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Survival Status and Predictors of Mortality among Colorectal Cancer Patients in St Paul's Millennium Medical College

Addis Ababa, Ethiopia;

Retrospective Cross Sectional Study

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Abstract

Background; Colorectal cancer (CRC) is among the top cancers in Ethiopia causing significant morbidity and mortality.

Objective; To determine the three years' post-operative survival status and determinants of mortality of colorectal malignancy at SPHMMC among patients who received treatment in the years 2013-2018 at SPHMMC, Addis Ababa, Ethiopia.

Methods

A cross-sectional study was conducted to determine the survival status of patients operated for colorectal cancer at SPHMMC from April 1st 2021-July 25th 2021. All patients who received their first surgical treatment from January 1st 2013 to December 31st 2018 at St Paul's Millennium Medical College (SPHMMC) were included.

Data was collected through a pretested data collection format, entered in to SPSS version 23. Data analysis was made by using descriptive analysis, Kaplan–Meier analysis, together with the log-rank test and Cox regression to estimate the survival curve and the presence of difference in survival among explanatory variables.

Result; Of the 97 colorectal cancer patients who were included in the analysis, 53 (54.6%) were dead at end of third year. The median overall survival time was 19 months (95%CI: 2.636-35.364). Stage at presentation (adjusted hazard ratio [AHR] = 2.96, 95% CI: 1.89-4.5) and the type of treatment given (i.e either surgery only, surgery followed by adjuvant chemo and/or Radiotherapy or neoadjuvant therapy followed by surgery followed by adjuvant therapy) (adjusted hazard ratio [AHR]=0.353, 95% CI:0.18-0.69) were found to significantly affect the overall survival status of patients.

Conclusion and Recommendation; According to this study late intervention and management modality of patients is found to significantly affect patient survival. The study recommends increasing public awareness/education about CRC symptoms.

List of abbreviations

CRC ; Colorectal cancer

CT; Computed Tomography

MRI; Magnetic Resonance Imaging

SPHMMC ; St Paul's Hospital Millennium Medical College

TNM ; Tumor, Node Metastasis

TASH; Tikuranbessa specialized hospital

US; United states

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Chapter I

1. Introduction

1.1 Background

Colorectal cancer is the second leading cause of cancer death in men and the third in women. It accounts for 10% of cancer related mortality making the life time risk of an individual to have Colorectal cancer 6% [1]. It is a cause of significant morbidity and mortality in Africa as well. In Ethiopia, it is the commonest cancer diagnosed in males and the fourth commonest in females [3]. Approximately 80% of colorectal cancers occur sporadically, while 20% arise in patients with a known family history of colorectal cancer. The incidence and magnitude as cause of ailment is decreasing in the developed world and increasing in the developing countries [1].

Colorectal cancer is mainly a disease of elderly according to most of the researches done so far with the peak incidence in 7th decade and it's not shown to have any sex predilection. But CRC occurs relatively at a much younger age in Ethiopia and other developing nations [3,4,5].

All Colorectal cancer originate from adenomas or flat dysplasia and they evolve in to different histology, Adenocarcinoma accounting for nearly 97% of the cases. Other less common histological subtypes include, Carcinoid, Lymphoma, Sarcoma and others.

Both genetic and environmental factors play an important part in the etiology of colorectal cancer. The majority of colorectal cancers are sporadic; approximately three-quarters of patients have a negative family history. In most Western populations, the average lifetime risk for colorectal cancer is in the range of 3–5% [1,2].

A diagnosis of colorectal cancer either results from an assessment of a patient presenting with symptoms, or as a result of screening which is the case in developed countries. Symptoms of colon and rectal cancers are nonspecific and generally develop when the cancer is locally advanced. The classic first symptoms are a change in bowel habits and rectal bleeding. Abdominal pain, bloating, and other signs of obstruction typically occur with larger tumors and suggest more advanced disease. Because of the caliber of the bowel and the consistency of the stool, left-sided tumors are more likely to cause obstruction than are right-sided tumors. Rectal tumors may cause bleeding, tenesmus, and pain. Alternatively, patients may be asymptomatic and/or present with unexplained anemia, weight loss, or poor appetite.

The predictive value of these symptoms for the presence of colorectal cancer in an elderly patient is limited, but they do warrant further clinical evaluation. With the widespread introduction of population screening for colorectal cancer, many individuals are diagnosed at a pre-clinical stage. In symptomatic patients, colonoscopy is the preferred method of investigation.

Colorectal cancer staging is based on tumor depth and the presence or absence of nodal or distant metastases under the tumor node-metastasis (TNM) staging system.

Once a colon or rectal carcinoma has been diagnosed, a staging evaluation should be undertaken.

The colon must be evaluated for synchronous tumors, usually

by colonoscopy. For rectal cancers, digital rectal examination and rigid or flexible proctoscopy with biopsy should be performed to assess tumor size, location, morphology, histology, and fixation. Endorectal ultrasound or MRI can be invaluable in staging rectal cancer and is used to classify the ultrasound T and N stage of rectal cancers .

CT scan should be obtained to evaluate for distant metastases. Pelvic CT scan, and sometimes MRI, can be useful in large rectal tumors and in recurrent disease to determine the extent of local invasion.

Among patients with obstructive symptoms, a water-soluble contrast study (Gastrografin enema) may be useful for delineating the degree of obstruction. It is important to avoid mechanical bowel preparation (for either colonoscopy or surgery) in a patient who appears to be obstructed. PET scan may be useful in evaluating lesions seen on CT scan and in patients in whom a risky or highly morbid operation is planned (pelvic exenterating,sacrectomy). Preoperative CEA is often obtained and may be useful for postoperative follow-up.

Management of CRC patients is best achieved by multimodality therapy involving surgery, and Chemo/Radiotherapy. The short and long term outcomes of management depends on several factors including socio-demographic and clinical and treatment factors as it was evidenced from several studies done so far on this area.

1.2 Statement of the problem

Colorectal cancer is malignancy arising from the colon and rectum. It is one of the common causes of morbidity and cancer death worldwide and in our country as well, being of a major clinical and public health importance. Early detection and timely management form the corner stones for good outcome. Little is known about the local prevalence and socio-demographics of CRC in Ethiopia which translated into the limitation in the capacity to early detection and timely management of cases.

Because of the long held belief that it is a disease of the elderly and uncommon in developing nations including Ethiopia, seeing relatively advanced disease in young adults is not uncommon. Researches showed young adults with CRC are diagnosed at least 6 months later than in older patients [6, 7].

This implies that, developing countries like ours are having their young and productive portion of the population being victimized, hence negatively affecting the counties' overall development. Researches assessing the management outcomes including perioperative and long term survival in our health institution are lacking.

1.3 Significance of the study

Colorectal cancer is among the leading causes of cancer related morbidity and mortality in the world. The knowledge and practice among Ethiopian health professionals is largely dependent on researches done in other parts of the world for the most part. Hence more studies are required in this area.

This study is believed to serve as an input for further studies in the country so that a better understanding of the pattern and prevalence of CRC will be there. Moreover it will serve as an input for studies comparing preoperative and long-term survival outcome of CRC patients. Like any other disease that we know of, the outcome also depends on how appropriately the patients are managed once diagnosed. We have to assess the quality of management by studying the outcomes and their determining factors.

This understanding should lead to the early detection, proper staging and adequate management of CRC. It would also impact different aspects of the health policy towards the handling of this common health problem.

Chapter 2

2.1 Literature review

Colorectal cancer (CRC) is the third most common cancer and cause of cancer death worldwide in both genders [1]. There is a marked variation in the incidence of colorectal cancer worldwide, with western countries having a high rate compared to Africa [8, 9]. However there is a rising incidence of colorectal cancer reported from various parts of Africa which were considered low incidence areas [10, 11, 12].

At diagnosis, the median age of patients with colon cancer is 68 and 72 years in men and women, respectively; the median age of patients with rectal cancer is 63 years in both genders [4]. In 2010, CRC among patients < 50 years old accounted for 4.8% and 9.5% of colon and rectal cancers, respectively [2, 8, 9]. Interestingly, recent studies on several continents have reported an increase in CRC incidence in this age subset and especially in individuals < 40 years.

In the USA an increase in the number of CRC diagnoses in the population younger than 50 years has been described and, in particular, this increase was observed in patients aged 20–35 years[6,8,9].According to the Surveillance, Epidemiology and End Results Program (SEER) database in the USA, around 5% of all CRC are diagnosed in patients < 45 years old[16].

In a retrospective cohort study done on the prognostic factors and survival of colorectal cancer, in Kurdistan province Iran showed, 1- to 5-year survival rate was 87% and 33%, respectively. The study showed that stages of the disease, older age, higher grade and stage of tumor grade to be significant predictors for poor survival outcome and the study found out that there was no statistically significant association between patients' gender, family history and site of tumor [31].

Similar results were found in a study done on determinants of healthcare utilization and predictors of outcome in colorectal cancer patients from Northern Iran [31].

Data from Oman showed that the median age was 56 years and a majority of the patients, 61.1%, were older than 50 years. Similarly, in Jordan, the median age was 62 for males and 58 for females. In Germany the median age at diagnosis was 70 years[33,34,35].

The five-year overall survival (OS) rate was 33%, much lower than the OS rate in developed countries. Highest five-year survival rate (72%) is in Israel and North Korea. Survival varies from 65% to 70% in North America, Europe and Australia, 63% in Germany and 55% in other developed countries [22, 23, 33]

However several studies have found out that, CRC diagnosis in young adults is carried out on average 6 months later than symptom onset due to low level of suspiciousness by probands and clinicians, sense of invincibility in young adults, and lack of medical insurance[6, 7]

Available evidence from cancer registries supports the perception that colorectal cancer is rare in Africa[18]. The age standardized incidence per 100000 ranges from as low as 1.5 in males and 2.5 in females in the Gambia to 8.5 in males and 7.1 in females in Zimbabwe[19]. This apparent rarity in incidence of colorectal cancer in African population can be attributed to dietary, environmental and lifestyle factors.

The crude incidence of colorectal cancer in Sub-Saharan Africa for both men and women was found to be 4.04 per 100,000 population, and about 24,711 new cases were estimated annually. This review also found that the major anatomical site of CRC was the rectum (in 46% of cases), followed by the cecum (17%). Approximately 25% of colorectal cancer patients in sub-Saharan Africa are younger than 40 years, and hereditary factors may contribute [23].

According to a study on CRC Surgery Trends in Kenya the mean age at presentation was 49.7 years (range 10–98 years). The peak age range was 41 to 50 years of age, and 27.3% occurred in patients 40 years or younger. The proportion in those 30 years of age was 11.3%. There were more males (60.6%), with an overall sex ratio of 1.53:1.00[15]. In a single institution based study in Kenya, 64% of all the patients presented at stages III and IV. In this study there was a significant difference among patients for whom surgery was done for curative intent and those for whom palliative surgery was performed; one-year survival was 94% for curative 74% for palliative surgery[18]. In Tanzania the mean age at diagnosis was 46 years and male to female ratio was 1.6:1[5, 17].

In Ethiopia, it is the first most common cancer among the male population .The overall survival probability of confirmed diagnosis of colorectal cancer was 47% at 36 months of follow-up. There is an increasing trend of colorectal cancer in Ethiopia over the past decades. According to

a study conducted two-year review of colorectal cancer at Tikur Anbessa Specialized Hospital, 2010-2011[3]. The median age at diagnosis was 46 and 52.8% of those diagnosed were under 50, which shows the majority of colorectal cancer patients in Ethiopia are young middle-aged adults [21]where as the median age at diagnosis was 70 in Germany[33].

According to the study done on the two-year review of colorectal cancer at Tikur Anbessa Specialized 36% were below the age of 40 years, 58% were men, nearly half came from Addis Ababa, and 20% presented as an emergency[3].

There are several factors which have so far been studied to have a negative relationship with overall survival outcomes of CRC patients. According to a study in Malaysian tertiary hospital no significant association was found between age, treatment modality , presence of Diabetes and HTN with survival rate of patients, on the other hand male sex, late stage of diagnosis , emergency surgery were found to contribute for the lower time adjusted post-treatment survival rate[30].

In a retrospective hospital based study in Ghana on the colorectal cancer survival rates, the median survival time was 15 months, the survival rates at the 1st, 2nd, 3rd, 4th and 5th years were 64%, 40%, 21% ,16% and 16%[33].

A study on the Survival Status and Predictors of Mortality among Colorectal Cancer Patients in Tikur Anbessa Specialized Hospital showed that the overall 1-, 3-, and 5-year survival rates of colorectal cancer patients were found to be 90.7%, 47.0%, and 21.7% respectively. The findings revealed that lower survival probability of confirmed colorectal cancer patients in TASH as compared with those of high- and middle-income countries. Age over 70 years, marital status, comorbidity, smoking, and alcohol consumption as well as stage and grade of tumor were found to be significant predictors of mortality [32].

In a study on the prognosis of CRC in TASH , pathological and clinical factors like primary tumour site, histopathology, tumour grade, size of the tumour, lymph node metastasis, distant metastasis and treatment modality were significantly associated with patients' survival time ($p < 0.05$)[21].

Around 34% of the patients had metastatic cancer at presentation. This is similar to a report from Oman (36.8) and Kenya (29.1%) but in contrast with reports from Germany (28.1%), in Ghana (24.9%), in Malaysia (24.3%), in Jordan (17.2%) and Iran (6.8%) of patients were metastatic [5,21,34]. The late presentation might be due to patients' low awareness of colorectal cancer sign and symptoms, lack of screening program, lengthy and poor referral system in Ethiopia. This might have contributed to the observed low survival of patients treated in Tikur Anbesa Specialized Hospital in Addis Ababa, Ethiopia.

On a hospital based retrospective study, on patients' survival rate in Ghana, the median survival time was 15 months. The overall survival rates at the 1st, 2nd, and 3rd years were 64%, 40%, 21% respectively. The survival rate for stage II was 34%, stage III: 12% and stage IV (0.0%). There was no statistically significant association between survival and age, sex, presence of comorbidity. The median survival time of patient who underwent chemotherapy was higher (30 months) compared to those who did not undergo chemotherapy (11 months) [20].

In a recently published paper from TASH a total of 422 colorectal cancer patients treated in Tikur Anbesa Specialized Hospital from January 2012 to December 2016 were considered in this retrospective study. Majority of the patients, (62.1%) were male and the median age at diagnosis was 46 years. Majority of patients had colon cancer 51.4% and 34.1% rectal cancer. Forty-five (31.3%) rectal cancer patients had adjuvant chemotherapy or radiotherapy after surgery, 31 (21.5) had adjuvant chemotherapy and radiotherapy after surgery and 23 (16%) did not receive any treatment [21].

The risk of death for metastatic cancer was 4.221 times to non-metastatic patients. For treatment modality, risk of death was 36.1% lesser and 47.9% in those patients who received adjuvant chemotherapy or adjuvant radiotherapy and who received adjuvant chemotherapy and adjuvant radiotherapy, respectively compared to patients who had only surgical resection [21].

Chapter 3

3.1 Objective

3.1.1 General Objective;

To assess the pattern and three years' post operative survival status and determinants of mortality of colorectal malignancy at SPHMMC among patients who received treatment in the years 2013-2018 at SPHMMC, Addis Ababa, Ethiopia.

3.1.2 Specific objective;

- To assess the incidence of CRC among all admitted patients at SPHMMC
- Determine the type of treatment provided to CRC patients
- Determine the overall survival of patients operated for CRC

Chapter 4

4.1 METHODOLOGY

4.1.1 Study area;

The study was conducted at St. Paul's Hospital Millennium Medical College (SPHMMC), the second biggest hospital in Addis Ababa which serves as a referral center for patients from Addis Ababa and the rest of Ethiopia..

There are different departments in the college including Surgery, Internal Medicine, GYN/OBS, and Anesthesiology etc.

The department of surgery has 15 consultants General Surgeons. During the study there were 15 senior residents who were involved in both elective and emergency care of patients. Most of the emergency surgeries were performed by senior residents.

4.1.2 Study period

The study was conducted from April 1st 2021 –July 25th2021at SPHMMC.

4.1.3 Study Design

Retrospective Cross sectional analysis of all patients operated earlier than December 31st 2018 but not earlier than January 1st 2013 was conducted.

4.1.4 Source Populations

All patients who were admitted to SPHMMC department of surgery in the years from January 1st 2013 to December 31st 2018.

4.1.5 Target Population; All patients who were admitted to SPHMMC department of surgery with the diagnosis of Colonic and/or Rectal cancer on the days January 1st 2013 to December 31st 2018

4.1. Sample Size Calculation

Sample size determination started by determining d (number of events) because the number of observed events matters beyond the total number of patients in survival data analysis. The required total number of events was calculated using the following formula.

$$d = \left(Z_{\alpha/2} + Z_{\beta} \right)^2 \frac{4}{\ln \Delta^2} \frac{d}{\text{Probability (of an event)}}$$

$$\text{Adjusting for a loss of 20\%. } n_{adj} = \frac{n}{1 - \text{loss}}$$

Z(critical value)=1.96

Confidence interval =95%

d(Margin of Error)=5%

p value =20% taken from overall survival

$$Z_{\alpha/2}=1.96$$

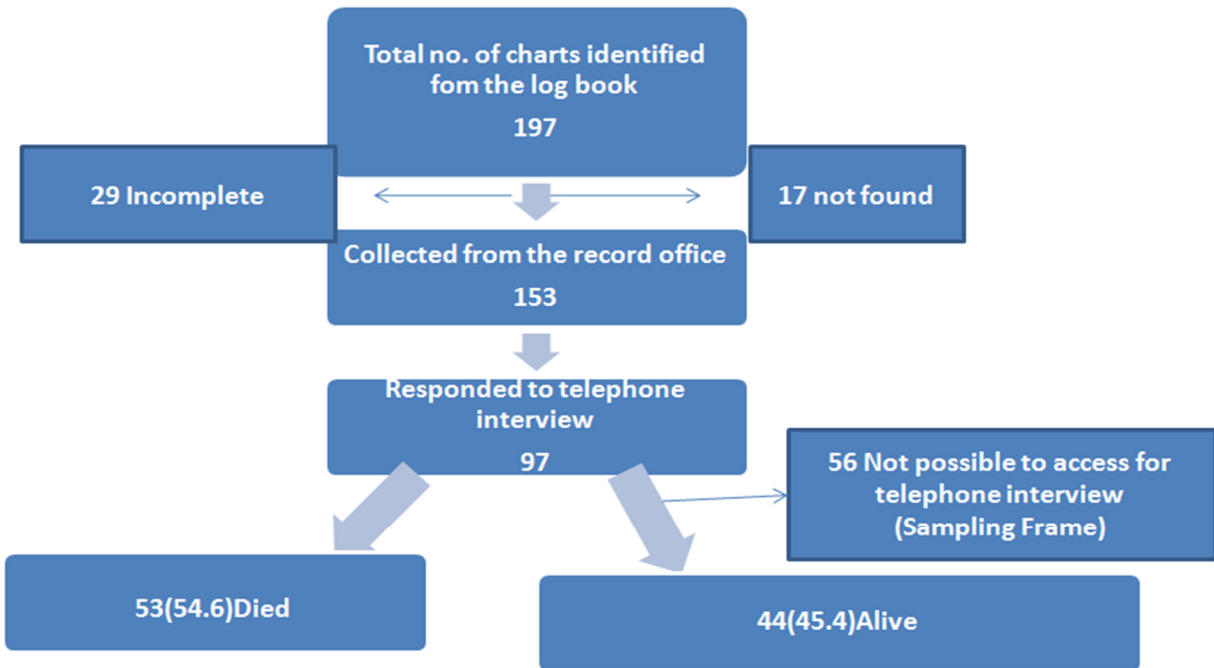
$$Z_{\beta}=0.84$$

The overall survival rate of 18.1% with a Hazard Ratio of 1.8 was taken from an institutional based study at TikurAnbesa Hospital [32]

n(sample size)=113

This formula was based on the one that was used to calculate the sample size of CRC patients to study the prognosis in TASH oncology department[20].

However, all CRC patients whose three years post operative survival could be traced were included in this study, making their total number 97.



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Fig. 1 Sampling procedure

4.1.7 Inclusion and Exclusion Criteria

4.1.7.1 Inclusion criteria

Those patients diagnosed with colorectal cancer in the study setting and who were operated at SPHMMC.

4.1.7.2 Exclusion criteria

Patients for whom first surgery was done at other institutions and are referred to SPHMMC.

Patients who had primary admission and operation on the Gyn/Obs side and are linked to surgery department in the same admission.

4.2 Variables

Dependent Variables(outcomes)	Non Dependent Variables
Primary outcome; survival	Age
	Sex
	Duration of illness
	Presenting symptom
	Primary location
	Stage at presentation
	Mode of presentation
	Co morbidity
	Type of Treatment
	Type of surgery

Table 1; Dependent and independent Variables

4.3 Operational definitions

Censored; patients who were alive at the end of the study time.

Event ; death

Survival status; whether the patients is dead or alive at the end of the study time

Time to death; time from the time patient was operated to death .

Co morbidity; derived from the international disease classification -10. The co-occurrence of any one of the diseases with CRC was labeled yes.

Incomplete Data; when any one of the independent variables were not found in the chart and patients registered phone not working.

Condition on discharge; whether the patient was discharged alive or died in the hospital

4.4 Data Collection

Patients were identified from the operation log books and medical records reviewed. Data collection format (DCF) including data on patient related factors, clinico-pathologic and treatment factors was prepared. DCF was pretested on 15 charts. The study participants' 1 year, 2 years, and 3 years post operative survival status was assessed via telephone interview. Five medical interns who were trained on research objectives and DCF did the data collection.

4.5 Data quality assurances

Data quality was assured by designing appropriate data extraction tool. The adapted data extraction tool was evaluated by research advisors. Pretest on 5% of medical record review was done on a confirmed diagnosis of patients enrolled in 2013 and 2018 one week prior to the actual data collection time. That was done to check the recorded variables.

Furthermore, the investigator supervised every aspect of the data collection. Random evaluation of the recording data extraction tool was done by the investigator. Review of data extraction tool filled was gathered and checked for completeness by the investigator on daily basis.

4.6 Data processing and analysis

Data was cleaned, coded and then entered using SPSS version 23 for analysis. Basic descriptive analyses on the Demographic and Clinic-pathological distribution was done on the 153 CRC patients whose medical records were reviewed, whereas analysis on the treatment related characteristics were performed on the 97 patients whose treatment outcome data was accessed through telephone interview.

The dependent variables were dichotomized in to death and censored. Survival table was used to estimate probabilities of survival after surgery for colorectal cancer at different time intervals. Kaplan–Meier analysis, together with the log-rank test and Cox regression was used to estimate the survival curve and the presence of a difference in survival among explanatory variables. The analyzed data is presented using tables.

4.7 Ethical Clearance

Written ethical clearance letter was obtained from St. Paul’s Hospital Millennium Medical College, surgical department and research directorate office after being evaluated by the Institutional Review Board, before conducting the research. We declare there is no conflict of interest. The data will be used only for the study purpose. Verbal consent was obtained for telephone interview.

4.8 Dissemination of the Results

The final report of this study will be prepared both in soft and hard copies and will be submitted to in SPHMMC surgical department, research directorate offices and SPHMMC library. The result will also be disseminated to any concerned body and will be published.

Chapter 5

5.1 RESULTS

5.1.1 Demographic and clinical characteristics of CRC patients

Out of the 153 patients 83(54.2%) were male. The mean age at diagnosis was 47.46 ± 14.97 and 56 patients (36.6%) were aged 40 and below. Only 27 (17.6%) patients had one or more co morbidity.

Rectal bleeding was the commonest presenting symptom occurring in 55 (35.9%) patients followed by abdominal pain in 30 (19.6%) of the non emergency cases. On physical examination, 69 (45.5%) patients had rectal mass and 16 (10.3%) patients abdominal mass where as the rest didn't have either. Rectum was the primary site of tumor in 74 (48.4%) of patients and recto-sigmoid in 23 (15%) where as the other parts of the colon accounted for the rest of cases. Majority of the cases (66%) presented at advanced stage of the disease i.e stages III and IV (table2).

Table2. Demographic and clinico-pathologic distribution of CRC among 153 CRC patients operated between January 1st 2013- December 31st 2018, at SPHMMC

Variable	Category		Percent (%)
Sex	Male	83	54.2
	Female	70	45.8
Age	=<40	56	36.6
	40-49	20	13.1
	50-59	29	19
	=>60	48	31.4
Comorbidity	Yes	27	17.6
	No	126	82.3
Presentation	Rectal bleeding	55	35.9
	Abdominal pain	30	19.6
	Emergency	43	28.1

	Other *	23	16.3
Physical finding	Abdominal mass	16	10.3
	Rectal mass	69	45.1
	None**	68	44.6
Location of tumor	Rectum	74	48.4
	Recto-sigmoid	23	15
	Rest of Colon ***	56	36.6
Stage at diagnosis	I	0	0
	II	52	33.9
	III	67	43.7
	IV	34	22.2
Mode of presentation	Elective	110	71.9
	Emergency	43	28.1
Duration of illness in weeks	=<1	30	19.6
	1-3	27	25.4
	4-6	39	25.8
	7-12	47	30.7
	>12	10	6.5
Type of emergency	Obstruction	36	85.1
	perforation	5	11.1
	bleeding	1	0.03
	appendicitis	1	0.03
Type of surgery	Tumor resection	99	64.9
	Diversion	54	35.1
Condition on discharge	Stable	139	90.8
	Death	14	9.2

*Other; tenesmus, difficulty during defecation, Fistula(urine through the anus, stool from the urethra), weight loss, appetite loss

**None; neither rectal or abdominal mass

***Rest of colon; cecum, ascending colon,decending colon, transverse colon

5.1.2 Survival outcome in relation to the demographic characteristics of CRC patients

Out of the 97 study participants who were operated between January 1st 2013-December 31st 2018 and whose post operative survival status could be accessed through telephone interview, 53(54.6%) of them died by the 3rd postoperative year while 44(45.4%) were censored.

Majority of the patients were from the age group 40-60 accounting for around 49.4% where as 24(24.7%) were aged 40 and below. Out of these, 45.8% of patients aged 40-60 died whereas around 50% of those aged 40 and below did so by the end of the study time. Around 13 of them had at least one co morbidity constituting 13.4% of the study participants while the rest 84(86.6%) didn't have any documented co morbidity. Out of those patients with co morbidity , 61.5% died by the end of the 3rd year where as 53.5% did so from those with no co morbidity(table 3).

Table3. Survival outcome at 3 years in relation to demographic characteristics of colorectal cancer patients in SPHMMC, Addis Ababa, Ethiopia

Variable	Category	Status at 3 rd year		Total
		Death	Censored	
Sex	Male	27(51.9)	25(48)	52(53.6)
	Female	26(57.7)	19(42.2)	45(46.4)
Age	<30	8(66.7)	4(33.3)	12(12.4)

	30-50	19(44.1)	24(55.8)	43(44.3)
	50-70	25(60.9)	16(39)	41(42.3)
	>70	1(100)	0	1(1)
Comorbidity	Yes	8(61.5)	5(38.4)	13(13.4)
	No	45(53.5)	39(46.4)	84(86.5)

5.1.3 Survival outcome in relation to clinical and treatment-related characteristics

The most common presenting symptom among the study participants was found to be rectal bleeding accounting for 35.9% (35 patients) of all, followed by abdominal pain accounting for 19.6%(19 patients). During physical examination rectal mass was found in 44 (45.1%) patients and abdominal mass was found in 10(10.3%) patients.

Rectum was found to be primary site of tumor in 47 patients (48.4%) and 15(15.4%) patients had rectosigmoid cancer the rest was accounted for by the other parts of the colon. Majority (56.7%) of the patients presented between 1and 3 month of onset of symptoms. Nearly 45.8% of those patients 40 years and younger had their presentations delayed by at least 7 weeks which is a higher percentage as compared to other age groups whereas 25% of them presented on Emergency basis comparable to other age groups(table 2).

Around 66% of the patients presented at advanced stage of the disease i.e stages III and IV. Among these patients 54(55.7%) were males and 43(44.3%). Among these 56(57.7%) were treated on elective basis where as 23(23.7%) presented on emergency basis. Based on the age group, 75% of patients among those 30 years and below and 64.5% of those between 40-60 years presented at later stage of the disease(table). In 50% of the patients who present at late stage rectum was the primary site of the tumor. All of the in hospital deaths (9) were form among those patients who presented at late stage. Majority of the patients (81.3%) and (80.9%) who had been diagnosed at stage III and IV respectively died by the end of the third year.

Around 74(76.3%) of patients presented on elective basis and the rest 23(23.7%)on emergency basis. Out of those who presented as elective cases,55.4% died where as 52.1 % of those

emergency presentations died. As to the treatment modalities, 65(67%) were treated with surgery only where as 30(30.9%) patients received surgery as well as adjuvant treatment in either the form of Chemotherapy or Radiotherapy and only 2 patients were found to have taken Neoadjuvant treatment. More than half (63%) of those patients treated with surgery alone died ,where as only 40% of those who took adjuvant therapy and none of those who got Neoadjuvant therapy died by the end of 3rd postoperative year. As to the type of surgery ,those patients who underwent definitive surgery were found to have a better survival 4 times greater than those who got only palliative surgery with AHR =4.1,95% CI, 2.33-7.1.

Table 4. Survival outcome in relation to clinic pathological and treatment-related characteristics of colorectal cancer patients in SPHMMC, Addis Ababa , Ethiopia.

Variables	Category	Status at 3 rd year		Total
		Death	Censored	
Stage of Disease	Stage II	1(3)	32(97)	33(34)
	Stage III	35(81.3)	8(18.6)	43(44.3)
	Stage IV	17(80.9)	4(19)	21(21.6)
Mode of presentation	Elective	41(55.4)	33(44.6)	74(76.3)
	Emergency	12(52.1)	11(47.8)	23(23.7)
Duration of illness in months	<1	8(42.1)	11(57.8)	19(19.6)
	1-3	9(52.9)	8(47)	17(17.5)
	4-6	15(60)	10(40)	25(25.8)
	7-12	19(63.3)	11(36.6)	30(30.9)
	>12	2(33.3)	4(67.7)	6(6.2)
Treatment Given	Surgery alone	41(60)	24(36.9)	65(67)
	Surgery with adjuvant therapy	12(40)	18(60)	30(30.9)
	Above plus neoadjuvant therapy	0	2(100)	2(2.1)
Type of surgery	Definitive	24(38)	39(62)	63(64.9)
	Palliative	29(85)	5(14.7)	34(35.1)

5.1.4 Overall survival rate of colorectal cancer patients

As Kaplan–Meier analysis showed that the overall survival rate was 43.7% at 36 months follow-up. The estimated cumulative survival rates of colorectal cancer patients at 12, 24 and 36 months were 54.4%, 45.9%, and 43.7% respectively. The overall median survival time of colorectal cancer patients was found to be 19 months (95% CI: 2.63-35.36). The probability of survival was highest at the first post operative day, but it relatively fell later as follow-up time increased.

Table 5 Survival time, cumulative survival probability and log-rank test for the study population according to patient related characteristics during three-year of follow-up (Kaplan–Meier method) of colorectal cancer patients in SPHMMC

Variable	Category	Median survival (mo)(95%CI)	1 year	2 years	3 years	Overall survival	Log-rank test(P-value)
Sex	Male	19	55.4	49.3	45.2	38.9	0.958
	Female	14	53.3	46.7	42.2	63.3	
Age	<30	2	33.3	33.3	33.3	21.3	0.354
	30-50	-	56.1	53.7	53.7	82.2	
	50-70	24	60.4	42.8	37.8	38.2	
	>70	0.75	-	-	-	0.25	
Co morbidity	Yes	9	44	35.2	35.2	26.3	0.354
	No	17	56.1	50	45.1	68.6	

5.1.5 Survival estimate among predictor variables

The study found that the median survival time of colorectal cancer patients treated with surgery alone was lower than those treated with adjuvant and neoadjuvant therapy; the three years survival for those patients treated with surgery only was 34.1% where as that for those treated with adjuvant therapy was 60%.

There was also significant difference in the cumulative survival among patients who presented with advanced and early stages ;stage II 97%, stage III 18.6% and stage IV 5.7% at three years .

Table 6 Survival time, cumulative survival probability and log-rank test for the study population according to clinical and treatment characteristics of patients during six-year of follow-up (Kaplan–Meier method) of colorectal cancer patients in SPHMMC

Variable	Category	Median survival (mo)(95%CI)	1 year	2 years	3 years	Overall survival	Log-rank test(P-value)
Stage of disease	II	-	97	97	97	83.4	<0.005
	III	4	30.2	20.9	18.6	33.2	
	IV	4	39.9	11.4	5.7	12.6	
Mode of presentation	Elective	18	59.5	51.4	44.6	67.8	0.481
	Emergency	10	46.4	41.3	41.3	33.4	
Duration of illness in months	<1	19	58.8	52.9	52.9	43.1	0.583
	1-3	17	58.8	47.1	47.1	43.7	
	4-6	24	56	44	40	67.7	
	7-12	5	43.3	36.7	26.7	26.1	
	>12	-	80	60		25.0	
Treatment given	Surgey alone	32.5	40.6	34.1	34.1	5	0.005
	Surgey with adjuvant therapy	90.3	80	66.7	60	-	
	Above plus Neoadjuvant	-			100	-	
Type of surgery	Definitive	87.9	70.5	62.3	60.7	-	<0.005
	Palliative	12.0	24.7	15.4	12.4	2	

5.1.6 Predictors of colorectal cancer mortality

As the multivariable analysis showed that patients aged below 30 were 0.99 times at higher risk to die (adjusted hazard ratio [AHR] = 0.99, 95% CI: 0.11-0.89) than those aged above 40 years old as a reference. Patients who present at stage II and III had 0.16 and 0.89 times (lower)mortality than those with stage IV disease; stage II (AHR =0.16,95% CI) and stage III(AHR=0.89,95% CI) when stage IV is use as a reference .

Table 7. Results of the bivariable and multivariable cox regression analysis of colorectal cancer patients in SPHMMC.

Variable	Category	Bivariable AHR()	Overall
Sex	Male		0.636(0.327-1.237)
	Female		
Age	<30	0.074(.006-0.898)	
	30-50	0.004(0.003-0.532)	
	50-70	0.054(0.004-0.723)	
	>70	-	
Comorbidity	Yes		1.244(0.453-3.418)
	No		
Duration of illness in months	<1	1.2(0.176-8.182)	
	1-3	3.95(0.758-20.58)	
	4-6	2.577(0.532-12.476)	
	6-12	5.672(1.13-28.3)	
	>12	-	
Mode of presentation	Elective		1.294(0.44-3.8)
	Emergency		
Stage at presentation	II		3.714(2.12-6.5)
	III		
	IV		
Treatment given	Surgery alone		0.43(0.205-0.895)

	Surgery with Adjuvant therapy		
	Above plus Neoadjuvant Therapy		
Type of surgery	Definitive		1.453(0.699-3.029)
	Palliative		

5.2 Discussion

This retrospective follow-up study aimed to assess the survival status and predictors of mortality among confirmed diagnosis of colorectal cancer at the SPHMMC.

With regards to age, the mean age at diagnosis of CRC was 47.9 ± 12.48 which is consistent with that of other studies done in Ethiopia and lower than that from studies in Germany [36] which is 70 years and from Kenya [15] which is 55.4 and UK where more than half of the patients were reported to be above 75 years [37]. In Zimbabwe among patients with colorectal cancer, black Africans tended to be younger than Caucasians, who were over-represented in the oldest age category; 32 % vs 2% were less than 50 years and 41% vs 78% were older than 60 years [17]. This indicates that CRC is more diagnosed in the youth in Ethiopia and other African countries. This could be due to the relatively higher healthcare seeking behavior of the youth and exposure to different risk factors which come along with economic growth.

According to this study, patients with age younger than 30 years were found to have decreased median survival as compared to those above 30 years. This could be due to the late stage presentation in these age group; 75% of those below 30 age present in advanced stage (III, IV) as compared to 63.5% of those above 30. This finding is contrary to the findings in other studies.

In this study more than half of the study participants were males, however there was no statistically significant difference in mortality between the two.

This study showed that the median survival was 19 months, and overall 1-, and 3-years, survival rates of colorectal cancer patients were found to be 54.4% and 43.7% respectively. This is significantly lower than the values from the study conducted in TASH which found a median survival of 34.8 months [32]. This was slightly higher than the result from a study done in Ghana

where the median survival time was found to be 15 months and the survival rates at 1st, 2nd and 3rd year were 64%, 40% and 21%[19].

The overall 1-year, 2 years and 3 years survival for stage II was 97%, 90.9% and 84.8% respectively. For stage III; 34.9%, 20.9% and 18.6% and for stage IV; 34.2%, 22.8% and 5.7% respectively. The survival at three years is lower than that from the study in black lion hospital in 2009 which was 60.8%, 44.5% and 20.9%[32] the median survivals for the respective stages were also lower from studies in TASH [20,32]. This could be attributed to the lack of oncology center at SPHMMC back in the years these research involved and although the patients were referred to TASH patient psychological and economical factors could play their roles in hampering the appropriate provision of those treatment modalities. As such, stage at initial diagnosis was found to be a factor that significantly affects survival status of patients post treatment.

In this study patients who received multimodality treatment in the form of surgery as well as adjuvant therapy; Chemo or Radiotherapy were found to have a significantly increased 1 year, 2 years and 3 years survival; 80%, 66.7% and 60% as compared to those who underwent only surgery as modality of treatment; 40.6%, 34.1% and 32% respectively. This is in line with the studies in Ethiopia, Ghana and Kenya [15, 20, 22, 32,]

The survival rate of patients with emergency presentation was shown to be lower than elective presentations by the end of one month post operatively indicating early post operative mortality in these group of patients. This could be due to the fact that emergency presentation hardly allows for proper patient optimization. The overall median survival was 10 months for emergency and 24 for elective cases. However no statistically significant association was found between mode of presentation and survival status.

Patients with co morbidity showed a lower survival by the 1st post operative month as compared to those without co morbidity; 61.5% versus 84.1% with a median survival of 9 and 19 months respectively. However no statistically significant association was found with survival status.

Those patients who underwent definitive surgery were found to have a better survival 4 times greater than those who got only palliative surgery with AHR =4.1, 95% CI, 2.33-7.1. This finding backs the conclusion that emergency and late stage presentation do have negative impact on the survival of patients and is in line with findings from TASH, South African studies [22, 38].

In conclusion the median survival of patients with CRC was found to be 19 months and overall survival at 3 years was 43.7%. This is lower than that found in the study from TASH. Contrary to most studies lower age at diagnoses was found to have significant effect in increasing the mortality at 3 years. Late stage at diagnosis and modality of treatment the patient took were important in determining the patients' survival rate.

Patients' sex, duration of illness and type of surgery were not found to have any statistically significant association with survival status.

Chapter 6

6.1 Conclusion

According to this study the occurrence of CRC is on the rise among the younger age group. Late stage at diagnosis and late intervention were found to significantly reduce patients' survival. In relation to this, being young was found to have a negative relationship with patient survival which is contradictory to most other studies and this probably is due to the late stage diagnosis of young patients. The other factor which is the implication of the negative impact of late stage at diagnosis is the type of surgery i.e patients managed with the minimum palliative surgery had shorter survival than those with tumor resection . Other factors which were found to be significantly related to patients' survival are management modality of patients, which is related to; one lack of proper staging of patients, and other lack of oncology treatment in the past at our hospital and the overwhelmingly high burden of patients from all over the country to TASH which has made the access to treatment very poor.

6.2 Recommendation; The study recommends early diagnosis of cases. Health education should be delivered in an institutionalized manner through different platforms to increase awareness about the risk factors and the common presentations of the disease. Attention should be given to proper staging of patients and rendering the appropriate modality of treatment.

6.3 Limitations; of this study are all the variables that we desired to study about were not included because of incompleteness of most of the charts. We couldn't also include as many number of patients as we planned because the patients couldn't be reached through their registered phone numbers. The other limitation is that it assess only 3 years post operative survival status because of lack of access of patients' documents.

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Annex

Data Collection Checklist

Patient Factors				
Name				
MRN				
Phone no.				
Age				
Sex	Male			
	Female			
Co mmorbidity	Yes	HTN		
		DM		
		RVI		
		Other		
	No			
Family history	Yes		1	>1
		First degree		
		Other		
	No			
	Not mentioned			
Smoking status	Smoker	Time in yrs	Not Specifi	
	Non smoker			
	Not mentioned			
Alcohol consumption	Yes	Time in years	Not specifi	
	No			
	Not mentioned			
Clinicopathological factors				

Duration of illness		In weeks	
Presenting Symptoms		Abdominal pain	Weight loss
		Rectal bleeding	Appetite loss
		Tenesmus	Signs of anemia
		Difficulty in defecation	Abdominal mass
		Symptoms of obstruction	Perianal mass
		Fistula	
Physical findings	Abdominal mass		
	Rectal mass		
	Not mentioned		
Primary location	Rectum		
	Rectosigmoid		
	Sigmoid		
	Descending Colon		
	Cecum		
	Transverse Colon		
	Ascending Colon		
	Anorectum		
	Hepatic Flexure		
	Splenic Flexure		
Stage at presentation	I		
	II		
	III		
	IV	Liver	
		Lung	
Bone			
Other			
Mode of presentation	Elective		
	Emergency		

Time of first visit to OPD/EOPD/SRC					
Treatment and outcome					
Date of surgery	•				
Treatment given	• Surgery				
	• Chemotherapy			Neoadjuvant	
	• Radiotherapy			Adjuvat	
Complications in the ward	• Yes	Time and complication			
	• No				
Condition on discharge	Stable				
	Death				
Status at follow up time period		1 year	2 nd year	3 rd year	
	Dead				
	Censored				
	Phone not working				