored or mixed race) remained 62 and 65 years, respectively. These data showed that SA black and white patients are at least 10 years younger in comparison to U.S. AA and U.S. white patients.

| Table 4 Descriptive histopathological analysis of CRC cases diagnosed at Charlotte Maxeke Johannesburg Academic Hospital between 2011–2015: Left versus right-sided colon cancer |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Demographic data                | Number of cases (%)             | Left-sided                      | Right-sided                     | Statistical analysis:         |
| Tumor site                      | 617                             | 426 (69%)                       | 191 (31%)                       | \( P < 0.0001^{***} \)         |
| Tumor subtype                   | 607                             | 419                             | 188                             | \( P = 0.02845 \)              |
| Invasive adenocarcinoma         | 596 (92)                        | 398 (66)                        | 162 (26)                        |                                |
| Mucinous adenocarcinoma         | 29 (5)                          | 9 (2)                           | 18 (10)\textsuperscript{***}   |                                |
| Signet ring cell adenocarcinoma | 20 (3)                          | 12 (3)                          | 7 (4)                           |                                |
| Neuroendocrine carcinoma        | 1 (0)                           | 0 (0)                           | 1 (0)                           |                                |
| Tumor grade                     | 587                             | 399                             | 188                             | \( P = 0.02845 \)              |
| LG                              | 533 (81)                        | 366 (92)                        | 167 (68)                        |                                |
| HG                              | 54 (9)                          | 33 (8)                          | 21 (11)                         |                                |
| AJCC TNM staging                | 350                             | 192                             | 153                             | \( P = 0.6086 \)               |
| I                               | 46 (13)                         | 28 (15)                         | 17 (11)                         |                                |
| II                              | 109 (31)                        | 60 (31)                         | 46 (30)                         |                                |
| III                             | 180 (52)                        | 96 (50)                         | 80 (52)                         |                                |
| IV                              | 15 (4)                          | 8 (4)                           | 10 (7)                          |                                |
| Tumor-infiltrating lymphocytes  | 338                             | 193                             | 145                             | \( P = 0.0210^{*} \)           |
| None                            | 220 (65)                        | 136 (70)                        | 84 (58)                         |                                |
| Mild–moderate                   | 118 (35)                        | 57 (30)                         | 61 (42)\textsuperscript{*}      |                                |
| Crohn’s like inflammatory response | 338                           | 193                             | 145                             | \( P = 1.0000 \)               |
| None                            | 258 (76)                        | 147 (76)                        | 111 (77)                        |                                |
| Mild–moderate                   | 80 (24)                         | 46 (24)                         | 34 (23)                         |                                |
| Lymphatic invasion              | 417                             | 254                             | 163                             | \( P = 0.0009^{***} \)         |
| Absent                          | 293 (70)                        | 194 (76)                        | 99 (61)                         |                                |
| Present                         | 123 (30)                        | 69 (24)                         | 64 (39)\textsuperscript{***}    |                                |
| Polyps                          | 392                             | 231                             | 161                             | \( P = 0.4468 \)               |
| Absent                          | 261 (67)                        | 150 (65)                        | 111 (69)                        |                                |
| Present                         | 131 (33)                        | 81 (35)                         | 50 (31)                         |                                |
| Polyp subtype                   | 131                             | 81                              | 50                              | \( P = 0.1484 \)               |
| Hyperplastic polyyp              | 3 (2)                           | 3 (4)                           | 0 (0)                           |                                |
| Pseudopolyyp                    | 2 (1)                           | 0 (0)                           | 2 (4)                           |                                |
| Sessile serrated adenoma        | 1 (1)                           | 0 (0)                           | 1 (2)                           |                                |
| TA                              | 68 (52)                         | 43 (53)                         | 25 (50)                         |                                |
| TVA                             | 57 (44)                         | 35 (43)                         | 22 (44)                         |                                |
| Polyp grade                     | 119                             |                                 |                                | \( P = 0.0615 \)               |
| TA                              | 64                              | 40                              | 24                              |                                |
| LG                              | 38 (59)                         | 21 (52)                         | 17 (71)                         |                                |
| HG                              | 26 (41)                         | 19 (48)                         | 7 (29)                          |                                |
| TVA                             | 55                              | 34                              | 21                              |                                |
| LG                              | 10 (18)                         | 3 (9)                           | 7 (33)                          |                                |
| HG                              | 45 (62)                         | 31 (91)\textsuperscript{*}      | 14 (67)                         |                                |
| BRAF V600E                      | 76                              | 42                              | 34                              | \( P = 0.0154^{*} \)           |
| Wildtype                        | 71                              | 42 (100)                        | 29 (65)                         |                                |
| Mutation                        | 5                               | 0 (0)                           | 5 (15)\textsuperscript{*}       |                                |

\*Statistically significant.

\***Statistically highly significant.

AJCC, American Joint Committee on Cancer; CI, confidence interval; CRC, colorectal cancer; HG, high grade; LG, low grade; TA, tubular adenoma; TNM, tumor node metastases; TVA, tubulovillous adenoma.
The frequency of young black patients younger than 50 years of age in this cohort (37%) was similar to that of young black SA CRC patients in the NCR 2014 report (32%). The majority of tumors occurred in the left colon, had an invasive adenocarcinoma subtype, LG tumors, and presented at an advanced TNM stage (III and IV). These findings were in concordance with international published data that reported an approximate 70% occurrence of left-sided CRC, with about 90% being of an invasive adenocarcinoma subtype, that was moderately to well differentiated, with approximately 50–60% of CRC cases presenting at a more advanced stage.\(^\text{17,18}\) Male and female patients had equal frequencies for tumor site (69% left-sided vs 31% right-sided). This finding is contrary to other studies showing right-sided colon cancer to be increased in female patients and left-sided CRC to be increased in males.\(^\text{19}\)

In the present analysis, with regard to polyps, conventional adenomas (TA, TVA, and villous adenomas [VAs]) are mostly found in the left colon,\(^\text{20}\) with TAs described as the predominant subtype (80%), TVAs accounting for 10–20%, and VAs less than 5%.\(^\text{21–23}\) In this study, polyps were found in 34% (140/408) of cases, with only 1% being sessile serrated adenoma (SSA), 4% hyperplastic polyps (HPs), 51% TAs, and 44% TVAs. TAs were mostly associated with LG dysplasia (60%), and TVAs that also occurred at a considerably high frequency than that stated in literature were mostly associated with HG dysplasia (83%) (\(P < 0.0001\)). The size of the adenomatous polyp (AP) was not recorded in the majority of reports, only the quantity of APs and grade of dysplasia. This study showed no association of APs with race, gender, or patient age; however, HG TVAs were more commonly found in the left colon (\(P = 0.0325\)). The transition from LG APs to more advanced APs or CRC takes approximately 3 years, suggesting that frequent surveillance colonoscopies for the earlier detection of CRC would benefit patients. Guidelines indicate repeat surveillance every 5–10 years for 1–2 small TAs (<1 cm) with LG dysplasia, and where 3–10 large APs are found (≥1 cm) or in those with HG dysplasia or with villous features, colonoscopy should be performed every 3 years.\(^\text{20,23}\)

The literature indicates that AA patients are more likely to have right-sided tumors than left.\(^\text{15,24,25}\) This SA study, however, showed no relationship between race and tumor site. BRAF V600E mutational analysis was carried out in 76 patients, and an association was only found in older white patients with right-sided colon cancers, possibly indicating development via the microsatellite instability CRC pathway.

CRC research in AA patients has demonstrated higher incidence and mortality rates, earlier age of diagnosis, more advanced stage of the disease, and a greater proportion of right-sided colon cancers in comparison to other ethnic groups. This has led American professional societies to change guidelines, recommending colonoscopy screening by 45 instead of 50 years of age, which has led to a great reduction in CRC incidence in this population group.\(^\text{26}\) Although statistically significant differences concerning stage and tumor site were not seen when comparing black versus ORG patients, later stage of disease and earlier age of onset in black patients remained significant factors, and a policy recommending earlier screening in this population group should be considered to reduce incidence rates.

In conclusion, this study shows that black SA CRC patients most likely follow a different carcinogenic pathway in comparison to other SA ethnic groups due to earlier age of onset. Black SA patients also seem to present at least a decade earlier when comparing Africans found in the Western world, with more left-sided CRC occurring in SA patients compared to a right-sided CRC association seen in AAs. Moreover, a lack of BRAF V600E mutation in the black SA CRC population in this study suggests that there is a different carcinogenic pathway in black SA CRC patients compared to other ethnic groups, which still needs to be evaluated in a larger cohort of patients. TVAs found at a frequent rate across different ethnic groups in SA patients could possibly suggest a dominant adenocarcinoma sequence in the development of the disease. The initiation of earlier screening and more frequent surveillance policies in black SA patients could possibly result in better management of the disease. Further epidemiological research linked to molecular characterization in SA population groups is still needed to assist in determining the underlying cause and designing more personalized treatment strategies for better management of the disease.

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