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Colorectal cancer treatment outcome and associated factors among patients treated at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

By

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This is to certify that the thesis prepared by Berhan Atsebeha entitled ***"****Colorectal cancer treatment outcome and associated factors among patients treated at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia."* and submitted in partial fulfilment of the requirements for the degree of Master of Pharmacy in Pharmacy Practice complies with the regulations of the university and meets the accepted standard concerning originality and quality.

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Abstract

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second cause of cancer death worldwide. It is a major public health problem and continues to be a disease of both the developed and developing nations. The objective of this study was to determine five year's survival and associated factors among patients treated for CRC at adult oncology unit of Tikur Anbessa Specialized Hospital (TASH). A hospital based retrospective cohort study was conducted and all patient charts with diagnosis of CRC from September 11, 2013 to September 10, 2014 were included for the study and tracked until September 10, 2019. The data was entered and analyzed using SPSS version 23.0. Survival curves were plotted using Kaplan-Meier method and prognostic factors for survival were determined using Cox regression model. Out of the 316 CRC patients, 181(57.3%) were male with 1.34 ratio. The mean age in years was 48.66 $\pm$ 13.58. Majority 115 (36.4%) of the patients were diagnosed with colon cancer, whereas, 112 (35.4%) and 89 (28.2%) patients were diagnosed with rectal and colorectal cancer respectively. Approximately, half (45.60%) of the patients were diagnosed at clinical Tumor Nodes Metastasis (TNM) stage-IV and 203 (64.2%) of patients were dead in the five years follow-up period with median survival of 19 months. The result of cox proportional hazard regression analysis showed that, being underweight (HR=1.72, 95% CI (1.19-2.48)), rectal cancer (HR=1.92, 95% CI (1.38-2.68)) and late stage of CRC (HR=2.71, 95% CI (1.67-4.41)) were associated with decreased survival. This study reflects that most patients diagnosed with CRC at TASH were predominantly presented at advanced stage and treatment outcome was poor compared to many African studies. Hence, a concerted effort has to be made to improve access to specialized medical faculties and public health education programs on CRC, which may be necessary for early detection and thereby improve treatment and CRC survival.

Keywords: Colorectal cancer, treatment outcome, mortality.

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Contents

Abbreviations and Acronyms

5-FU:	5-Fluorouracil
BMI:	Body mass index
CAPEOX or CAPOX:	Capecitabine and Oxaliplatin
CRC:	Colorectal Cancer
DM:	Diabetes mellitus
DNA:	Deoxyribonucleic acid
EFMOH:	Ethiopia Federal Minister of Health.
EGFR:	Epidermal Growth Factor
FAP:	Familial Adenomatous Polyposis
FOLFIRI:	5-Fluorouracil, Leucovorin, and Irinotecan.
FOLFOX:	5-Fluorouracil, Leucovorin, and Oxaliplatin.
FOLFOXIRI:	5-Fluorouracil, Leucovorin, Oxaliplatin, and Irinotecan
HMIS:	Health Management Information System
HNPCC:	Hereditary Nonpolyposis Colorectal Cancer
HUCSH:	Hawassa University Specialized Hospital.
IBD:	Inflammatory Bowel Disease
NCCN:	National Comprehensive Cancer Network
OS:	Overall survival
RUQ:	Right Upper Quadrant Pain
TASH:	Tikur Anbessa Specialized hospital
TNM:	Tumor Nodes Metastasis
VEGF:	Vascular Endothelial Growth Factor

List of tables

List of figures

1. Introduction

1.1. Background

Cancer is a generic term for a large group of diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and/or spread to other organs. Other common terms used are malignant, tumors, and neoplasms. Cancer can affect almost any part of the body and has many anatomic and molecular subtypes(1). Cancer is the second leading cause of death globally and is responsible for an estimated 9.6 million deaths in 2018. Globally, about 1 in 6 deaths is due to cancer. Approximately 70% of deaths from cancer occur in low- and middle-income countries(1). There is wide variation over time among the different geographic areas due to variable exposure to risk factors, introduction, and uptake of screening as well as access to appropriate treatment services. (2). Over the years, the cancer burden has shifted to less developed countries, which currently account for about 57% of cases and 65% of cancer deaths worldwide(3). During the last two decades, the incidence of cancer has increased in an ascending pattern worldwide. It is expectable that with an increase in life expectancy, adapting western lifestyle, and the growth of industrialization, the burden of cancer in sub-Saharan African countries is likely to increase in the new millennium(4). In Ethiopia, cancer accounts for about 5.80 % of total national mortality. Although population-based data do not exist in the country except for Addis Ababa, it is estimated that the annual incidence of cancer is around 60,960 cases and the annual mortality is over 44,000. For people under the age of 75 years, the risk of being diagnosed with cancer is 11·3% and the risk of dying from the disease is 9·4% (3).

Colorectal cancer (CRC) is the malignant growth of the tumor that begins from the inner wall of the colon or rectum. Most CRCs arise from adenomatous polyps. These neoplasms are usually benign, but some develop into cancer over time. Approximately two-thirds of these cancers will arise from the colon, and the remainder will form in the rectum. One-third of patients with CRC usually have systemic metastasis at their initial diagnosis. The liver is the most commonly metastasized organ for primary CRC (5).

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the second cause of cancer death worldwide. It is a major public health problem and continues to be a disease of both the developed and developing nations (6).

In Africa, CRC presents in late stages and relatively on younger patients (7). The International Agency for Research on Cancer (IARC) publishes sets of estimates of global incidence and mortality through the GLOBOCAN (Global cancer incidence, mortality, and prevalence) project. Accordingly, this data indicates that colorectal cancer is the 5th most common cancer in sub-Saharan Africa (8).

The incidence of CRC in Sub–Saharan Africa was found to be 4.04 per 100,000 populations. From this East African data contributed to 1.57 per 100,000 population (8). Although slight regional variation in prevalence has been reported, according to data from GLOBOCAN in Africa, CRC is the fourth most common fatal malignancy. It is ranked as the third most common amongst all types of cancers in North Africa, while in East, Central, South, and West Africa it is ranked as fourth. It is noted that many of these nations lack official cancer registries, which may reduce the accuracy and reliability of the data (9).

Colorectal cancer is among the few cancers that can be prevented by the removal of precancerous tissue; therefore, early detection is crucial (10). The therapeutic modalities available to the patient with colorectal cancer are similar to those used in other solid tumors. Surgery, radiation, and chemotherapy all have roles in both localized and advanced disease, but how each of these strategies is used, and sequencing depends on the location and extent of disease and the goal of therapy (11).

The 1-year and 5-year relative survival rates for individuals with colorectal cancer are 83.2% and 64.3%, respectively. Survival continues to decline to 57.6% at 10 years after diagnosis. When colorectal cancers are detected at a localized stage, the 5-year relative survival rate is 90.1%. After cancer has spread regionally to involve adjacent organs or lymph nodes, the 5-year survival rate drops to 69.20 %. When the disease has spread to distant organs, the 5-year survival rate is 11.7% (12).

Over the past years, several research groups have suggested numerous factors associated with the survival of CRC patients (13). However, the extent of tumor infiltration to the bowel wall, adjacent lymph node metastases, and distant metastasis are the major contributing factors. Although various studies have reported a strong correlation between CRC stage and its prognosis, it has also been argued in other studies that the prognosis for a patient with CRC is much influenced by factors relating to patients characteristics and the tumor but not just the anatomical extension of the tumor (14).

1.2. Statements of the problem

Historically CRC rates were far lower in low- and middle-income countries (LMICs) than high-income countries, but now globalization has changed the game entirely. Incidence rates of CRC at an East African hospital have increased by over 300% in 2 decades (15).

Besides the rise in the incidence of CRC, there are increased mortality rates in both males and females among some low-resource countries. This may reflect a lack of prevention measures, proper and early diagnosis, and treatment modalities. Indeed, low socioeconomic status was found to be associated with later CRC stage at diagnosis and less aggressive treatment. However, other factors may contribute to the higher burden in Blacks, since CRC death rates are substantially higher in Blacks than in Whites even within the same socioeconomic gradient (2).

Outcome studies from America suggest worse outcomes for African Americans in comparison to the Whites (16). Worse treatment outcomes are tied to treatment access, screening practice, and the presence and nature of co-morbidities. The disparities in CRC mortality are also related to certain areas of deficiency such as knowledge of family history, access to care obstacles, the impact of migration on CRC, and paucity of clinical data (7).

Standard treatment for CRC has progressed from 5-fluorouracil mono-therapy to combination chemotherapy (5-Fluorouracil and Irinotecan and/or Oxaliplatin) and more recently to biological agents targeted at angiogenesis and the epidermal growth factor receptor (EGFR) (17). However the treatment protocols in developing countries still rely on older molecules, which may have contributed to a poor outcome.

Several research groups have suggested numerous factors associated with the survival of CRC patients. However, the extents of tumor infiltration to the bowel wall, adjacent lymph node metastases, late-stage at diagnosis, obesity, distant metastasis are the major contributing factors. Recent studies have shown that the survival of CRC in sub-Saharan African is very low due to late presentations and lack of modern specialized systems for treatment (14).

The Colorectal cancer mortality rate is correlated to the stage of the diagnosis. When CRC is diagnosed in its early stage and treated, the patient will have a greater chance of survival.

Screening of average-risk individuals can reduce CRC mortality by detecting cancer at an early, curable stage and may decrease CRC incidence by detecting and removing polyps. There is direct evidence from randomized controlled trials that screening using fecal occult blood testing and flexible sigmoidoscopy will reduce mortality from CRC. And there is evidence from case-control studies and cohort studies that colonoscopy has the potential ability to prevent cancer death due to early detection of cancer (18).

Knowing the above evidence; as far as our knowledge, still there is no published evidence-based research done in Ethiopia that assesses treatment outcome and associated factors among patients treated for CRC. Therefore the purpose of this study is to fill the gap in knowledge of survival and contributing factors for treatment outcome; and to determine the association between socio-demographic and clinical characteristics and treatment outcome in patients treated for CRC in TASH.

1.3. Significance of the study

Ethiopia does not have a routine screening scheme like many developing countries in the world. Consequently, patients present at a late stage, which results in significantly high morbidity and mortality related to CRC (19). The late presentation mostly requires costly and advanced treatment methods presenting a challenge to the inadequately resourced health institutions. So this study will forward the necessary recommendations to different stakeholders in the area.

There is no study done on CRC in Ethiopia. Hence, the result of this study would help to provide information regarding the treatment outcome of CRC and associated factors. This would in return help to improve the service provided to CRC patients and hence improve survival.

Only 1 in 5 low- and middle-income countries have the necessary data to drive cancer policy (1). So, the finding of this study will also be used as input for policymakers and serve as a baseline survey for further investigation on CRC management in TASH.

1.4. Literature review

1.4.1. Epidemiology of colorectal cancer

The GLOBOCAN estimates global incidence and mortality of 36 cancers in 185 countries based on the reports generated from the database for all cancers combined. Accordingly, CRC is the fourth commonly diagnosed cancer (6.1%). Lung cancer (11.58%), female breast cancer (11.55%) and prostate cancer (7.06%) being the 1st, 2nd and 3rd commonly diagnosed cancers respectively. And CRC is the second leading cause of death (9.2%) next to lung cancer (18.4%) only (20).

The point retrospective case study carried out in Iranian cancer institute, from 1995 to 2009 with confirmed CRC, 66.5% of them were rectal cancer, and 33.5% of them are diagnosed with colon cancer(21).

The incidence of CRC is lowest in developing countries like India and countries in Africa. In Nigeria, the incidence of CRC is put at 3.4/100,000 compared with 35.8/100,000 each year in the United States of America (USA). Despite this low incidence of CRC in Nigeria, the outcome of treatment remains poor due largely to late presentation, ignorance, poverty, and superstition (22).

In South Africa, CRC is the fourth most common cancer in both men and women. The crude incidence is 7.17/100,000/year for men and 5.80/100,000/year for women, and CRC ranks sixth in cancer-related mortality (23).

According to a retrospective hospital-based study done in Ghana by Agyemang *et al*, the number of new cases of CRC has increased by 8-fold per year from an average of 4.1 new cases in the 1960s to an average of 32.6 new cases in 2010 (14).

A retrospective analysis using the Cancer Disease Hospital (CDH) registry database was done in the largest cancer hospital in the capital City (Lusaka) of Zambia which serves as the national referral center. Accordingly, 234 of the charts were found to have CRC. Geographically, 111 (48%) subjects resided in Lusaka and 1 (0.4%) outside of Zambia. The CRC is the 6th most common cancer in Zambia, with an incidence rate of 4.8/100,000, prevalence 3/100,000, and

mortality rate of 3.8/100,000 (24). A total of 241 CRC cases were identified in the Eritrean National Health Laboratory (NHL) database between 2011 and 2017. The cumulative age-standardized incidence rate was 9.97 per 100,000 (25).

Based on 2013 data from the Addis Ababa Cancer Registry, CRC accounted for 5.70 % of all cancer cases next to breast cancer (30.20 %) and cancer of the cervix (13.40 %) (3). It has become the second leading cause of death, next to Breast cancer in the adult population (26).

1.4.2. Factors associated with prognosis of colorectal cancer

The stage at diagnosis of CRC is the most important prognostic factor. For example, in the USA, 5-year relative survival was 90.1% for patients with localized stage, 69.2% for patients with regional spread, and 11.7% for patients with distant tumor spread (27).

According to a study done by Bouvier *et al*, using two French population-based cancer registries, the risk of recurrence between 5 and 10 years was associated with male sex (hazard ratio (HR) of 0.66 (0.44–0.97)), a context of perforation (HR perforation Vs. elective surgery 3.17 (1.35–7.42)) and advanced age (28).

According to the retrospective study done at the Iranian Cancer Institute; tumor grade was the only factor significantly related with recurrence (21).

According to national survival data Saudi Arabia, age and tumor extent were significant prognostic factors of survival in patients with colon cancer; the risk was higher in patients with distant metastasis (hazard ratio [HR], 2.53; 95% confidence interval [CI], 1.17-5.45). In patients with rectal cancer, the risk was lower in males (HR, 0.66; CI, 0.45-0.98), but higher in patients with unknown tumor extent (HR, 3.70; 95% CI, 1.66-8.24) (29).

A Single Center Study was done in Oman. On Log rank univariate analysis, age, BMI, diabetes, hypertension, metformin use, stage, clinical nodal status for rectal cancer, TNM status, site of metastasis, surgical intervention, chemotherapy, radiotherapy, chemotherapy regimen, site of recurrence and administration of 2^{nd} line chemotherapy were significant factors affecting overall survival (OS). On Cox regression multivariate analysis none of the factors independently affected the OS (30).

Survival Rate and its Predictors in Colorectal Cancer Patients was done in Southern Iran, and the primary diagnosis method, income status, history of alcohol use, primary treatment method and history of metastasis have significant relationship with survival rate (31).

According to the study done in Komfo Anokye Teaching Hospital, Ghana; Family history (HR= 3.44), Chemotherapy (HR= 0.23), BMI (HR= 1.78) and both chemo/radiotherapy (HR= 3.63) were the significant social and clinical factors influencing the overall survival. Pathological

factors such as TNM tumor stage, depth of tumor invasion, lymph node metastasis, and distance metastasis were significantly associated with overall survival (14).

Despite the rarity of CRC in Nigeria, treatment outcome still remains poor due to late presentation. Eighteen (56.3%) patients presented more than 6 months after the onset of symptoms. Twenty-one (65.6%) patient's presented with the features of intestinal obstruction; 17 (53.1%) with rectal bleeding. Most patients present when they become obstructed or have a severe change in bowel habits at which stage the disease is already late and treatment modalities will be palliative and not for the cure (22).

Data of 233 patients treated for CRC between 2005 and 2010 at various Nairobi hospitals, overall 5 years mortality rate was 29.4%. Factors significantly associated with mortality in this study were male gender, presence of co-morbidity, recurrence, curative intent, disease stage and receipt of chemotherapy (7).

2. Objectives

2.1. General objective

The general objective of the study was to assess treatment outcomes and associated factors among patients diagnosed with CRC at the adult oncology unit of TASH.

2.2. Specific objectives

- To determine a five years survival rate in patients with CRC at TASH.
- To determine predictors of CRC treatment outcome at TASH.

3. Methodology

3.1. Study area and period

The study was conducted at the adult oncology unit of TASH which was established in 1972. The hospital is located in Lideta Sub-City, Addis Ababa, Ethiopia. It is the largest teaching hospital affiliated with the College of Health Sciences, Addis Ababa University, and serves as a training center for undergraduate and postgraduate medical, pharmacy, and other health science students. It is also an institution where specialized comprehensive and clinical services that are not available in other public or private institutions are rendered to the whole nation, of which radiation treatment is one of them. The hospital serves more than 500,000 patients per year in its 20 outpatient specialty clinics, inpatient, and emergency departments.

Treatments offered at the TASH oncology unit include chemotherapy, surgery, and radiotherapy. The department of Oncology has two radiotherapy machines (cobalt-60), 36 beds in the inpatient chemotherapy ward, and 12 outpatient chemotherapy beds. Six clinical oncologists serve the department. The Department of Surgery has two colorectal surgeons. Currently, the Department of Radiology is equipped with two computed tomography scans and one magnetic resonance imaging unit (32,33). The study was conducted from October 1, to December 1, 2019.

3.2. Study design and period

A hospital based retrospective cohort study was conducted.

3.3. Population

3.3.1. Source population

The source population was all patients treated for CRC at the adult oncology unit of TASH.

3.3.2. Study population

The study population was all patients treated for CRC from September 11, 2013, to September 10, 2014, and who fulfill the inclusion criteria of the study.

3.3.3. Eligibility criteria

Inclusion criteria's:

- First visit TASH for CRC from September 11, 2013, to September 10, 2014.
- All patients who started treatment at TASH.

Exclusion criteria's:

- Patients' who had incomplete data and/or medical record that lack of key data elements.
- Patient's lost to follow up.

3.4. Sample size and sampling procedure

All patients treated for CRC who fulfills the inclusion criteria were included for the study and five years charts were retrospectively reviewed. As a result, there were 362 patients with CRC visited oncology unit of TASH from September 11, 2013, to September 10, 2014, and 316 patients fulfilled the inclusion criteria and hence were included in the study (see Fig. 1 below).

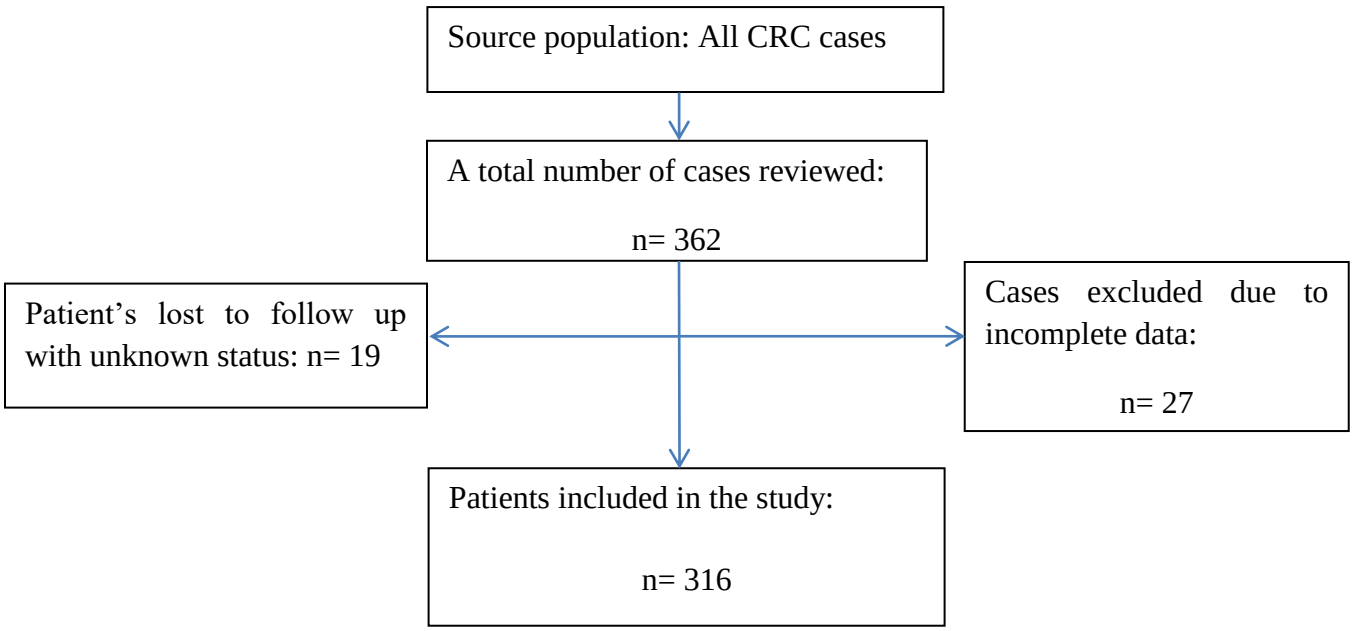


Figure 1. Study population selection procedure

3.5. Study variables

Dependent variable:

- Five year survival.

Independent variables:

- Socio-demographic and lifestyle characteristics (age, sex, marital status and social drug use history).
- Clinical and pathological characteristics at diagnosis (duration of symptom/s, tumor location, TNM tumor stage, histologic cell type, level of histologic cell differentiation and Body mass index).
- Medical history (Comorbidity, Previous Cancer history).
- Treatment-related characteristics (Mode of treatment/s, chemotherapy regimen, chemotherapy cycle and type of surgery).
- Follow up related characteristics (Disease recurrence, in-hospital medical event/s and surgical complication/s).

3.6. Data collection technique

The registration logbook of the oncology department was used to get the card numbers of patients who were diagnosed with CRC during the study period. After getting the card numbers, patient charts were retrieved from the TASH oncology unit archive and documentation office. Data were collected by reviewing the medical charts of patients treated for CRC at the adult oncology unit of TASH and by phone interview (Annex-I). All the information's documented on the patients' medical charts for five years starting from the patient's first visit were tracked. Additional information was collected by calling patient and or patients' relative using the phone number recorded on patients' medical record to confirm status of missed patients from follow up.

Data were collected by two trained pharmacists who had a one-day training prior to data collection on how to collect data using the data abstraction format.

3.7. Data quality control

To ensure data quality, a pre-test was done on 5% of the study population to ensure the agreement of the data abstraction format and phone interview with the need of the study. Any error found during the process of the pre-test was corrected and modification was made into the final version of the data abstraction format. Supervision and checking were made by the principal investigator to ensure consistency of the collected data. All collected data were examined for completeness during data management, storage, and analysis.

3.8. Statistical analysis

The collected data was entered and analyzed using Statistical Package for the Social Sciences (SPSS) software version 23.0. Descriptive analysis was used to describe the pattern of each independent variable. Categorical variables were summarized as percentages, and continuous variables were summarized as means, standard deviations (SDs), and medians. Survival curves were plotted using Kaplan-Meier method and prognostic factors for survival were determined using Cox regression model. Univariate Cox-regression analysis was used to determine the association of different variables with survival. However, Univariate cox regression does not take into account the effect of confounding factors which may affect the relationship between dependent and independent variables. Then multivariable analysis was performed using the Cox-regression model, on variables that have a p-value of <0.20, to determine the independent prognostic factors for survival. Estimation of hazard ratio (HR) at a 95% confidence level was done using the Cox regression model. Proportional hazard (PH) assumptions, as one of cox model assumptions were initially tested using log-log plots. Convergence, divergence, or crossing of log-log plots violates PH assumptions. The lines of the log-log plots were parallel. So, proportional hazard assumptions were approved. A *p*-value less than 0.05 was considered statistically significant.

3.9. Ethical Considerations

Ethical approval of the study was obtained from AAU, CHS, School of pharmacy ethical review board (approval number: ERB/SOP/104/06/2019). Before data collection, written permission was obtained from the oncology unit of TASH. The collected data was secured in a lockable cabinet, no identifiers were used and data was analyzed in aggregate to maintain confidentiality and anonymity of information.

Before asking the required information during a phone call, the study participants were detailed on the purpose of the study and utilization of the information they are providing. Then, Informed consent was taken.

3.10. Definition of terms

Body Mass Index (BMI): is a measure of weight in relation to height. It is the most practical way to estimate if a person is underweight, at a healthy weight, overweight, or obese. The interpretations are: Underweight (BMI < 18.5), Normal (BMI $\geq$ 18.5 and < 25), Overweight (BMI $\geq$ 25 and < 30) and Obese (BMI $\geq$ 30). These indexes were taken at the time of diagnosis of CRC (34).

Early stage CRC: Refers to stage I and stage II CRC according to American Joint Committee on Cancer (AJCC) tumor/node/metastasis (TNM) classification and staging for CRC (35).

Late stage CRC: Refers to stage III and stage IV CRC according to American Joint Committee on Cancer (AJCC) tumor/node/metastasis (TNM) classification and staging for CRC (35).

Treatment outcome: refers to the status of the patient after starting treatment until the end of the review period. Death and alive are the two treatment outcomes considered.

Recurrence or "Relapse": is here used to indicate the reappearance of a disease after complete eradication (36). Recurrences (i.e., local recurrence or distant metastasis) were obtained from the patient's medical record according to the diagnosis of clinicians involved in the management and the follow-up of CRC patients.

Comorbidities: Comorbidities can be defined as other chronic episodic disorders like asthma (i.e. acute episodes of signs and symptoms that can come and go for years) or chronic progressive conditions like cardiovascular disease (37). Any distinct additional entity that has existed or may occur during the clinical course of a patient who has the index disease under study. Diseases that are "not directly related in either pathogenesis or management and do not share an underlying predisposing factor" (e.g. type 2 diabetes mellitus and irritable bowel syndrome) (38). In this study it refers to, any chronic medical diseases except malignancies.

In-hospital medical event/s: are any complications of major comorbid diseases. Hospital-acquired pneumonia, Hematologic toxicities (Neutropenic fever, Anemia), GI toxicities (Mucocities, Diarrhea), Deep vein thrombosis etc.

Lost to Follow-up: is defined as absence from the clinic, without known death or transfer to another facility, for at least 3 months since last scheduled visit (39). It was obtained from the patient's medical record according to the diagnosis of clinicians involved in the management and the follow-up of CRC patients.

4. Results

4.1. Socio-demographic and lifestyle characteristics

A total of 362 patient's medical records with a diagnosis of CRC were reviewed for the study. Forty six of them were excluded from the study due to loss to follow-up with unknown status and incomplete medical record /lack of key data elements. Out of the 316 study participants, males comprised (181, 57.3%). The majority (101, 32.0 %) of the study participants were under 40 years old. The mean age at the time of diagnosis was (48.66, SD± 13.58) years. The majority (144, 45.6%) of the patients was from Addis Ababa, and being married accounted for the highest proportion (249, 78.8%) (Table 1).

Table 1: Socio-Demographic Characteristics of CRC Patients in Tikur Anbessa Specialized Hospital, Ethiopia 2013-2014

Variables		Frequency	Percent (%)
Sex	Male	181	57.3
	Female	135	42.7
Age (in a year)	Under 40	101	32.0
	40-49	50	15.8
	50-59	72	22.8
	60-69	81	25.6
	70 and above	12	3.8
Region	Tigray	6	1.9
	Afar	14	4.4
	Amhara	46	14.6
	Oromia	69	21.8
	Somali	1	0.3
	Benishangul-Gumuz	2	0.6
	SNNP*	23	7.3
	Gambella	1	0.3
	Harari	6	1.9
	Addis Ababa	144	45.6
	Dire Dawa	4	1.3
Marital Status	Single	33	10.4
	Married	249	78.8
	Divorced	16	5.1
	Widowed	18	5.7

*SNNP: Southern Nations Nationalities and People

Regarding social drug use history, 9.50% (n=30) of the patients had a known history of tobacco use, 13.90% (n=44) drunk alcohol, and 20.30% (n=64) of them chew khat (Table 2).

Table 2: Admission Details of CRC Patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

Variables		**Frequency**	**Percent (%)**
Tobacco use	Yes	30	9.5
	No	274	86.7
	Unknown	12	3.8
Alcohol use	Yes	44	13.9
	No	249	78.8
	Unknown	23	7.3
Khat use	Yes	64	20.3
	No	228	72.2
	Unknown	24	7.6

4.2. Medical history

Regarding the previous medical history, 18 (5.70%) of the study participants had a known history of other cancer, of which 4 of them had ovarian cancer. Around 1/4th of (n=80) of the study participants had a history of comorbid diseases and hypertension accounted for the highest percentage (27, 33.75%). Out of 316 study participants, 14 (4.4%) had documented history of radiation exposure (Table 3).

Table 3: Medical History of CRC Patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

Variables		**Frequency**	**Percent (%)**
Previous Cancer history	Yes	18	5.70
	No	298	94.30
Cancer type	Ovarian	4	22.20
	Nasal	3	16.70
	Breast	8	44.40
	Other*	3	16.70
Comorbidities	Yes	80	25.3
	No	236	74.7
Comorbid disease	DM	18	22.50
	Hypertension	27	33.75
	Heart Failure	5	6.25
	Asthma	3	3.75
	DM and HTN	21	26.25
	Others**	9	11.25
Radiation exposure	Yes	14	4.40
	No	207	65.50
	Unknown	95	30.10

Others* Esophageal (2), Prostate (1). Others** Retroviral infection (6), chronic kidney disease (3).

4.3. Clinical and pathological characteristics

As shown in Table 4, 25.9% (n=82) of the study participants presented with rectal bleeding, 24.1% (n=76) with right upper quadrant (RUQ) pain, and 1.3% (n=4) of them were presented with rectal bleeding and RUQ pain combined. The average duration of symptoms in months since the onset of symptoms was 9.3 months. Slightly higher proportions of the study participants (115, 36.4%) were diagnosed with colonic cancer. Almost all (309, 97.80%) of the patients were diagnosed with a histological cell type of adenocarcinoma. With regard to the level of histological cell differentiation, 60.8% (n=192) were well differentiated. A BMI of the study participants was calculated and majorities (182, 57.60 %) of them were in the normal BMI range.

Table 4: Clinical and Pathological Characteristics of CRC Patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

Variables		**Frequency**	**Percentage (%)**
Clinical presentation	Rectal Bleeding	82	25.9
	Intestinal Obstruction	35	11
	Tenesmus	54	17.1
	RUQ Pain	76	24.1
	Constipation	32	10.1
	Rectal bleeding and constipation	8	2.5
	RUQ pain and constipation	17	5.4
	Rectal Bleeding and RUQ pain	4	1.3
	Rectal bleeding, constipation and RUQ pain	8	2.5
Duration of symptom	< 6 months	122	38.6
	6- 12 months	128	40.5
	> 12 months	66	20.9
Primary tumor location	Colon	115	36.4
	Rectal	112	35.4
	Colorectal	89	28.2
Histological cell type	Adenocarcinoma	309	97.80
	Unknown	7	2.20
Level of histological differentiation	Well-differentiated	192	60.8
	Moderately differentiate	91	28.8
	Poorly differentiated	21	6.6
	Undifferentiated	12	3.8
BMI	Underweight	43	13.6
	Normal	182	57.6
	Overweight	79	25
	Obese	12	3.8

As illustrated in Figure 2, the findings from this study showed that almost half (144, 45.60%) of the patients were diagnosed to have CRC with clinical TNM stage IV. From those patients who had documented metastatic cancer, the liver was the primary site of metastasis in the majority (n=88, 61.1%) of the patients. Lung, bone and other sites comprises 28.5% (n=41), 6.9% (n=10) and 3.5 % (n=5), respectively.

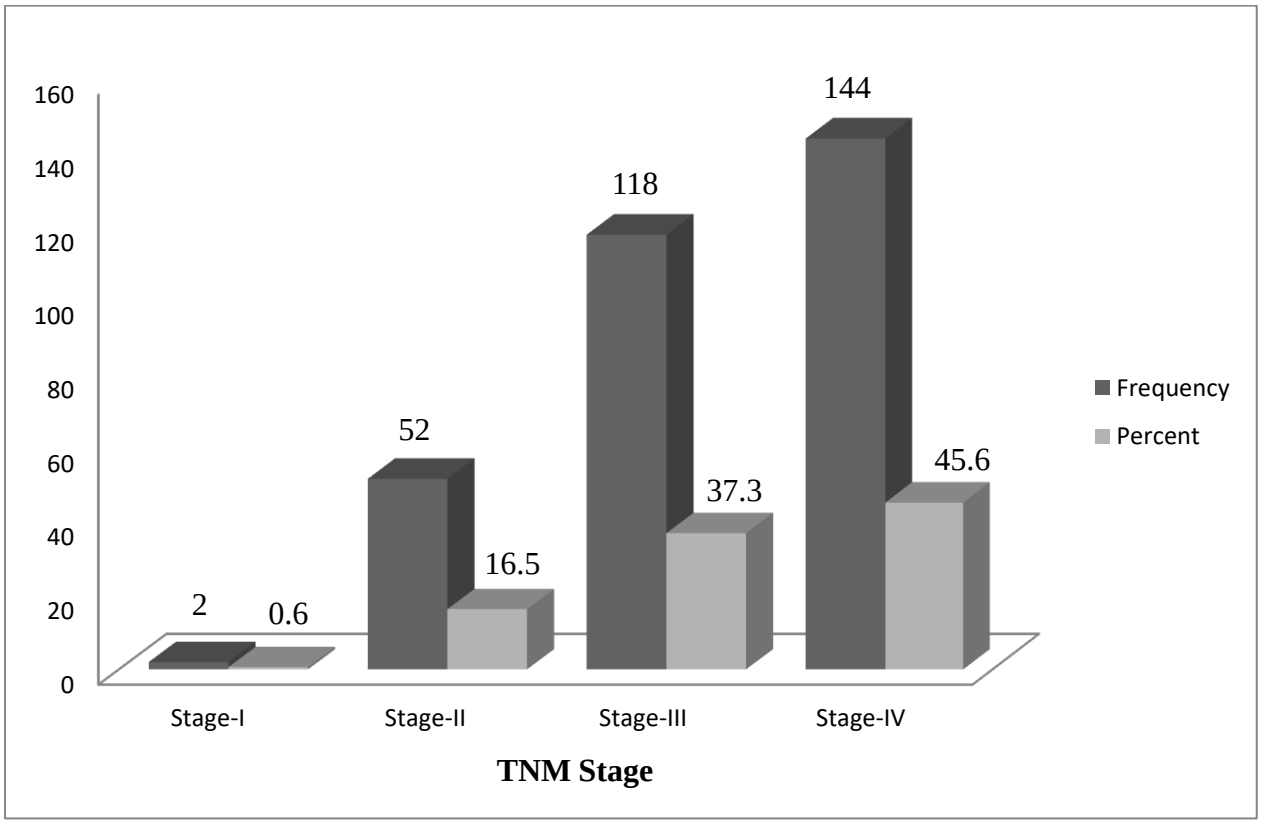
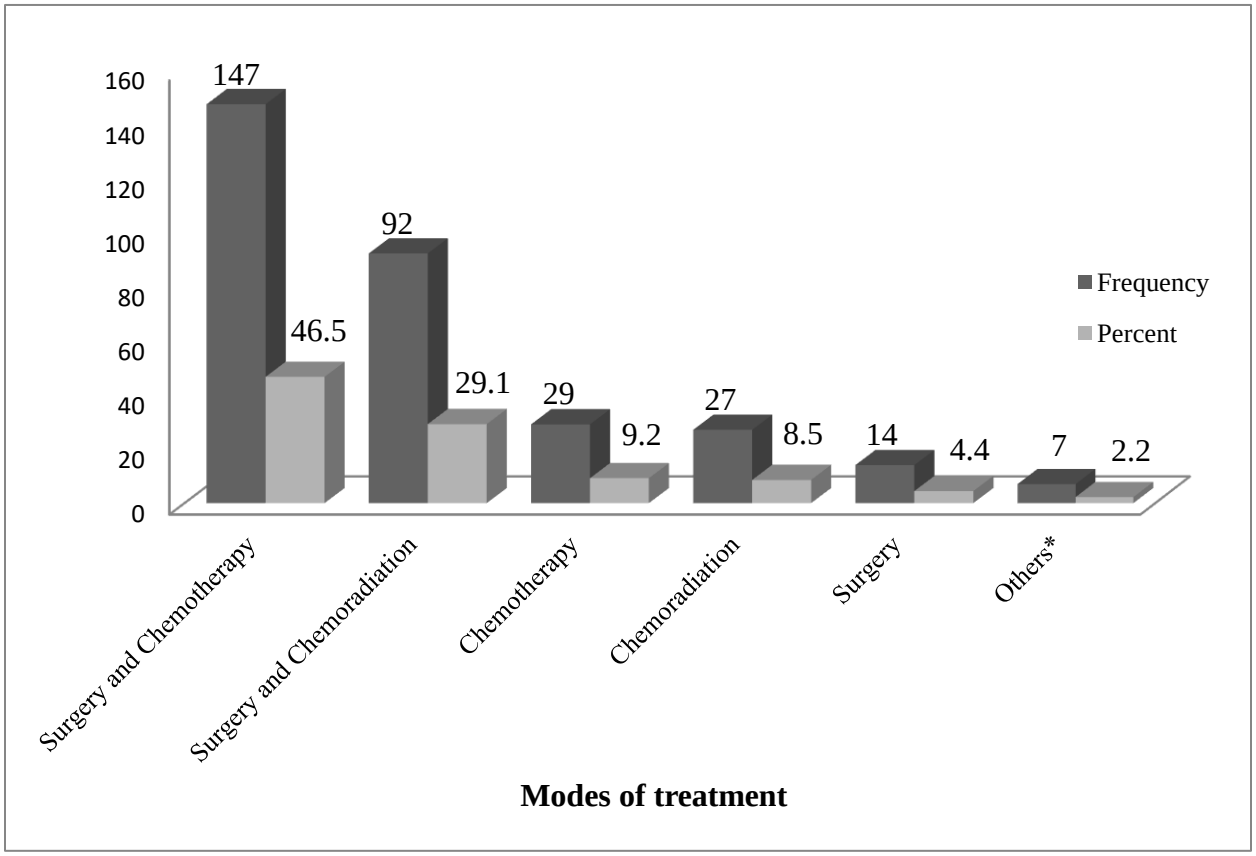


Figure 2. TNM-stage of CRC patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

4.4. Treatment-related characteristics

With regard to treatment modalities used for the treatment of CRC, a combination of surgery and chemotherapy was the primary mode of (147, 46.5%) followed by combination surgery and chemo-radiation (92, 29.1%) and chemotherapy alone (29, 9.2%), as shown in Figure 3 below.



Others* Radiation alone; radiation plus surgery

Figure 3. Modes of treatment for CRC patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

Chemotherapy regimen used in the treatment of CRC, number of cycles given and type of surgery done among study participants are presented in Table 5 below. Among 285 (93.35%) patients who were on chemotherapy, more than half of patients (165, 55.6%) took a regimen containing Folinic Acid +Fluorouracil + Oxaliplatin (FOLFOX). From patients who were eligible for taking chemotherapy, most of (220, 74.6%) of the patients with CRC took ≤6 cycles of chemotherapy, while 25.6% (n=75) of patients took >6 cycles of chemotherapy.

Among 253 patients that underwent a surgical procedure, tumor resection (103, 40.7%) was the most common surgical procedure employed in the treatment of CRC followed by colectomy (97, 38.33%) and colostomy (52, 20.6%) (Table 5).

Table 5: Chemotherapy Regimen and Surgical Procedures for CRC Patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

Variables		**Frequency**	**Percentage (%)**
Chemotherapy regimen	FOLFOX	164	55.6
	FOLFRI	23	7.8
	CAPOX	44	15.0
	Fluorouracil plus Leucovorin	49	16.6
	Capecitabine (Xeloda)	14	4.7
	Irinotecan	1	0.3
Chemotherapy cycle/s given	≤ 6	220	74.6
	> 6	75	25.4
Type of surgery	Hemi colectomy	74	29.2
	Transverse colectomy	13	5.1
	Sigmoid colectomy	10	4.0
	Anterior resection	30	11.9
	Abdominoperineal resection (APR)	73	28.9
	Colostomy	52	20.6
	Unknown/ Not specified	1	0.4

4.5. Follow up characteristics

As illustrated in Table 6 below, 176 (55.7%) of the study participants developed in-hospital medical event/s during their follow up period. Ninety-nine patients (56.3%) developed neutropenia, 46 patients (26.1%) developed anemia, and 12 patients (6.8%) developed hypovolemic shock during their follow up period. About 247 patients had a record regarding surgical complications; from this 58(23.5%) had developed a surgical complication. Major bleeding episodes (24, 41.1%) were the common surgical complication developed followed by perforation (15, 25.9%) and surgical site infection (14, 24.1%). Five patients had discharge from the surgical site.

Among 316 patients, the disease recurred in 29.1% (n=92) of the patients during the follow-up period. From those who presented with disease recurrence 88 (95.7%) patients were put on second-line treatment. And among the second-line mode of treatment, chemotherapy alone accounted for the highest percentage (72, 81.8%) (Table 6). Among those who started second-line chemotherapy only, 39(44.30%) patients took the FOLFRI regimen. The rest of patients who were on second-line chemotherapy, they took FOLFOX (18, 20.5%), CapOx (12, 13.6%), Capecitabine (9, 10.2%), Fluorouracil plus Leucovorin (8, 9.1%) and Irinotecan alone (2, 2.3%).

Table 6: In-Hospital Medical Event/s and Disease Recurrence for CRC Patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

Variables		**Frequency**	**Percentage (%)**
In-hospital medical event/s	Yes	176	55.7
	No	140	44.3
In-hospital medical event type	Neutropenia	99	56.3
	Anemia	46	26.1
	Hypovolemic Shock	12	6.8
	Others*	19	10.8
Surgical complication	Yes	58	22.9
	No	189	74.7
	Unknown	6	2.4
Type of surgical complication	Perforation	15	25.9
	Major bleeding episodes	24	41.4
	SSI (Surgical Site infection)	14	24.1
	Discharge	5	8.6
Disease recurred	Yes	92	29.1
	No	224	70.9
Second-line treatment	Yes	88	95.7
	No	4	4.3
Second line mode of treatment	Chemotherapy	72	81.8
	Chemo-radiation	8	9.1
	Surgery and chemotherapy	8	9.1

Others*: GI toxicities, Pneumonia, Sepsis, DVT (Deep Vein Thrombosis)

4.6. Predictors of CRC survival

Based on univariate cox regression analysis, variables that have a p-value of < 0.2 were used in multivariate analysis. Hence, Age (p=0.059), marital status (p=0.105), BMI (P=0.004), level of histological cell differentiation (p=0.191), tumor location (p=0.0001), TNM tumor stage (p=0.0001), surgery as a mode of treatment (p=0.197), surgery plus chemotherapy receipts (p=0.013) and disease recurrence (p=0.102) were included in the multivariate cox regression analysis.

After controlling different demographic, clinical, pathologic, and other factors; BMI (p=0.01), tumor location (p=0.006) and TNM clinical stage (p=0.014) were significantly associated with survival. Whereas, factors like age (AHR= 1.23, 95% CI (0.73-2.06), p=0.43), marital status (AHR=0.68, 95%CI (0.40-1.16), p=0.159), histological grade (AHR=0.64, 95%CI (0.23-1.75), p=0.38), surgery (AHR=1.4, 95%CI (0.87-2.26), p=0.168), surgery plus chemotherapy (AHR=0.71, 95%CI (0.38-1.34), p=0.295) and disease recurrence (AHR=1.10, 95%CI (0.80-1.51), p=0.55) were not significantly associated with CRC survival (Table 7).

On univariate Cox regression patients taking surgery plus chemotherapy as a mode of therapy has an increased hazard ratio (CHR=1.76, 95% CI (1.13-2.75), p=0.013), but this was not statistically significant on multivariable analysis, p=0.295 (Table 7).

Table 7: Association of categorical Variables with Survival of CRC Patients in Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014

Variables	CHR (95% CI)	P-value	AHR (95% CI)	P-value
Age				
Under 40	1			
40-49	1.05(0.67-1.65)	0.827	1.23 (0.73-2.06)	0.43
50-59	1.44 (0.98-2.11)	0.059	0.97 (0.63-1.51)	0.9
60-69	1.23 (0.86-1.77)	0.256	1.11 (0.74-1.68)	0.614
70 and above	1.19 (0.59-2.40)	0.624	1.24 (0.59-2.62)	0.57
Marital Status				
Single	1			
Married	0.68 (0.43-1.08)	0.105	0.68 (0.40-1.16)	0.159
Divorced	0.94 (0.47-1.88)	0.855	0.86 (0.39-1.93)	0.721
Widowed	0.64 (0.30-1.34)	0.232	0.73 (0.32-1.66)	0.454
BMI				
Normal	1			
Underweight	1.72 (1.19-2.48)	**0.004**	1.725 (1.34-2.62)	**0.01**
Overweight	0.99 (0.71-1.39)	0.957	1.261 (0.88-1.81)	0.21
Obese	0.63 (0.26-1.54)	0.311	0.63 (0.24-1.62)	0.339

AHR: Adjusted Hazard Ratio; CHR: Crude Hazard ratio; CI, confidence interval

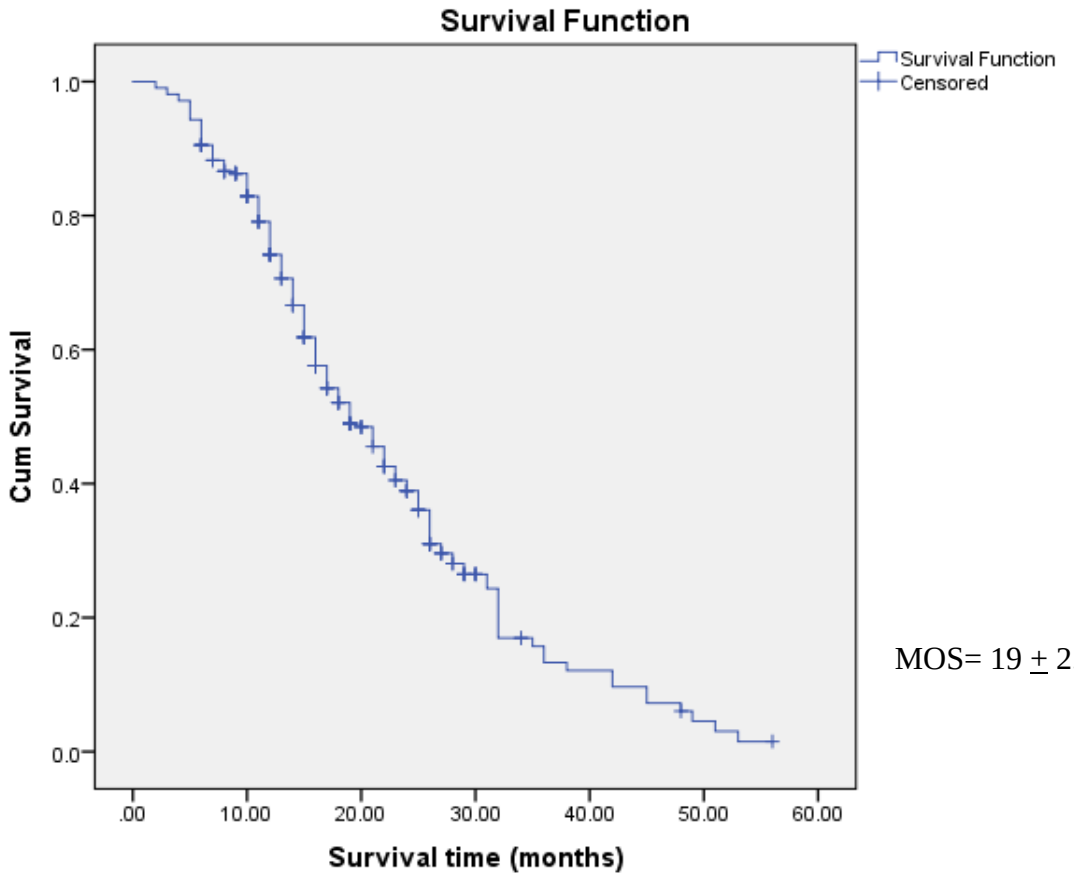
Table 7: (continued)

Variables	CHR (95% CI)	P-value	AHR (95% CI)	P-value
Histological cell differentiation				
Well-differentiated	1			
Moderately differentiate	1.22 (0.90-1.66)	0.191	1.13 (0.81-1.57)	0.485
Poorly differentiated	1.09 (0.64-1.87)	0.749	1.12 (0.64-1.96)	0.7
Undifferentiated	0.54 (0.2-1.47)	0.231	0.64 (0.23-1.75)	0.38
Tumor location				
Colon	1			
Rectal	1.92 (1.38-2.68)	**0.0001**	1.64 (1.15-2.33)	**0.006**
Colorectal	1.27 (0.88-1.84)	0.203	1.13 (0.76-1.68)	0.533
TNM Tumor Stage				
Early Stages (Stage-I & II)	1			
Late Stages (Stage-III & IV)	2.71 (1.67-4.41)	**0.0001**	2.60 (1.57-4.28)	**0.0001**
Surgery				
No	1			
Yes	0.8 (0.57-1.12)	0.197	1.4 (0.87-2.26)	0.168
Surgery plus Chemotherapy				
No	1			
Yes	1.76 (1.13-2.75)	**0.013**	0.71 (0.38-1.34)	0.295
Recurrence				
No	1			
Yes	0.79 (0.60-1.05)	0.102	1.1 (0.80-1.51)	0.55

AHR: Adjusted Hazard Ratio; CHR: Crude Hazard ratio; CI, confidence interval

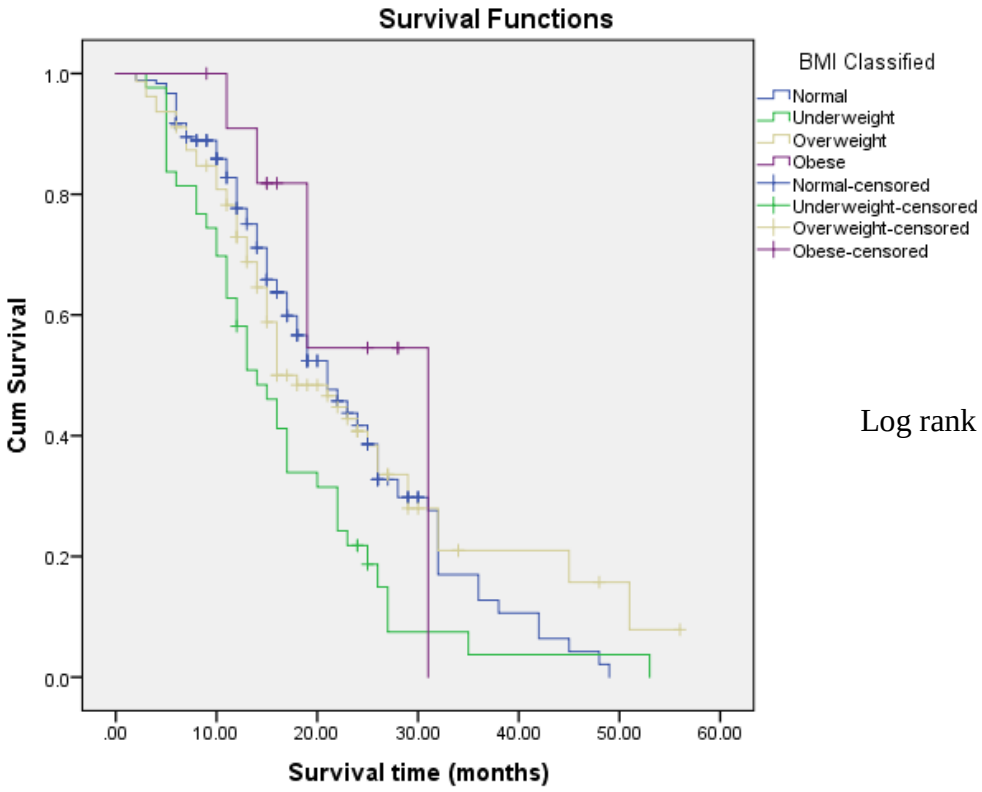
4.7. Kaplan–Meier plots of the Survival function

The overall survival curve is shown in Figure 5. The median estimated survival time was 19 months with 95% CI (16.60–21.40). The survival was lower among underweight patients, patients diagnosed to have rectal cancer and diagnosed in late-stage (stage-III and IV) of the disease, as depicted in fig.4.1, fig.4.2 and fig.4.3 respectively.



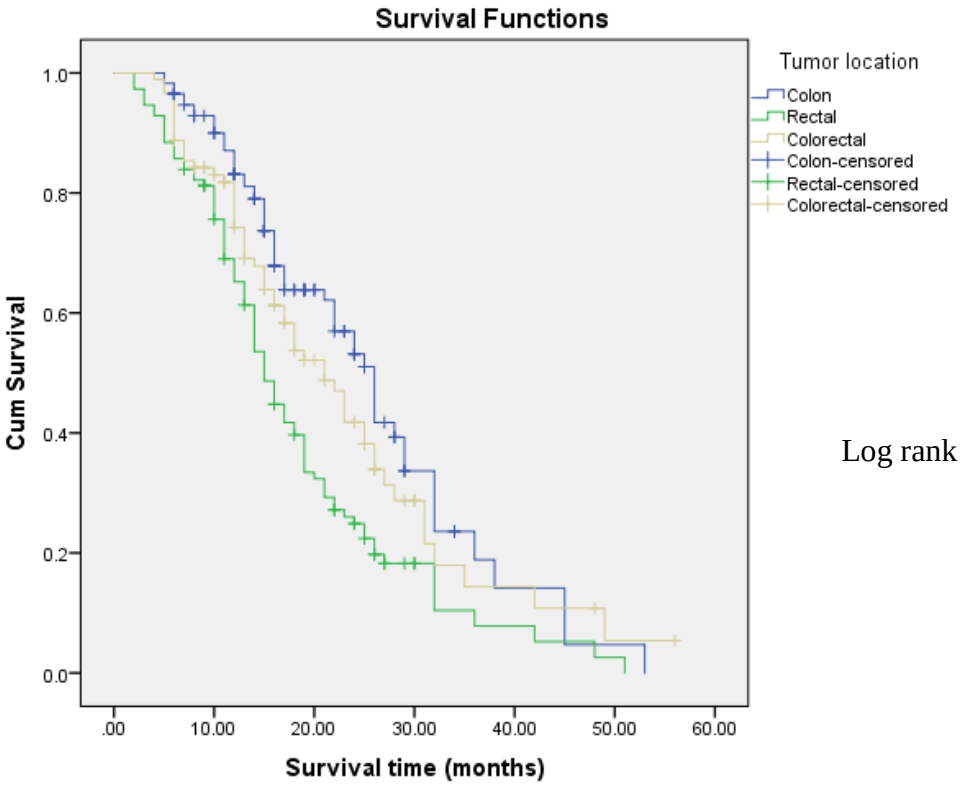
MOS= 19 ± 2.4 months.

Figure 4. Overall 5 year's survival function curve in CRC patients at Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014



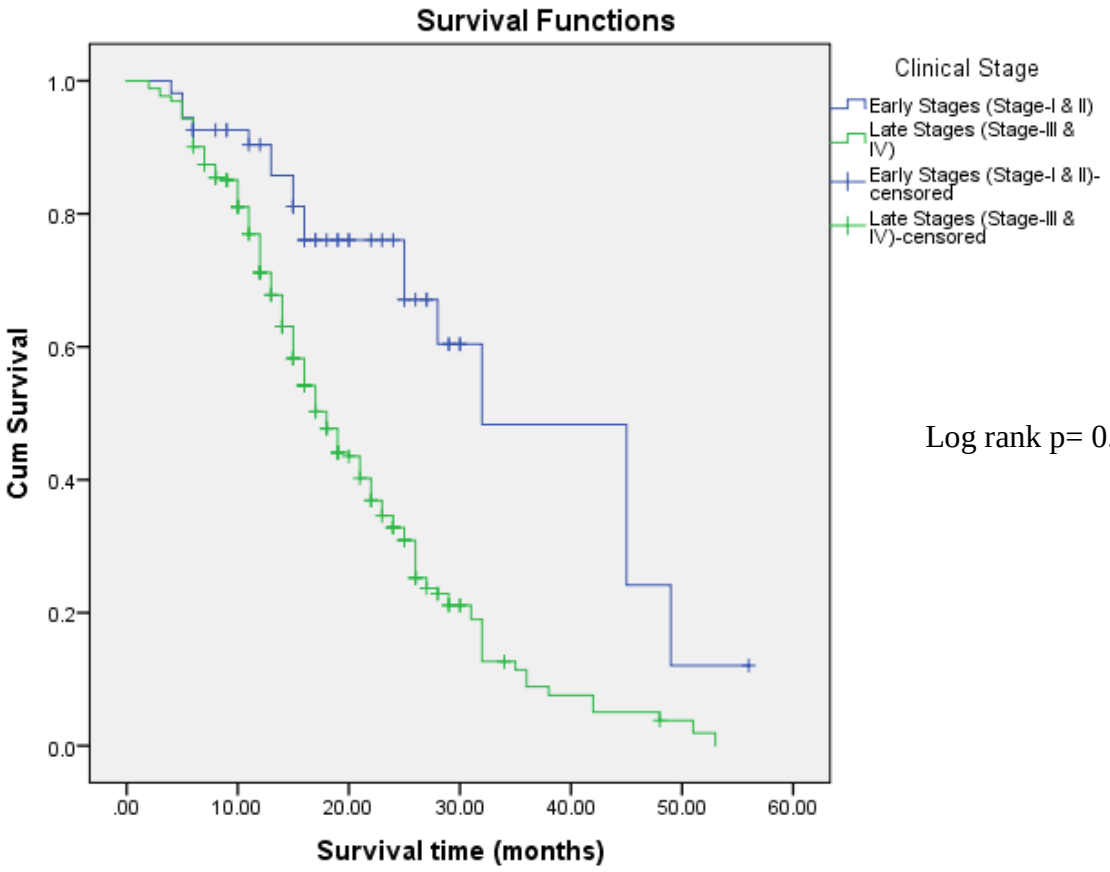
Log rank p= 0.009

Figure 4. 1. Influence of BMI on the survival of CRC patients at Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014



Log rank p= 0.0001

Figure 4. 2. Influence of tumor location on the survival of CRC patients at Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014.



Log rank p= 0.0001

Figure 4. 3. Influence of TNM clinical stage on the survival of CRC patients at Tikur Anbessa Specialized Hospital, Ethiopia, 2013-2014.

5. Discussion

The five year survival rate of CRC at TASH was 38% and factors associated with survival are BMI, cancer location and stage of the disease.

Time to initiation of adjuvant chemotherapy is significantly associated with survival of CRC patients. It is usually accepted that adjuvant chemotherapy should begin within 8 weeks after surgery, and most clinical trials mandate that it should be started within 6 to 8 weeks after surgery (40). Lack of modernized infrastructure for cancer care and the unavailability of curative treatment for patients are also some of the factors identified for the poor cancer survival in Sub Saharan Africa (14). In this study, the five-year survival rate was 35.8% with a median survival time of 19 months, which was lower than the study reported from different studies: a retrospective hospital-based study in Ghana (53.4%), South Africa (59.3%), Kenya (70.6%), Nigeria (62.5%), Saudi Arabia (55.4%), Pakistan (46%) and Sweden (62.8%) (7,14,22,23,29,41,42). This might be due to the presence of poor prognostic factors in the study populations like; late presentation since the onset of symptoms, advanced stage at diagnosis, and disease recurrence. Late initiation of adjuvant chemotherapy in the study population may have also contributed to poor survival.

There have been conflicting findings on the association between BMI and colorectal cancer survival. Studies have proposed that increasing levels of insulin and insulin-like growth factors as well as increasing insulin resistance in obesity may negatively influence CRC survival (49). This study found that being underweight was significantly associated with poor survival. Similar result was reported by Tang *et al* (44). On contrary, a recent meta-analysis and a study by Boyle *et al* reported that being overweight or obese was significantly associated with poorer survival in patients with CRC (34,50). Therefore, it is advisable that patients with CRC maintain a healthy normal weight which will help to improve their survival. In this study, 3.8% (12) had obesity, which is similar to the study done in Taiwan (3.8%) (44). This finding is much lower than the study done in Australia (29.4%) (34). This may be due to sedentary life style in westerns.

Tumor location influences survival. According to results from cox regression, patients with rectal cancer had about 1.92 times more hazard of death compared to patients with colon cancer (HR= 1.92; 95% CI: 1.38, 2.68, *p*=0.0001). Similar results were reported in other studies done elsewhere (21,29,51). This might be due to the possibility of rectal carcinoma being an aggressive and highly metastatic subset of the CRC (52). Globally the incidence of rectal cancer is less than colon cancer (6.1% Vs 3.9%) (20). The result of this study showed that among 316 CRC patients came to TASH; 35.4 % of patients were diagnosed with rectal cancer. A similar result has been reported by Cervantes A *et al*, in which the incidence of rectal cancer in the European Union is 125,000 per year, i.e. 35% of the total colorectal cancer incidence (46). But much lower than a report from Iranian cancer institute, in which 66.5% where diagnosed as rectal cancer (21).

The stage at diagnosis of CRC is the most important prognostic factor. When identified early, cancer is more likely to respond to effective treatment and can result in a greater probability of surviving, less morbidity, and less expensive treatment (1). In the present study, patients diagnosed at the late stage (stage III and IV) of the disease were associated with decreased odds of survival than that of patients who were diagnosed at an early stage of the disease (stage I and II) (HR= 2.71; 95% CI: 1.67, 4.41, *p*=0.0001). Similar results were reported in many other studies (7,27,29,30,51). In this study, 262 (82.9%) of the patients were diagnosed at a late stage of the disease (stage III and IV CRC). This is in line with the EFMOH report on national cancer control plan, in which about 80% of reported cases of cancer are diagnosed at advanced stages. (3) This result is also supported by other studies done in east Africa Kiarie G *et al* (69.2%), Biniam L *et al* (61.7%), El-bolkainy TN et al (72.6%) (7,25,45). But it is higher than the study done in different Europe; Boyle T *et al* (32.5 %) (34). This may be due to less awareness of the society regarding early symptom/s of CRC. Lack of screening modalities in the public may have also an impact.

Age is considered as the most important risk factor for CRC, because greater than 90% of patients diagnosed are older than 50 years (10). The mean age of CRC patients in TASH was 48.66 (SD± 13.58) years which is higher than the study done in Pakistan (33.3 ± 7.9 years) but lower in decades than that of the study done in Israel (71.5 ± 14.3) (41,43).

This study also showed that many patients were from Addis Ababa and Oromia region. This can be explained by the facts that people in Addis Ababa and nearby regions relatively can easily access to TASH for diagnosis and treatment.

When identified early, cancer is more likely to respond to effective treatment and can result in a greater probability of surviving, less morbidity, and less expensive treatment (1). The result of the study showed that more than half of the patients (61.4%) came to TASH, after 6 months since the onset of the symptoms. This is supported by the study done in Ghana, in which 57% of patients came to the hospital after 6 months since the onset of the symptoms (14). The late presentation of the patients could be due to the lack of interventions such as screening programs and public education on cancer prevention and inaccessibility to specialized centers.

Degree of histological differentiation remains paramount predictor of prognosis in colorectal cancer, which is vital for the choice of therapeutic options. Pathological differentiation of most lesions (60.8%) in the present study were well-differentiated which is much greater than the study done in Oman (10.3%) (30), Saudi Arabia (22.6%) (29) and Pakistan (6%) (41), and less than a study done in Egypt (75.8%) (45).

6. Limitation of the study

Patients who were diagnosed and treated only at TASH were included in this study; hence this may not be a true reflection of the situation in the country. It may be difficult to generalize based on the finding of this study.

Due to retrospective nature of the study, some patients chart with CRC may be missed.

The documentation on some of patients medical record was incomplete and it was difficult to find complete information on some of the variables; like family history, history of social drug use (Cigarette smoking, alcohol, khat chewing), radiation exposure, and surgical complications. Hence, it is difficult to draw a clear conclusion on those variables, as these factors may be associated with CRC treatment outcomes.

In spite of these limitations, the study provided useful information's and formulated the necessary recommendations to different stakeholders in order to improve cancer survival.

7. Conclusion

Colorectal cancer treatment outcome in TASH was poor when compared to different studies. Most patients in TASH were diagnosed with late stage of the disease. Factors significantly associated with this poor survival were being underweight, rectal cancer and late-stage of the disease (stage-III and IV).

8. Recommendations

Based on the findings from this study, the following recommendations can be given:

- ⇨ In this study, large proportions of some variables had unknown status (social drug use, radiation exposure and surgical complications) and obese patients had improved survival. Retrospective nature of this study did not allow a follow-up, which would have been a better design to determine association these variables with treatment outcome and explain this finding. So, further prospective study or prospective study that is bridged with this retrospective study should be conducted to explore this.
- ⇨ The poor survival rate of CRC patients could be due to lack of awareness regarding early sign and symptoms. So there is a need for intensified public health education, to increase public awareness on the early signs and symptoms of colorectal cancer. This will greatly improve survival through early detection.
- ⇨ Significant proportions of the study population are excluded due to incomplete data. Hence, all patients' medical records should be computerized and medical recording should be improved.
- ⇨ Most of CRC patients present to TASH at late stage of the disease and $\geq$ 6 months since symptom onset. Therefore, there is a need for increased access to specialized medical faculties; which may be necessary for early detection and thereby improve CRC survival.
- ⇨ Obese patients in this study are found to have a good relative survival. So further study should be conducted to identify this factor and its association with survival of CRC patients.

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Annex

Annex-I: Data abstraction format

Date: ____/_____/____

Treatment outcome and associated factor of colorectal cancer patients at Tikur Anbessa specialized hospital oncology center.

1. Socio demographic and lifestyle characteristics:

1.01. Patient initials: _____

1.02. Age (at the time of diagnosis; in years): _____

A. □ < 40

B. □ 40-49

C. □ 50-59

D. □ 60-69

E. ≥70

1.03. Sex:

□ Male □ Female

1.04. Home/ residence (Region): _____

1.05. Tobacco use

□ Yes □ No □ Unknown

1.06. Alcohol use

□ Yes □ No □ Unknown

1.07. Khat use:

□ Yes □ No □ Unknown

1.08. Marital status:

□ Single □ Divorced

□ Married □ Widowed/er

2. Medical History

2.01. Previous cancer

□ Yes □ No □ Unknown

2.01.01. If yes; cancer type:

A. Ovarian C. Breast

B. Nasopharyngeal D. Other, specify: _____

2.02. History of major comorbid diseases

□ Yes □ No □ Unknown

2.02.01.If yes, specify:

□ DM □ HF

□ HTN □ Asthma

□ DM plus HTN □ Other, specify: _____

2.03. Had radiation exposure for comorbidities:

□ Yes □ No □Unknown

2.03.01. If yes, specific region of exposure

A. Abdominal area C. Other specify _____

B. Pelvic area

3. Clinical and pathological characteristics:

3.01. Body mass index (kg/m^2):_____

□ < 18.5

□ 18.5-24.9

□ 25-30

□ ≥ 30

3.02. Clinical presentation:

□ Rectal bleeding

□ Intestinal obstruction

□ Tenesmus

□ Abdominal pain/ RUQ pain

□ Constipation

□ Rectal bleeding and constipation

□ RUQ pain and constipation

□ Rectal bleeding, constipation and RUQ pain

□ Other specify: _____

3.03. Duration of symptom/s (since onset): _____

□ < 6 months

□ 6- 12 months

□ > 12 months

3.04. Histologic cell type

□ Adenocarcinoma

□ Squamous Cell Cancer

□ Others (specify): ……..

3.05. Level of histological cell differentiation (Histological Grade):

□ Well differentiated

□ Moderately differentiated

□ Poorly differentiated

□ Undifferentiated

□ Unknown/ Unspecified

3.06.

Cancer location:

□ Colon □ Colorectal

□ Rectal

3.07. Stage of the disease at diagnosis (TNM classification):

□ I □ IIIA □ IVB

□ IIA □ IIIB □ IVC

□ IIB □ IIIC □ Not known/ unspecified

□ IIC □ IVA

3.07. If stage IV, primary site/s of metastasis:

□ Liver □ Skeletal / Bone

□ Pulmonary/ Lung □ Other specify:……

4. Treatment

4.01. Date of commencement of treatment _____/_____/_____

4.02. Mode of treatment used:

□ Surgery

□ Radiotherapy

□ Chemotherapy

□ Chemo-radiation

□ Surgery and chemotherapy

□ Surgery, radiotherapy and chemotherapy

4.03. If chemotherapy,

4.03.01. Chemotherapy Regimen:

□ FOLFOX

□ FOLFRI

□ CapOx

□ FOLFOXIRI

□ Fluorouracil plus Leucovorin

□ Capecitabine (Xeloda)

□ VEGF, (bevacizumab, ziv-aflibercept, or ramucirumab) added

□ EGFR (cetuximab or panitumumab) added

□ Irinotecan

4.03.02. Cycle/s given: _____

4.04. If surgery was done,

4.04.01. Type of surgery performed:

□ Hemiclectomy

□ Transverse colectomy

□ Sigmoid colectomy

□ Anterior resections

□ Abdominoperineal resection

□ Colostomy/bypass/no surgery

□ Other: _____

4.04.02. How many times performed: _____

5. Follow up Characteristics

5.01. Major in-hospital medical event.

□ Yes □ No □ Unknown

5.01.01. If yes; Major in-hospital medical event type:

□ Neutropenic □ Hypovolemic shock

□ Anemia □ Others Specify:_____

5.02. Was there surgical complication/s:

□ Yes □ No □Unknown

5.02.01. If yes; surgical complication type:

□ Perforation □ Discharge

□ Major bleeding episodes □ Others; Specify_____

□ SSI (Surgical Site infection)

5.03. Disease recurred.

□ Yes □ No □ Unknown

5.03.01. If yes; time to recurrence _____

A. Within a year

B. Second year

C. Third year

D. Beyond three year

5.03.02. Was there a second line treatment?

□ Yes □ No

5.03.02.01. If yes; second line mode of treatment?

□ Surgery

□ Radiotherapy

□ Chemotherapy

□ Chemo-radiation

□ Surgery and chemotherapy

□ Surgery, radiotherapy and chemotherapy

5.03.02.01.01. If chemotherapy, chemotherapy regimen:

□ FOLFOX

□ FOLFRI

□ CapOx

□ FOLFOXIRI

□ Fluorouracil plus Leucovorin

□ Capecitabine (Xeloda)

□ VEGF, (bevacizumab, ziv-aflibercept, or ramucirumab) added

□ EGFR (cetuximab or panitumumab) added

□ Irinotecan

5.03.02.01.02. Cycle/s given: _____

5.04. Status of the patient?

□ Alive □ Dead