COMPLICATED COLORECTAL CANCER: PREVALENCE IN KWAZULU-NATAL TEACHING HOSPITALS

By

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2018

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As the candidate's supervisor I have/have not approved this thesis for submission.

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DEDICATION

My parents, my mother Phyllis Ntombise Mothae, my late father Lovecan Mothae

My other parents Nomalungisa Sishuba, the late Lindiswa Salvina and Spalding Dengana

My sisters, Moliehi, Lipuo and late Lemohang Mothae

My niblings Ziningi, Neo, Thato and Amohelang Mothae

My bosses Mr Manogaran S Moodley and Mr Subash Chirkut for never giving up on me

My friends Viwe Sineke, Nozipho Zulu, Unathi Mgandela and Mondi Zungu-Dlamini for their unending support

ACKNOWLEDGEMENTS

I herewith acknowledge Professor Thandinkosi E Madiba for bestowing his time to supervising this research project towards the degree of Master of Medicine.

OVERVIEW

Colorectal cancer (CRC) is the third most common cancer in the world and was listed as the fourth most common cancer in South Africa in 2004 [1]. The average person's lifetime risk of CRC is 5% [2]. The incidence of CRC is higher in people aged 50 and older; however, recent literature shows an increasing incidence of CRC in patients younger than 50 years [3]. Young age is considered a poor prognostic factor, these patients usually present with advanced stages and more aggressive histopathologic disease. Survival ultimately depends on the stage at diagnosis. Five-year survival for localized disease is 90%, 60% for regional disease and 10% for metastatic disease [3].

Due to lack of recognized screening programs in South Africa, a significant number of patients with CRC present to surgical units with complicated colorectal cancer (CCC). These complications range from obstruction, perforation, fistula and bleeding and are associated with a worse prognosis. Approximately 30% of patients with CRC present with complications [4]. Of these, 8-10% present with obstruction, and approximately 3% with perforation. Morbidity and mortality associated with emergency surgery is very high [5].

Since there is lack of data on CCC in South Africa, this study was undertaken to establish the prevalence of CCC among patients presenting to the KwaZulu-Natal teaching hospitals.

The main objectives were (i) to establish the prevalence of CCC in our setting, (ii) to analyse and compare the complication rates amongst different racial and age groups in KwaZulu-Natal, (iii) to determine treatment outcomes, and (iv) to compare our findings to other parts of the world.

This study was undertaken using collected data from the Colorectal Cancer Database that is archived at the University of KwaZulu-Natal's Department of General Surgery. The ongoing database, which commenced in the year 2000, had accrued a total of 1824 patients with CRC by the end of 2015.

Four hundred and thirty-one of these patients in this cohort were found to have CCC (23.6%). Patient's demographic details, clinical presentation, complication type and site as well as the type of intervention and outcome were reviewed. Interestingly no patients presented with bleeding as the cause of CCC. The complications in this cohort were managed via stent, diversion, resection or a combination of these procedures.

From this study of CRC over a 16-year period in KwaZulu-Natal, 23.6% patients presented with complications. The male to female ratio was 1.2:1.

ABSTRACT

Background

Colorectal cancer (CRC) is the third most common +cancer in the world. According to National Cancer Registry in 2004, was listed the 4th most common cancer in South Africa. The average person's lifetime risk of CRC is 5%. Majority of CRC is sporadic, with only 20% associated with inherited and inflammatory bowel disorders. Incidence increases with increasing age and genetic mutations. CRC incidence higher in people aged 50 and older. Unfortunately the incidence of CRC is escalating in patients younger than 50. Young age is considered a poor prognostic factor, usually presenting in advanced stages, with more aggressive histopathologic features. Other risk factors depend on lifestyle and behaviour (diet, smoking, alcohol, obesity). Survival depends on the stage at diagnosis. Five year survival for localized disease is 90%, 60% for regional disease and 10% for metastatic disease. Due to lack of recognized screening programs in South Africa, a large number of patients with CRC present to surgical units with complications of colorectal cancer. Morbidity and mortality associated with emergency surgery is very high. It is estimated that about 30% of patients with CRC present with complications such as obstruction, perforation, bleeding and fistulas. Of these 8-10% present with obstruction, and approximately 3% with perforation. These complications are associated with the worst prognosis.

Aim

There is a lack of data on complicated colorectal cancer in South Africa. The study was therefore undertaken in order to establish the prevalence of complicated colorectal cancer among patients presenting to the KwaZulu-Natal teaching hospitals.

Methods

This is a retrospective analysis of a prospectively collected data. The on-going KwaZulu-Natal colorectal cancer database was established in 2000. The database now comprise 1944 patients with colorectal cancer (CRC). Of these, 448 patients presented with complicated colorectal carcinoma and these patients form the basis of this analysis.

Results

Four hundred and forty eight patients with complicated colorectal carcinoma were accrued during the period 2000 - 2016. There were 244 (54.5%) males and 204 (45.5%) female. There were 165 Indians, 163 Africans, 92 White and 28 Coloured patients. The mean age at presentation was 56.4± 14.4years. Seventy patients (16.1%) were young patients, presenting at or under the age of 40 years. A total of 382 (20%) patients presented with malignant obstruction, 71 (4%) with perforation and 28 (1.5%) with malignant fistula. Twenty-five patients presented with combined obstruction and perforation and eight had combined malignant obstruction and fistula. The most common sites for malignant obstruction were sigmoid and rectum; the sigmoid colon and caecum were the most common sites for perforation and the rectum and sigmoid colon predominated among patients with malignant fistula. The majority of the patients presented as stages II, III and IV at 26.3%, 26.6% and 29.7% respectively. The median follow up period was 11 months for all three groups of complications (range 1-180 months for malignant obstruction, 1-94 months for perforation and 1-94 months for malignant fistula)

Discussion

The proportion of patients with complicated colorectal cancer was 23%.The mean age for the cohort was 56.4±14.4 years, considerably less than 63-72 years reported in the world literature. The age at presentation for Blacks was the youngest being about one to two decades younger than the other population groups. Whites were oldest at presentation in comparison to other races and their mean age approximated the world literature. These population differences in age distribution mimic that seen in the general population of patients with CRC in KwaZulu-Natal, where Blacks were a decade younger than the other population groups. The proportion of patients presenting with obstructing CRC in this study was 20%, it fell within the range of published series and did not differ between races or gender. Perforation was the second most common complication (4%) in this study. Contrary to obstruction and fistula, perforation seemed to have an equal sex incidence. The 1.5% fistula rate in this series compares favourably with the literature.

In malignant obstruction resection rate was 68% with a five-year survival rate of 70%. Patients with perforation had the highest resection rate at 97% and they achieved the best an overall five-year survival of 85%. Malignant fistula had the lowest resection rate at 32% and the five-year survival was the poorest at 60% compared to the other neoplastic complications in this series.

Conclusion

The prevalence of complicated colorectal cancer in our setting is similar to that reported in the literature. The prevalence is the same across all population groups and the sex incidence is similar, but the age at presentation is younger in Blacks. The site distribution varied according to the complication, with obstruction associated more frequently with left-sided disease and fistula involving the sigmoid and rectum.

The resection rate was dependent on the type of complication. The resection rate was better for malignant perforation and obstruction than malignant fistula. The fistula population also had a worst survival rate. Patients who underwent resection had a zero in-hospital mortality rate.

The perforation status did not impact on long-term outcome. Patients with malignant fistula appeared to have the worst outcome. Presentation of CCC (and CRC in general) at a younger age in our setting in Black patients highlights the need for more research in developing countries.

CHAPTER 1

LITERATURE REVIEW

Colorectal cancer (CRC) is reported as the third most commonly diagnosed cancer in males and the second in females [1]CRC is the third most commonly diagnosed cancer and the third leading cause of cancer death in both men and women in the United States [6]. The highest incidence rates are reported in developed countries such as Australia, New Zealand, Europe, and North America. Africa and South-Central Asia report lower rates [7].CRC is said to be the second most common cancer in Europe and the incidence is steadily increasing [8]. In 2012 the annual number of new CRC reported was 447000, and 215000 fatalities in Europe [8]. In most Indian cancer registries, the incidence of CRC is reported to be amongst the lowest in the world [9] . However, the incidence rates of CRC in Indian immigrants to the United Kingdom and USA are much higher, supporting the concept of life style and dietary habit in the causation of CRC [9]. CRC is strongly associated with advanced age, a western-style diet and a sedentary lifestyle [10]. Recently, there's been an increase in the incidence of CRC in patients younger than 50 7. The average person's lifetime risk of developing CRC is approximately 5% [2].

In most parts of the world, CRC has a higher incidence in men than women.
The overall mortality rate for CRC has been reported to be 35% higher in men well as the incidence of rectal tumours 31% versus 24% in women [11].

It is generally accepted that CRC occurs less frequently in underdeveloped countries when compared to Western countries [12]. CRC is the fifth most common malignancy in Africa although it tends to be more common in Northern Africa [13]. Epidemiological data on the occurrence of cancer in Sub-Saharan Africa (SSA) is sparse, and obtaining population-based cancer survival data is even more difficult due to various logistical difficulties [12]. A significant number of younger Black patients under the age of 50 are presenting with CRC in SSA, unfortunately this has been under-reported in the literature [10].

The majority of CRCs are sporadic, 50-60% [14]. The two most common hereditary syndromes include hereditary non-polyposis colon cancer (HNPCC) and familial adenomatous polyposis (FAP)[14]. Diet and lifestyle are important identifiable risk factors in the sporadic cancers; with diets high in animal fat, protein, processed food, alcohol and smoking being the most commonly cited dietary issues [14].

The stage of the disease at diagnosis is directly proportional to the survival [14].The five-year survival for localised disease is reported to be 90%, 68% for regional disease and 10% for metastatic disease [11].Interestingly, recent studies have shown a relative rightward shift in the location of colon cancer over the past three decades [11]. Also in the last three decades, in the US, there has been a change in the racial distribution of the disease with high mortality rates seen in Blacks than Whites [6].

Graham et al analysed data from 19 different countries in SSA and found the highest incidence of CRC to be in Zimbabwe and South Africa[12]. They also reported the data collection systems to be of poor quality; possibly resulting in under reported local statistics [15]. The incidence of CRC in SSA is said to be higher in males with a peak incidence over the age of 75, a crude incidence of 4.04 per 100 000 population [12]. Despite poor record keeping in SSA these authors noted South African registries to be of the highest quality [15]. Furthermore, they noted that the rates in different ethnic populations were comparable in South Africa due to the diverse demographic structure [12]. Graham et al also found that, in SSA, the major anatomical site of CRC was the rectum (46%), followed by the caecum (17%). These trends are similar to those found in the Western World [12].

Studies from as far afield as Western Africa have shown similar trends. Irabor, reported the incidence of CRC in Nigeria to be increasing, and that the average annual incidence was 27 patients per year [16]. He also noted that, although the incidence rates were increasing, it was still about one tenth of that seen in developed countries.

Irabor hypothesised that this decreased incidence may be due to the different dietary lifestyles of many West African nations. Possible cancer protective factors may be present in the staple starchy, high-fibre, spicy, peppery foodstuff as well as a diet low in animal protein [16]. He suggested that geographical location of West African nations, and their weather, was another possible protective factor [16]. The same study noted that patients in SSA presented at an advanced stage of the disease [16]. He attributed this to poverty, lack of local resources and poor education.

There has been some data focussing specifically on the South Africa population. Cancer registry statistics shows an increase in incidence of CRC in South Africa over the last decade [17]. According to the South African National Cancer Registry of 2011, CRC was ranked the fifth most common cancer in males and the sixth in females in South Africa [17]. Findings by Graham et al [12] have shown that, in South Africa, the incidence is highest in Whites, followed by the Asian and then Coloured populations, with Blacks having the lowest reported incidence [12]. The epidemiology of CRC in White South Africans therefore appears to follow the classic Western trend. Moreover, Segal found that, despite the long-established Western dietary habits in urbanized South African Blacks living in the Witwatersrand, Black South Africans still had a much lower incidence of CRC than White South Africans [18]. According to the 1993–1995 South African Cancer Registry, in African patients, CRC was responsible for 2.0% of all cancers [17]. Over this period the incidence rates for African males and females were 2.1 and 1.6 per 100 000 'world' population. The corresponding rates for White males and females were far higher, 24.7 and 19.3, respectively, per 100 000 [17], demonstrating that the incidence in Blacks was less than one tenth that in Whites. This was despite the three to four generations of "westernization" among Blacks. Although international screening guidelines exist, there are no set guidelines in South Africa. Despite this a large number of cases present to the surgical clinics with complications of CRC, such as tumoral obstruction, perforation, and fistula. [19]

CHAPTER 2

RESEARCH QUESTION

Research question

What are the clinicopathological trends in patients with complicated colorectal carcinoma presenting to KwaZulu-Natal teaching hospitals?

Hypothesis

The incidence of complicated colorectal cancer is more common in our setting compared to the world standard.

Aim

To establish the prevalence of complicated colorectal cancer in patients presenting to KwaZulu-Natal hospitals and to document management outcomes in our setting.

Objectives

To analyse patients presenting with complicated colorectal cancer over the 16-year period from year 2000 to 2015 in KwaZulu-Natal

To determine the prevalence of complicated colorectal cancer in KwaZulu-Natal

To establish the clinicopathological patterns of complicated colorectal cancer amongst different racial groups in KwaZulu-Natal

To document treatments and outcomes of colorectal cancer in KwaZulu-Natal

CHAPTER 3

METHODOLOGY

STUDY SETTING

The study was undertaken at the Colorectal Unit situated at Inkosi Albert Luthuli Central Hospital (IALCH), a tertiary referral hospital situated in Durban. The data used were extracted from the Colorectal Cancer database archived in the Department of General Surgery at the University of KwaZulu-Natal. Patients with CRC are referred from various teaching hospitals in KwaZulu-Natal to IALCH where they are seen in the multi-disciplinary clinic (MDC).

STUDY POPULATION

All patients referred with histologically proven CRC are entered into the Colorectal Cancer Database. The database was started in 2000 and collection is ongoing. Patients with Complicated Colorectal Cancer (CCC) are initially seen at their regional hospital where the first surgical intervention is undertaken prior to referral to IALCH for decision-making in the MDC. Patients presenting with complete obstruction are managed initially at the base hospital. Patients with incomplete obstruction are referred to the Colorectal Unit at IALCH for evaluation with regard to further management, which is either a diverting colostomy or stent insertion. Population groups were defined as Africans (Blacks, Coloureds, Indians and Whites according to the criteria devised by the South African Government.

For the purpose of this dissertation, “African” and “Black” are used interchangeably and the word “Black” has been used throughout in this manuscript. Patients’ data for this study have been extracted from the database between 2000 and 2016.

STUDY DESIGN

This is a descriptive cohort study involving a retrospective analysis of prospectively collected data extracted from the database. Data of all patients with CCC accrued between 2000 and 2015 were extracted from the database and analysed. Those with subacute obstruction underwent investigation such as colonoscopy or contrast enema to make the diagnosis of malignant obstruction. The decision to perform a defunctioning colostomy versus stent insertion was based on the feasibility of stent insertion. This was a clinical decision. Those patients who presented with a complete obstruction underwent emergency exploratory laparotomy and the diagnosis of the malignancy was made intra-operatively and confirmed with histology. Parameters analysed were age, sex, race, clinical presentation, duration of symptoms, co-morbidities, location of tumour, stage of disease, complications, type of intervention, histology, resection margins, post-operative complications, oncotherapy and follow up.

All patients with CRC are followed up in the Oncology and Colorectal Clinics at IALCH and Addington Hospital, Durban. Diagnosis of perforation was made either on the basis of gross operative findings and confirmed by histology or entirely on pathologic review of the histopathology. A free perforation was defined as a perforation into the peritoneum with localized or generalized peritonitis. A contained perforation was defined as perforation into a confined space localized by peritoneum, omentum, or bowel.

The diagnosis of a malignant fistula was made by virtue of the presence of the fistulous tract diagnosed clinically either on imaging or histology. Tumour location was sub-grouped into proximal colon, distal colon and rectum. The proximal colon included the caecum, ascending colon, hepatic flexure and transverse colon. Distal colon included splenic flexure, descending colon and sigmoid colon. Sites documented as 'recto-sigmoid' were classified under 'rectum'. Complications were classified into three major groups: obstruction, perforation and fistula. For the purposes of this study, "bleeding" was regarded as a symptom and was not included under "neoplastic complications". Tumours were staged according to the TNM (tumour, node and metastasis) and UICC numeric staging in the CRC database. T stage was based on the histology of the resected specimen and the M stage was made at surgery or on radiological assessment. For the purposes of analysis the UICC staging was used in this dissertation.

INTERVENTION

Obstruction was managed with resection, diverting colostomy, stent insertion or a combination of these modalities. All patients with perforation underwent resection. Management options for fistula included resection, diverting colostomy or stent insertion. The management of the complication was dependent on the patient's presentation. Patients presenting with acute complete obstruction were scheduled for immediate surgery.

The decision on resection versus diverting stoma depended on the resectability of the tumour. Patients with sub-acute obstruction were considered for insertion of self-expanding metal stent (SEMS). SEMS were used as palliative treatment for malignant colorectal obstruction. The term "successful insertion of stent" refers to successful deployment of stent followed by relief of symptoms. "Failure of insertion" refers to failure of the stent to deploy. Palliative stents were placed in patients who were considered either unfit for surgery or with irresectable tumours. Where the tumour was considered to have borderline resectability, a stent was inserted as a 'bridge to surgery'.

Following stent insertion, when patients were considered operable and the tumour irresectable, the patients were offered neo-adjuvant therapy and were then re-assessed for possible resection. Treatment was considered as palliative if there was either a non-resectable tumour, metastatic cancer or patients were physically unfit for curative oncological resection. All stents were inserted via colonoscopy under radiological guidance using an image intensifier. *Boston Scientific Colonic Walls Stents* (*Boston Scientific, MA, USA*) were the stents deployed. Procedures were performed under conscious sedation.

FOLLOW-UP

Patients were followed up in the Oncology and Colorectal Clinics at IALCH and Addington Hospital. Deaths were established from hospital records or obtained from the Department of Home Affairs (South African Government).

DATA MANAGEMENT

Data were collected on a dedicated proforma and subsequently transcribed onto an MsAccess Database. Data were analysed using Ms-Excel, in which different ethnic groups were compared. Continuous data are presented as either mean and standard deviation or median values (range). One-way analysis of variance (ANOVA) was used to compare ages of the different population groups.

ETHICS STATEMENT

The proposal for this study was reviewed and approved by the University of KwaZulu-Natal's Biomedical Research Ethics Committee (Ref: BE246/15).

CHAPTER 4

RESULTS

At the end of 2015, the database comprised 1944 patients with CRC of whom 615 were Blacks, 753 Indian, 89 Coloured and 367 White. Of these, 448 patients presented with complications (25.1%). When stratified according to population groups 161of the 615 Black patients presented with complications (26%), 157 of 753 Indian patients (21%), 25 of 89 Coloured patients (28%) and 88 of 367 White patients (24%). Of the 431 patients with CCC, 244 were male and 204 were female resulting in a male to female ratio of 1.2:1. The mean age at presentation was 56.4 $\pm$ 14.4 years with a range from 18 to 92 years. The age distribution is shown in Figure 1. The age at presentation peaked in the seventh decade. The average age at presentation was 49.65 $\pm$ 15.36 years for Blacks, 54.97 $\pm$ 11.9 years for Indians, 54.97 $\pm$ 11.9 years for Coloureds and 64.47 $\pm$ 11.63 years for Whites. Seventy patients (16.1%) were young, presenting at or under the age of 40 years. The age at presentation was similar in all complication categories. The proportion of patients presenting with complications aged 40 years or younger was 15.7% for obstruction, 22.9% for perforation and 22.25% for fistula.

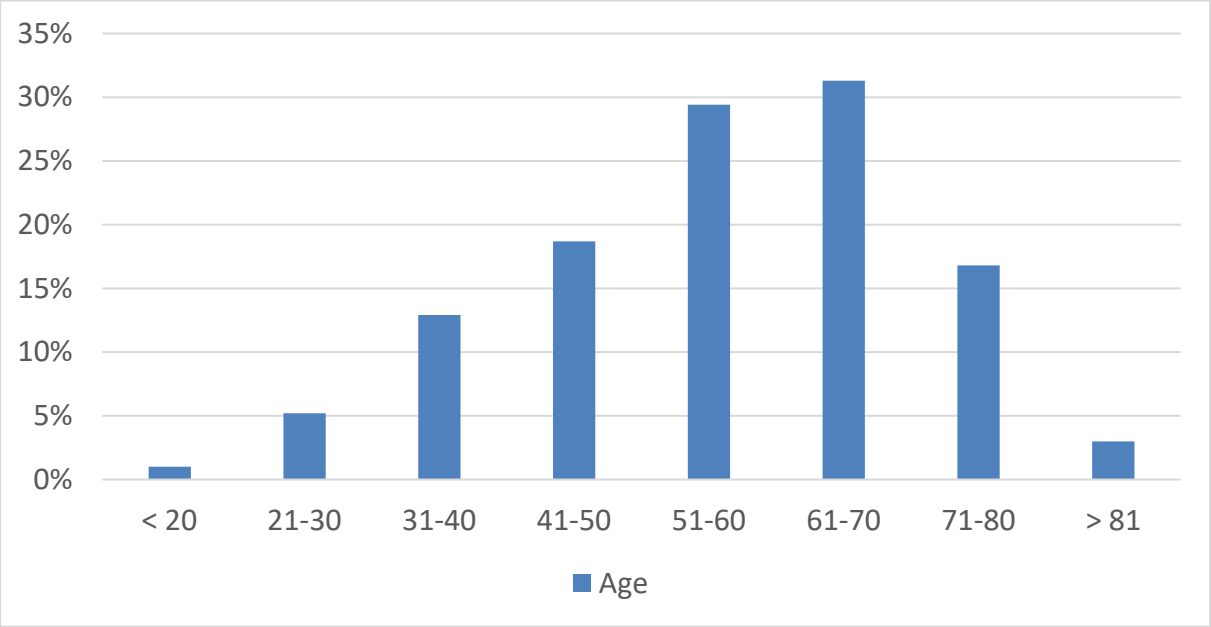

Figure 1

Age distribution in patients with complicated colorectal cancer.

Table I shows the profile of patients presenting with CCC. A total of 382 patients presented with malignant obstruction (20%). Perforation occurred in 71 patients (4%) and malignant fistula in 28 patients (1.5%). Twenty-five patients presented with combined obstruction and perforation and eight had combined malignant obstruction and fistula. One patient presented with a diaphragmatic hernia. The CCC group had a slight male preponderance at 54%. When looking at individual complications there was a slight male preponderance for obstruction, perforation occurred with equal incidence in both sexes and females predominated in patients presenting with fistula. The mean age at presentation was highest for obstruction at 56.6 ± 14.51 and lowest for perforation at 52.4±14.81. The proportion of patients presenting under the age of 40 years was lower for obstruction when compared to perforation and fistula. Age distribution for the different population groups is shown in Table II.

TABLE I

PATIENT PROFILE OF PATIENTS WITH COMPLICATED COLORECTAL CANCER

	Total with complications	**Obstruction**	**Perforation**	**Fistula**	**Other**
Overall (n=1944)	448(23.1%)	382 (19.7%)	71 (3.7%)	28 (1.5%)	-
Males	244	212	37	14	1
Females	204	170	34	14	0
M:F ratio	1.2:1	1.3:1	1:1	1:1	-
Mean age (years)	56.4 $\pm$ 14.4	56.8 $\pm$ 14.3	52.4 $\pm$ 14.9	57.5 *	71
Age range (years)	18-92	18-92	19-82	26-69	71
$\leq$ 40 years	70 (15.6%)	57 (15.0%)	17 (23.9%)	6 (22.2%)	1
> 40 years	378	325	54	22	0

Please note: Some patients had more than one complication.

* Median

TABLE II

AGES OF DIFFERENT POPULATION GROUPS PRESENTING WITH COMPLICATIONS OF COLORECTAL CANCER

Overall	**Obstruction (mean ± SD)**	**Perforation (mean ± SD)**	**Fistula (median)**
Black	50.55 ± 15.87	42.78 ± 14.36	43
Indian	55.55 ± 11.66	54.09 ± 10.2	61
Coloured	58.35 ± 15.71	59 median	73
White	64.71 ± 11.25	63.78 ± 12.87	53.5

Site distribution is shown in Table III. The most common sites for obstruction were the sigmoid colon and the rectum, with equal frequency at both sites. Following this was the caecum and then the ascending colon. The most common site for perforation was the sigmoid colon followed by caecum and ascending colon. Among patients with malignant fistula, the most common site was the rectum followed by the sigmoid colon.

Staging is shown in Table IV. The majority presented as stages II, III and IV. In patients with obstruction, the most common stage was IV followed by II and III respectively. Among perforation, the most common stage was III followed by stage II and IV respectively. In fistula stages II and IV were similar.

Figure 2 compares staging of the CRC cohort (1824) with the CCC (431) cohort. In patients with CCC, there was a higher proportion of patients with stages II, III and IV when compared to the overall cohort. Figure 3 shows survival of the whole group of patients and figure 4 shows survival stratified according to complication.

TABLE III

DISEASE DISTRIBUTION IN PATIENTS WITH COMPLICATED COLORECTAL CANCER

Site *	**Obstruction n=382**	**Perforation n=71**	**Fistula n=28**	**Other n=1**
Ascending + caecum	59 (15.5%)	19 (26.8%)	1 (3.6%)	0
Hepatic flexure	14 (3.7%)	3 (4.2%)	0	1 (100%)
Transverse	24 (6.3%)	4 (5.6%)	1 (3.6%)	0
Splenic flexure	22 (5.8%)	3 (4.2%)	0	0
Descending	30 (7.9%)	5 (6.9%)	0	0
Sigmoid	120 (31.4%)	28 (39.4%)	9 (32.1%)	0
Recto-sigmoid	40 (10.5%0	2 (2.8%)	2 (7.1%)	
Rectum	73 (19.1%)	7 (9.8%)	15 (53.6%)	0

* Please note: Some patients had tumour at multiple sites

TABLE IV

STAGING IN PATIENTS MANAGED FOR COMPLICATED COLORECTAL CANCER

Stage	Overall	Obstruction	Perforation	Fistula
I	20 (4.5%)	18 (4.7%)	1 (1.4%)	0 (0%)
II	118 (26.3%)	99 (25.9%)	26 (36.6%)	8 (28.6%)
III	119 (26.6%)	93 (24.4%)	34 (47.9%)	3 (10.7%)
IV	133 (29.7%)	125 (32.7%)	9 (12.7%)	6 (21.4%)
Not staged	58 (13%)	47 (12.3%)	1 (1.4%)	11 (39.3%0

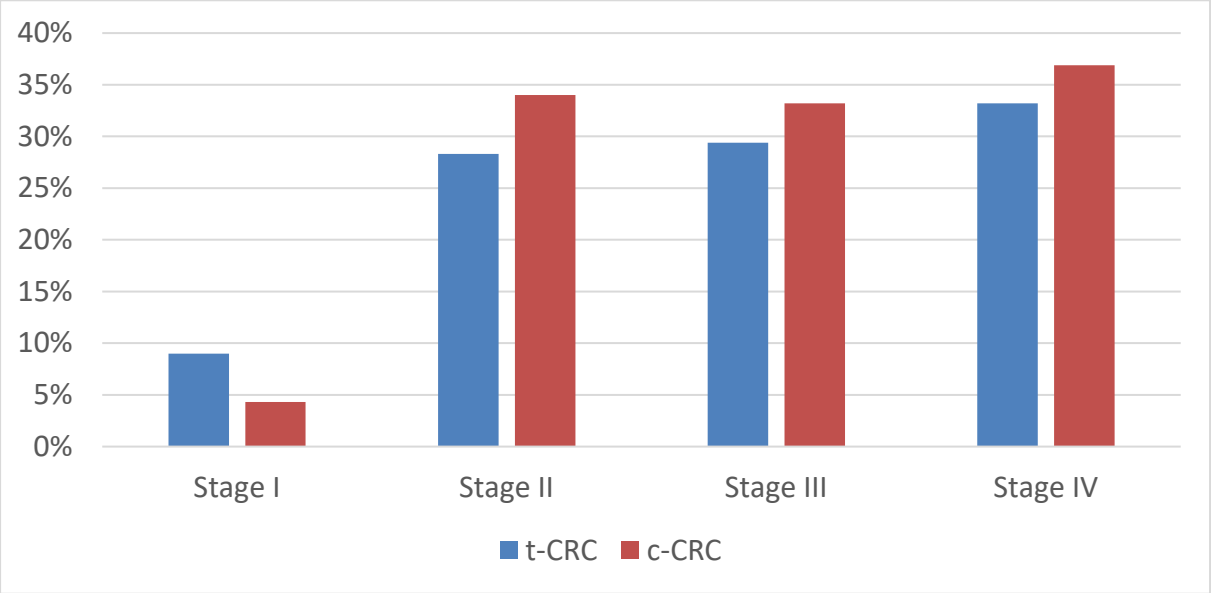

Figure 2

Comparing the stage of disease at presentation of patients with complicated colorectal cancer compared to all patients with colorectal cancer (t-CRC = total with CRC; c-CRC = total with complications).

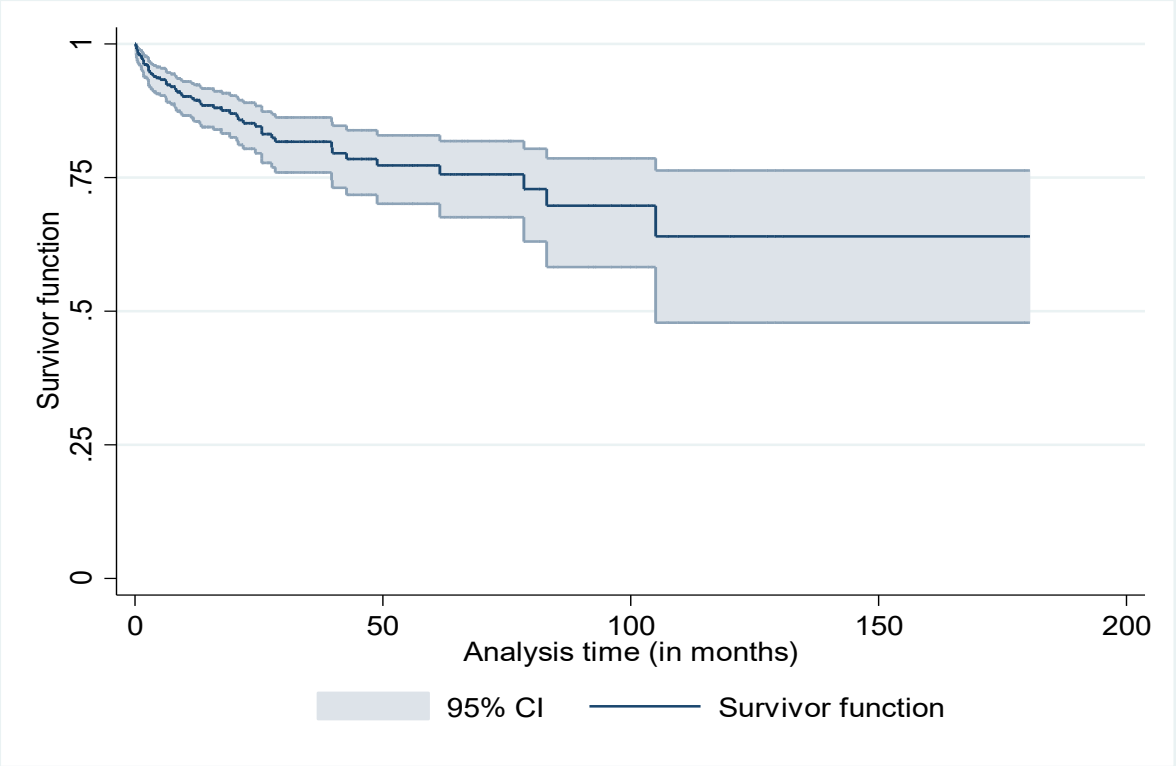

Figure 3

Survival of the whole group of patients presenting with complicated colorectal cancer.

CHAPTER 4.1

MALIGNANT OBSTRUCTION

There were 364 patients with malignant obstruction of whom 202 were males, resulting in a male to female ratio of 1.3:1. The mean age was 57.2 $\pm$ 14.9 years. Ages for different population groups are shown in Table II. Black patients were a decade younger than the other population groups. The most common site was the sigmoid colon followed by the rectum. Metastatic disease at presentation occurred in 122 (33.5%). Management of malignant obstruction is shown in Table V. A total of 239 patients underwent resection (65.7%). Seventy-four percent of patients received a diverting colostomy, nine patients had a colostomy post resection. Resection procedures are shown in Table VI.

The most common surgical resection undertaken was a sigmoidectomy followed by right a hemicolectomy. Thirty-two patients underwent total colectomy due to either a distended proximal colon or multiple lesions and a total of 47 stents were inserted. Two hundred and twenty-four patients had R0 resections (95%), 12 had R1 resections and three had R2 resections. The objective of stent insertion was palliation in 40 patients (85%) and bridge to surgery in seven patients (13%). Stent insertion was successful in 41 patients (87%) with failure in six patients (13%). One of the six patients (two %) developed a perforation as a consequence of the stent insertion.

TABLE V

THE MANAGEMENT OF 382 PATIENTS WITH MALIGNANT COLORECTAL OBSTRUCTION

Management	**N**	**%**
Resection *ab initio*	233	-
Stent followed by resection	5	-
Colostomy followed by resection	9	-
Total undergoing resection	***247***	***64.6%***
Colostomy *ab initio*	89	-
Failed stent -> colostomy	5	-
Total undergoing colostomy	***94***	***24.6%***
Conservative de novo	2	-
Failed stent -> conservative	1	-
Total managed conservatively	***3***	***0.8%***
Stent insertion	41	10.7%
Bypass	5	1.3%

TABLE VI

SURGICAL PROCEDURES UNDERTAKEN IN PATIENTS WITH MALIGNANT OBSTRUCTION

Procedure	**N**	**%**
Sigmoid colectomy	75	19.6%
Right hemicolectomy [1]	74	19.3%
Subtotal colectomy	34	8.9%
Left hemicolectomy [2]	41	10.7%
Transverse colectomy	7	1.8%
Bypass procedure	5	1.3%
Abdominoperineal resection	9	2.4%
Anterior resection	20	5.2%
No resection	117	30.6

Legend

[1]Includes extended right hemicolectomy

[2]Includes extended left hemicolectomy

CHAPTER 4.2

MALIGNANT PERFORATION

Seventy-one patients developed perforation, which accounted for 4% of the total cohort of patients with CRC. The male to female ratio was 1.1:1. Mean age was 52.4 $\pm$ 14.8 years. Blacks were the youngest and were one to two decades younger when compared to the other population groups. The most common site was the sigmoid colon followed by the ascending colon and caecum. Metastatic disease was seen in eight patients (Table IV). Procedures undertaken are shown in Table VI. Perforation occurred at the tumoral site, and was contained in the vast majority, free perforation occurred in only two patients. None of the patients presented with localized or generalized peritonitis. The most common site of perforation was the sigmoid colon (27) followed by the caecum and ascending colon (19), rectum (nine), descending colon (five), hepatic flexure (four) and transverse colon (four). Twelve patients (25%) presented with colonic obstruction and the perforation was discovered at the time of emergency resection. The remaining patients underwent elective surgery with the perforation identified either at operation or on pathology.

Sixty-nine patients had a contained neoplastic perforation and were managed by resection (97%). One patient with obstruction presented with a proximal caecal perforation; in this patient the tumour was deemed irresectable and a colostomy was fashioned. Another patient sustained a colonic perforation proximal to the tumour at colonoscopy. He immediately underwent laparotomy and a colostomy was fashioned as the tumour was deemed irresectable. There was no postoperative mortality in this group of patients. A total of 61 patients had R0 resections (88%), seven patients had R1 resections and one had a R2

resection. The majority of patients presented as stages II (26, 36.6%) and III (34, 48%). Only eight patients presented as stage IV (11.3%) and one as stage I (two %). No patient had peritoneal carcinomatosis or peritoneal metastases. Three patients had a resection with residual microscopic disease (R-1 resection) at the circumferential margin (6.4%). All proximal and distal margins were free of tumour.

Table VII

SURGICAL PROCEDURES UNDERTAKEN IN 71 PATIENTS WITH MALIGNANT COLORECTAL CANCER PERFORATION

Procedure	**N**	**%**
Right hemicolectomy [1]	25	35.2%
Sigmoid colectomy	23	32.4%
Subtotal colectomy	5	7.0%
Left hemicolectomy [2]	6	8.5%
Transverse colectomy	3	4.2%
Abdominoperineal resection	3	4.2%
Anterior resection	3	4.2%
No resection	3	4.2%

Legend

[1]Included extended right hemicolectomy

[2]Includes extended left hemicolectomy

CHAPTER 4.3

MALIGNANT FISTULA

There were 28 patients with malignant fistula (1.5%) identified, 12 were male, resulting in a male to female ratio of 1:1.3. The most common site was the rectum followed by the sigmoid colon. The median age was 52.4 years. Blacks were one to two decades younger when compared to the other population groups. The secondarily involved organs are depicted in Table VIII. Colovesical and rectovaginal fistulae were the most common fistula at 50% and 39.2% respectively. Fistula management is demonstrated in Table IX. The majority of the patients underwent diverting colostomy (64%) and eight underwent resection 28.6%). Table X shows the surgical procedures performed to address the malignant fistula. The most common procedure was a sigmoid colectomy followed by abdominoperineal resection. Most patients with fistula had stage II and IV disease at 28% and 21% respectively. One patient with malignant enterocutaneous fistula underwent conservative management.

TABLE VIII

SECONDARY ORGANS ON PATIENTS WITH COLORECTAL MALIGNANT FISTULAE

Secondary organ	**n**	**%**
Bladder	14	50
Vagina	11	39,2
Small bowel	3	10.7
Bladder and small bowel	1	3.6
Skin	1	3.6

* Some fistulae communicated with more than one organ

TABLE IX

MANAGEMENT OF 27 PATIENTS WITH MALIGNANT COLORECTAL FISTULA

Management	**N**	**%**
Colostomy	18	64.3
Total undergoing resection	8	28.6
Resection	*7*	
Stent followed by resection	*1*	
Stent only	1	3.6
Conservation management	1	3.6

TABLE X

SURGICAL PROCEDURES UNDERTAKEN IN PATIENTS WITH CRC

COMPLICATED BY MALIGNANT FISTULA FORMATION

Procedure	**N**	**%**
Sigmoid colectomy	5	17.8
A-P Resection	2	7.1
Right hemicolectomy	1	3.6
Extended left hemicolectomy	1	3.6
No resection	19	67.8

CHAPTER 4.4

FOLLOW-UP

Patients were followed up in the Oncology and Colorectal Clinics in IALCH and Addington Hospital. The duration of follow-up varied depending on patients' adherence on their appointments.

Malignant obstruction

Median follow-up for obstruction was 11 months (range 1-180 months). Twenty-three of the patients who underwent resection developed recurrence (9.6%). All 23 developed local recurrence, with 8 of these developing additional metastatic disease. After 180 months, the overall survival was 60%. One hundred and ninety-one patients died during the follow up period of this study. The five-year survival rate was 70% (Figure 4). The median disease free interval was 20.5 months (range 9-107 months). Of the 242 patients without metastatic disease at presentation, 22 progressed during follow-up (9%). The median progression free interval was 13 months (range 8-74 months). Among those who underwent surgery, there were no postoperative deaths.

Malignant perforation

Median follow-up for perforation was 11 months (range 1-94 months). At 140 months, overall survival was 85%. Of the 69 patients who underwent resection, 11 developed local recurrences (15.7%). Five-year survival for perforation was 85% (Figure 4). The median disease free interval was 12.5 months (7-36 months). Of the 63 patients without metastatic disease, seven progressed. The median progression free interval was 13 months (range 9-36 months).

Malignant fistula

Median follow-up for fistula was 11 months (range 1-94 months). At 80 months, 54% of patients with fistula had survived. Five-year survival was 60% (Figure 4). Of the nine patients that underwent resection, one developed a local recurrence (14%) after an interval of 20 months. Out of the seven patients undergoing resection, two had R1 resections (28.6%) and five had R2 resections (71.4%). Of the 21 patients with no metastatic disease, two progressed (10%) after a median interval of 11.5 months.

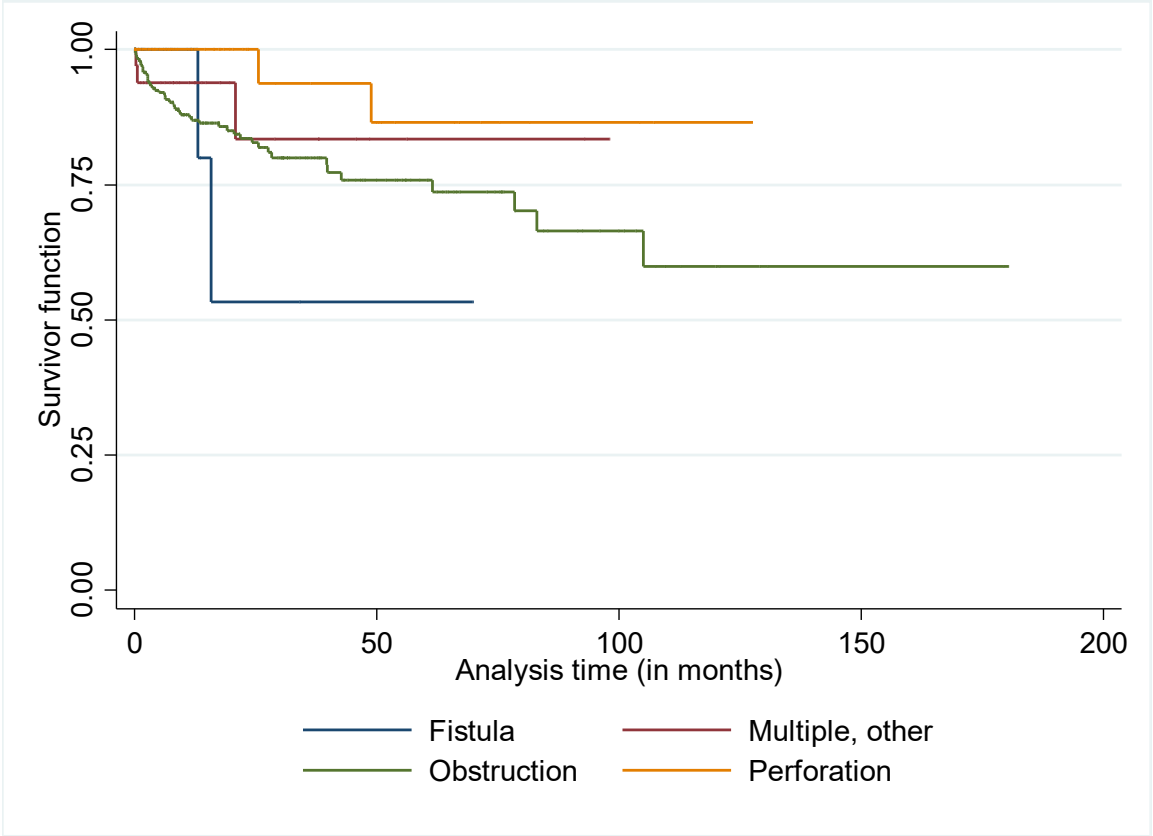

Figure 4

Survival curves showing survival stratified according to complication.

CHAPTER 5

DISCUSSION

This study investigated patients presenting with CCC, there were a total of 1824 patients with CRC identified over a period of 16 years, Four hundred and thirty-one patients (23.6%) presented with complications. The mean age for the cohort was 55 years, considerably less than the 63-72 years reported in the world literature [2,5].

Interestingly, the age at presentation for Blacks is the youngest reported internationally, being about one to two decades younger. White patients were the oldest at presentation in comparison with other races and their mean age approximated the world literature. These population differences in age distribution mimic that seen in the general population of patients with CRC in KwaZulu-Natal, where Blacks were a decade younger than the other population groups [20].

Up to 30% of CRCs present with complications, namely obstruction or perforation [4]. In the majority of cases of CCC surgery is the primary treatment [21]. Patients who present with acute colonic emergencies are often elderly and frail with multiple comorbidities. Moreover, upon emergency presentation, these patients are generally in a poor physical condition due to dehydration, malnutrition and electrolyte imbalance.

Emergency colorectal procedures requiring laparotomy are less likely to involve a primary anastomosis and are associated with higher morbidity and mortality due to the patients' insufficiently optimized metabolic state [5,22]. The surgeon has to manage unanticipated factors including septic shock as well as the technical demands of an oncologic resection without adequate work-up work up [23]. It is well reported that patients with stomas experience significant morbidity, poor quality of life, body dysmorphism and psychological distress [24,25]. The risk factors predictive of poor outcome include age, peritonitis, systemic sepsis, tumour stage, cardiopulmonary co-morbidities, ASA grade and the presence of distant metastasis at presentation [4,21,26-29]. These complicated presentations, which result in emergency surgery, are also associated with a longer hospital stay [30].

Risk factors for mortality have been shown to be emergency surgery, age greater than 70 years, weight loss greater than 10% within 6 months, neurological history, ASA score greater than zero or equal to three and preoperative renal failure. The mortality rate ranges from 0.5% if no risk factors were present to 50% if all factors were present [31] .

There was no in-hospital mortality in this cohort of patients with obstructed colorectal cancer. The author postulates that this is due to the fact that the study patients were younger in comparison to the world literature. Mortality and morbidity rates for emergency surgical decompression are 15-20% and 50%, respectively, as opposed to a mortality rate of 0.9-6% when patients undergo elective surgery [24,32].

Studies suggest that the resection rate is generally inferior in emergency surgery vs elective surgery (77% vs 85%) and that the oncological resection is inferior after emergency surgery when compared to elective surgery (60% vs 70%) [33]. Resection rate in this series depended on the type of complication the patient presented with. Perforation had the highest resection rate at 97% and malignant fistula had the lowest resection rate at 32% with obstruction achieving a resection rate of 68%.

Follow-up studies have shown that patients who present with these complications have a poor prognosis [33].Emergency operations are associated with decreased overall survival rate at 5 years (75% versus 86% for elective intervention) [34]. CCC presents at a more advanced stage and this also impacts the overall long-term prognosis [35]. Five-year overall survival rate in this series was 85% for obstruction, 70% for perforation and 60% for malignant fistula

5.1. Malignant Obstruction

The definition of large bowel obstruction varies widely across the published literature, with no universally accepted description that stratifies the degree of obstruction requiring emergency surgery [36]. Terms such as sub-acute obstruction, partial obstruction and sub-occlusion further add to confusion [36]. Aslar et al [37] defined obstruction as the combination of absolute absence of flatus or stool for at least 24 hours, abdominal distension and the presence of dilated colon on radiography. As patient information concerning symptoms at the time of presentation may be vague and the clinical signs subjective, this researcher defined obstruction as colorectal disease requiring emergency operative decompression at presentation thereby altering the conventional elective management of CRC.

The proportion of patients presenting with obstructing CRC differs worldwide. The reported incidence of complete obstruction ranges from 7 to 40% [24,36,38-40]. Accepted as a surgical emergency, patients with complete large bowel obstruction are often managed at district hospitals. Factors such as the hospital location and the clinician's definition of obstruction may in part explain the wide range in incidence reported in the literature [36,40,41]. The proportion of patients presenting with obstructing CRC in this study was 20%, it fell within the range of published series and did not differ between races or sex.

European studies reveal a mean age of presentation for malignant colon obstruction to be in the seventh decade of life [40,42]. In contrast, our study showed a younger age (mean 50.5 for Blacks, 55.6 for Indians, 58.4 for Coloureds and 64.7 for Whites) at presentation. In this cohort, Black patients were the youngest at presentation, mean age 50.55±15.87. The mean age at presentation for White patients was 64.7 years, which is similar to that in the Western literature which is quoted as 68-72 years (68 in males and 72 in females.

We believe that the younger age of presentation for this cohort is due to the fact that Black patients have been shown to present at a young age [36,43] and we have a larger number of Black patients in this study cohort.at 36.7%.

In this study almost 90% of the strictures were located at or distal to the splenic flexure [24,44].Although some studies have demonstrated no differences in the incidence of right- and left-sided obstruction from CRC [45], others document the left colon to be the more common site of obstruction [38]. Similarly, in this study, the left colon was involved more frequently, 45% compared to 25%, in the proximal colon. Opinion suggesting that the splenic flexure is at greatest risk of obstruction due to acute angulation [46] was not confirmed in our study and that of Moolla et al [36]; the most common site of obstruction in this study was the sigmoid colon and rectum both at 31%, with only a small number of patients obstructing at the splenic flexure at 6%.

CRC causing obstruction tends to be associated with a more advanced stage and with a greater incidence of liver metastases [38,46-48]. This statistic was echoed in this study, although the predominance of stage IV disease was marginal at 34%. The optimal management of obstructing CRC remains controversial due to the paucity of randomized controlled studies. For obstructing colonic cancers, resection and diversion has been the mainstay of treatment in the unprepared colon, particularly for left-sided obstruction or in patients with peritonitis. The emergency management of acute left-sided colonic obstruction remains controversial. The following options are available (i) diverting loop colostomy or ileostomy and subsequent resection which can be in the form of two or three stage procedure, (ii) resection with end colostomy (Hartmann's procedure), (iii) resection and primary anastomosis and (iv) SEMS [49,50].

Colostomy is part of the staged management for left-sided colonic obstruction. During the first stage, the obstruction is relieved by the performance of a colostomy. At the second stage the tumour is resected and the colostomy is either reversed or, alternatively, the colostomy can be closed at a third stage. The advantage of offering a colostomy at presentation is to offer a lower risk surgery to decompress the colon and then allows for delayed staging and patient optimisation prior to the definitive resection [50]. There is no evidence to suggest benefit in mortality with either primary anastomosis or staged procedures [50-52].

While there is consensus concerning the emergency management of tumoral obstruction of the right and transverse colon, recent studies have demonstrated the potential safety of resection and primary anastomosis for right-sided lesions in unprepared bowel [49,53-55]. The colonic segment containing the tumour and its mesentery are resected along with the entire dilated proximal colon as far as the ileo-caecal valve and an ileo-colic (or ileo-rectal) anastomosis is made between non-distended intestinal segments [53]. This method has the advantage of removing the unexplored proximal colon and any synchronous lesions (synchronous cancer is present in approximately seven% of cases), and of performing the anastomosis in the well-vascularized terminal ileum [53].

Resection and anastomosis has remained controversial for left-sided tumours, however, there is increasing evidence that primary anastomosis is the procedure of choice for left sided colonic obstruction [54,55]. Treatment options for an obstructed left colon carcinoma, beyond the left flexure, includes resection of the left colonic segment with primary anastomosis, subtotal colectomy with primary anastomosis, and resection of the colonic segment involved with end colostomy and Hartmann's procedure. Total or subtotal colectomy with primary anastomosis is advisable in patients with an obstructed left colon and dilated proximal colon.

Other indications requiring a total colectomy or subtotal colectomy include the presence of synchronous tumours, damage to the proximal colon preventing an anastomosis or caecal distention with threat of perforation [49,53]. Total colectomy under these circumstances, is safe and the procedure of choice. [56]

Diverting colostomy and Hartmann's resections retain a place in the emergency management of obstructive cancer, particularly in unstable patients. Other candidates for non-anastomotic surgery include patients in whom resection is thought to be unlikely due to morbidity or in patients with advanced colorectal cancer, classified as either locally irresectable, metastatic and or peritoneal carcinomatosis[49,53]. Malignant recto-sigmoidal obstruction usually requires an emergency surgical decompression by colostomy [24]. Isolated stomas have a high complication rate, especially when performed as an emergency. The colostomy may be permanent in patients with advanced disease or those with high-risk morbidity for further surgery [49,53]. A stoma, whether permanent or temporary, causes considerable psychological distress and has a significant impact on the patient's daily life [24,57,58].

Colonic stents were introduced in the 1990s and have been used for: (i) palliation for inoperable cancer, or for patients unfit for definitive surgery; or (ii) as a bridge to surgery. This procedure allows prompt relief of obstructive symptoms, thus avoiding the need for emergency surgery or colostomy [24,59].The placement of a metallic stent in the colon was first published as a palliative measure in 1991 by Dohmoto[60]. Tejero and colleagues [59] modified the technique of stent placement using fluoroscopy.

Emergency surgery delays the commencement of chemotherapy. Hence, stent placement converts a major emergency procedure to a minor procedure thereby by allowing time to investigate and stage the disease, assessment for synchronous cancers, optimisation of comorbidities and nutrition and commencement of chemotherapy [61-63]. This further allows for possible immediate restoration of intestinal continuity, thereby converting an emergency major procedure into an elective major resection without a stoma [49,53].

Although colorectal SEMS are expensive, they have been established to be more cost-effective than surgery as a result of the shorter hospital stay, shorter intensive care stay, decreased stoma rate and fewer complications [64-66]. Also, these patients have a reduced recovery time, which is beneficial in such patients who have limited life expectancy [64-66]. Recent systematic reviews and meta-analyses that reviewed the use of SEMS have showed variable technical and clinical success rates at comparable mortality rates [21,67-69]. However, there have been conflicting results regarding complication rates of stents, namely perforation [70-72]. A systematic review of 88 studies with 1,785 patients managed with SEMS in the acute setting, achieved a median clinical success rate for relieving obstruction of 92% and a perforation rate of 4.5 % [69]. Comparatively, the overall success rate in our study was 87%, with a perforation rate of 4%. Failure of placement of SEMS in six patients (13%) in this study was due to inability by the endoscopic operator to pass the guide-wire safely across the stenosis**.**

In the bridge-to-surgery setting, although the success rate of SEMS insertion has been reported to be as high as 93% [62],it is not always feasible. This may be due to technical inability to place the stent or lack of experienced operators. Colorectal stenting was utilised for palliation in 85% of the cohort and as a bridge to later surgical resection in 15%.

Colorectal SEMS-related complications may be classified as early or late. Early complications are defined as adverse events that develop within 30 days following SEMS insertion; late complications are those that occur thereafter. Major early complications include perforation (0% to 12.8%), stent migration (0% to 4.9%), re-obstruction (0% to 18%), pain (0% to 7.4%) and bleeding (0% to 3.7%) [62,73-77]. Late complications include stent re-obstruction (4.0% to 22.9%), stent migration (1.0% to 12.5%) and perforation (3.8%-6.9 %)[73,74,76,77]. Covered SEMS area higher risk factor for migration (5.5% vs. 21.3% in the uncovered SEMS group) [78]. Most re-obstructions are caused by tumour ingrowth, although tumour overgrowth, faecal impaction and mucosal prolapse may also lead to stent re-obstruction [73,79] . The re-obstruction rate tends to be lower for covered SEMS compared to uncovered ones. This is believed to be related to the lower rate of tumour ingrowth [66,73,78].

The potential for tumour dissemination during the stent insertion procedure have been debated [62]. The European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommends SEMS placement as the preferred treatment for palliation of incurable CRC obstruction only[62,77]. It has been observed that the survival rate following potentially curative resection for obstructed cancer was worse than that in non-obstructed patients with comparable disease stage [47]. The five-year survival in this study was 70%. Resection rate was influenced by the complication in this series. Malignant obstruction achieved a resection rate of 68%.

5.2. Malignant Perforation

Perforation can either occur at the site of the cancer or proximal to a complete obstruction. It may present either as a free perforation, with peritoneal spillage, or as a localized perforation with an abscess. Perforation was the second most common complication (4%) in this study. Contrary to obstruction and fistula, perforation seemed to have an equal sex incidence. The clinical course of patients with malignant colorectal perforation depended on the onset of symptoms, as well as the patient's nutritional status, age, and co-morbidities [33]. Whereas patients with free perforation generally present in extremis, those with contained perforation tend to present in a more elective fashion, albeit with signs of infection, such as fever and leucocytosis [80]. The predominant symptoms of perforation in this series were abdominal pain, abdominal distension and change in bowel habit.

As seen in most series [39,47] the sigmoid colon was the most common site of the primary lesion; this incidence differs from the disease distribution of CRC in the world literature and in South Africa [43], where the rectum is the most common site. The greater tendency for perforation in the sigmoid colon compared to other regions is unknown but may be related to the narrower diameter of the lumen in this portion of the colon. There was no difference in sex distribution. Similar observations have been made by others [39].

The vast majority of the perforations were contained neoplastic perforations with no clinical signs of peritonitis, and all were confirmed at the time of surgery. The four percent rate of perforated CRC established in this study falls within the 2.6 – 10% reported in the literature [38,39,47,81,82]. Only 27% of patients required emergency surgery due to associated malignant large bowel obstruction. Tumour stages in perforated cancers are reported to be higher when compared to uncomplicated cancers [38,83]. This finding was echoed in this study. Perforation

usually occurs near or at the site of the tumour, and it is associated with high postsurgical morbidity and mortality rates [39,47]. This high morbidity and resultant mortality appears to decrease the 5-year survival rate by up to 20% [47,84].

The operative treatment of CRC regardless of perforation or obstruction depends primarily on the location of the lesion and the operable fitness of the patient[85,86]. Our resection rate of 97% in this study attests to the fact that the operation of choice for perforated CRC is resection. Circumstances which may lead to the modification of the surgical procedure include the presence of a free perforation with clinical peritonitis or an obstruction in addition to perforation. This may cause dilatation of the proximal bowel thereby potentially affecting the safety of an anastomosis. A segmental colectomy, adhering to oncologic principles is feasible in the majority of cases with contained perforation [33]. Subtotal colectomy with primary anastomosis may be considered for patients with left-sided perforation and associated obstruction resulting in distension and ischaemia of the proximal colon[33,87]. Otherwise, resection of the neoplasm with proximal colonic diversion and a Hartmann's procedure may be indicated if there is local peritonitis. All patients in whom the tumour was resectable in this series, however, were managed by colectomy and primary anastomosis.

In the study by Alvarez et al [38] the mortality rates for perforated lesions was 29%. The main causes of death were sepsis and MODS.The long-term outcome depends on other factors such as disease stage, presence of poor prognostic factors, physiological status of the patients and not the perforation status .Therefore provided these patients with perforated CCC receive the same oncologic resection as non-perforated CRC, the short and long-term outcome should be quite similar

There was no in-hospital mortality. The zero mortality rate in this study is striking when compared to the reported 5-40% in-hospital mortality for perforated colorectal cancer in other series [39,45,47,80,81,83,84,88,89]. The zero mortality in this series may be explained by the fact that patients in this study did not undergo emergency laparotomy except when there was an associated obstruction and, even under these circumstances; the reason for the emergency procedure was the presence of colonic obstruction. Another possible explanation for the extremely low operative mortality may be that all these patients were attended to timeously at their local hospital and were thus not physiologically compromised from delay in presentation. It is possible that patients with free perforation, and thus with severe physiologic compromise, may have been selected out and demised prior to arrival. This low mortality equivalent to findings in the study by Zielinski et al reporting on contained perforation [80]. This author postulates that these are due the contained neoplastic perforation, thus avoiding peritonitis.

In contrast to obstructing CRC which has been repeatedly shown to be associated with advanced disease [38,48], reports on perforated CRC have yielded conflicting results. Some studies have suggested a greater incidence of metastatic disease, more advanced disease stage, and greater residual tumour burden at the time of presentation for perforated colorectal cancer [38,47,80,81,90]. Other studies have shown perforated cancers to be less advanced compared to obstructing cancers [38,39]. The reason for this difference may be related to a presumed longer time required to cause complete obstruction, resulting advanced stage at diagnosis, as opposed to the shorter time needed for tumour necrosis resulting in perforation [39].

Our R-0 resection rate compares favourably with other studies reporting 62–68% in patients with perforated CRC[80]. This author shares the assertion by Zielinski et al that, whether or not the malignant process extends to the circumferential margin is dependent not on the perforation itself but rather on the extent to which the malignant process has permeated through the bowel wall along with the necrosis as it causes the perforation [80].

The long-term prognosis of patients with neoplastic perforation is unclear in the literature, some studies report a negative effect on patient outcome [39], while other studies report perforation as a positive predictive feature [39,91,92]. These conflicting data stem from the tendency of previous studies to not clearly differentiate between free and contained perforation or between neoplastic and proximal perforation.

Two studies have reported a poorer survival and higher recurrence rates with perforation proximal to the tumour compared to non-perforated tumours, suggesting that tumour cell spillage into the peritoneal cavity may result in peritoneal dissemination and negative influence on the patients' survival [39,80]. Survival seems to be related to the cause and the site of the perforation in relation to the tumour itself. Consensus dictates that this patient population should receive aggressive surgical intervention and appropriate adjuvant oncologic therapy [39]. Another series has suggested that, when the immediate post-operative morbidities have been corrected and, if adequate oncological surgery has been performed, the long-term outcomes are similar to those of non-perforated controls [39,45,80,93]. Therefore, an aggressive surgical approach based on adequate oncologic resection principles is indicated. This further suggests that perforation with tumour spillage into the contained area of perforation, if it occurs, does not reach a degree that results in tumour implantation and as such is not an indicator of poor prognosis [39,45,80,93].

In this series resection rate was dependent on the type of complication as well as tumour site. Patients with perforation had the highest resection rate at 97%. The reported overall five-year survival of 85% is encouraging. The best survival rate was achieved in patients who presented with perforation.

5.3. Malignant Fistula

A fistula is an abnormal epithelium-lined connection between two epithelial surfaces. The most common cause of colovesical fistulae is diverticular in origin, followed by malignancy and Crohn's disease[94-96].Commonmalignancies resulting in rectovaginal fistulae include those of the cervix, rectum, uterus, or vagina[97,98]. In the context of malignant fistula, invasive tumour erodes into luminal structures such as the vagina, resulting in fistulisation[97]. Fistulae may also occur following radiation treatment[98]. The added combination of neo-adjuvant therapy and surgery render the tumour bed or site of anastomosis particularly vulnerable to the development of rectovaginal fistula[98]. The most common tumour associated with malignant fistula is CRC. However, colon cancer alone has a much lower incidence of fistula formation, reported as 0.5-0.6 %[94,96,99-102]. The 1.5% fistula rate in this series compares favourably with the literature. Colovesical fistulae most commonly occur following sigmoid colon malignancy[94,99]. They occur more frequently in men as the interposing uterus in women is protective[94,99].Indeed, many women who present with colovesical fistula, have had a previous hysterectomy[94,99]. Rectovaginal fistulae resulting from colorectal or gynaecological malignancy typically occur proximal to the sphincter[97].

Presenting symptoms most commonly arise from the urinary tract. The classical findings are pneumaturia and faecaluria[95,96,103]. Other symptoms include dysuria, frequency of micturition, haematuria and a combination of these [96,103]. Diagnostic verification of colovesical fistula is necessary not only to establish the presence of the fistula but also the anatomic region of the colon involved in order to guide subsequent surgery[95,96]. Options include CT scan, cystoscopy, cystography, contrast enema and colonoscopy[95,96].

The management of both colovesical and rectovaginal fistulae is determined by the underlying aetiology as well as the resectability of the tumour. In the context colovesical fistulae, surgical intervention is essential to avoid complications such as cystitis and pyelonephritis [103]. The management options colovesical fistulae described in the literature include conservative management, resection of the bladder and the colon with or without interposition of the omentum and diverting stoma [94,101].Diverting colostomy can be used as a covering stoma prior to resection of the fistula or can be used as permanent colostomy in patients who are considered not fit for definitive management and are considered for palliative treatment [94,101].

There is scarce literature describing the management of malignant colovesical fistulae and the available literature make no comment of the use of flaps following resection and repair of the respective hollow organs [99-102,104].We do not use flaps in our unit. Surgery is, for the most part, determined by the site and the aetiology of the colonic lesion [94].Resection of the diseased segment is an essential component in achieving cure[99]. Definitive surgical options include either a resection with primary anastomosis, primary anastomosis with a temporary diverting stoma, Hartmann's procedure or 3-stage procedures [99,103]. A single stage resection is

recommended as the treatment of choice for uncomplicated colovesical and rectovaginal fistula from colonic carcinoma[94,101,103].

The first step to evaluate the surgical correction of these fistulae is addressing resectability of the primary[97]. Typically the resection incudes an *en-bloc* resection of the fistula[94,96,97]. The resulting defect in the secondary organ should be closed primarily [103]. In irresectable disease a proximal diverting stoma is recommended to improve quality of life[73].

In colovesical fistulae, there needs to be local resection of the bladder of the bladder involved [95]. Should resection of the bladder potentially reduce the overall capacity, considerations should be given to reconstructive procedures to provide adequate bladder capacity continence [95]. For more extensive tumours, pelvic exenteration is another option[104].A single stage procedure may not be feasible when there is extensive inflammation, abscess, complex fistulae, radiation, irresectable malignancy or poor surgical fitness (94). Conventionally, the management of colovesical fistula has been performed as a three stage procedure, namely, diverting colostomy, repair of the fistula and closure of colostomy [95,103].More recently colovesical fistulae are repaired in a single-stage procedure has been reported with success[94,95,103].

Controversy remains over the decision to perform a single stage versus multistage procedure to correct colovesical fistulae. The presence of previous radiation, intestinal obstruction, abscess, concurrent reconstruction of the bladder and an unprepared bowel all dictate that the intestinal tract should be defunctioned prior to attempted repair [95]. Malignant colovesical and rectovaginal fistulae may be associated with colorectal stenosis. The endoscopic management of a colorectal stenosis with an associated fistula may involve the use of a SEMS [94,102];more

specifically, a covered SEMS [102]. This technique has the advantage of securing the device to the stenotic bowel segment preventing movement as well as covering the opening of the fistula, even in the presence of neoplastic, fragile tissue[102].

Where a stent cannot be placed due to technical reasons, a colostomy becomes the only feasible option suitable. Palliative surgical options for both colovesical and rectovaginal fistulae, in patients who are either unfit or do not wish to undergo major resection surgery or in the presence of irresectable disease, included a defunctioning ileostomy or colostomy [94,98,99,103]. The use of stents for the palliation of malignant fistula has been described[105,106]. The procedure is only feasible if the fistula is associated with a stricture

Malignant fistula had the lowest resection rate at 32%. The R0 resection rate was 78% in this patient group. Reportedly invasion of the bladder from CRC does not carry a poorer prognosis,so long as an *en-bloc* resection of colon and bladder is performed[101].The 5-year survival with macroscopic tumour clearance reported in the literature is 56-62% [101].Five-year survival for malignant fistula in our cohort was the poorest at 60% compared to the other neoplastic complications in this series.

5.4. Limitations

The limitations of this study are that the duration of follow-up was very poor. Follow-up is a major problem in our geographic society, with socio-economic status and difficulties with transport for face-to-face follow-up being major drivers of the poor follow-up. Also, it is likely that other patients with a perforated colorectal cancer were managed locally and might have been too ill to be sent to our regional units.

The strength of the study is that it specifically addresses contained perforation of colorectal cancer as opposed to free perforation and it differentiates direct neoplastic perforation from proximal perforation. This is an improvement on previous studies, whose weakness was failure to differentiate between free and contained perforation as well as neoplastic and proximal perforation. Moreover, this work is the first report to address this condition in South Africa and in Africa.

Follow-up was limited as some patients were lost to follow-up.

CHAPTER 6

CONCLUSIONS

The prevalence of complicated colorectal cancer in our setting is similar to that reported in the literature. The prevalence is the same across all population groups and the sex incidence is similar, but the age at presentation is younger in Blacks. The site distribution varied according to the complication, with obstruction associated more frequently with left-sided disease and fistula involving the sigmoid and rectum.

Full oncological resection was performed in the majority of patients with malignant obstruction and perforation. The majority of patients presenting with malignant fistula underwent a diverting colostomy. The resection rate was dependent on the type of complication. The oncological resection rate was better for malignant perforation and obstruction than malignant fistula. The fistula population also had a worst survival rate. Patients who underwent resection had a zero in-hospital mortality rate. Contained perforation rarely resulted in clinical peritonitis in our patient cohort. We feel this contributed to the zero post-operative mortality.

The perforation status did not impact on long-term outcome. As such patients with obstruction and perforation who had oncological resections should have similar short and long-term outcomes as non-complicated colorectal cancer. Patients with malignant fistula appeared to have the worst outcome in this study group. Earlier presentation of CCC (and CRC in general) in our setting in Black patients highlights the need for more research in developing countries. In the absence of randomized controlled trials, intra-operative management will remain at the discretion of the operating surgeon.

Stenting at centres with expertise is an attractive alternative for obstruction and for fistula, however, patient selection remains key in deciding on whether or not to use a stent.

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