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SURVIVAL STATUS AND PREDICTORS OF MORTALITY AMONG COLORECTAL CANCER PATIENTS IN TIKUR ANBESSA SPECIALIZED HOSPITAL: A RETROSPECTIVE COHORT STUDY

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ABBREVIATIONS AND ACRONYMS

ACS: American Cancer of Society

ACG: American College of Gastroenterology

AJCC: American Joint Committee of Cancer

AHR: Adjusted Hazard Ratio

BMI: Body Mass Index

CI: Confidence Interval

CRC: Colorectal Cancer

CSS: Cause-Specific Survival

NCI: National Cancer Institute

SRPT: Surgical Removal of Primary Tumor

SSA: Sub Saharan Africa

TASH: Tikur Anbessa Specialized Hospital

US: United States

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Introduction: Colorectal cancer is the commonest cancer type that has a great public health impact both in developed and developing countries. Impacts from the disease have shown decreasing trends in developed counties; whereas, Mortality from the diseases and reduced survival are still the highest and steadily rising in developing countries.

Objective: To determine the survival status and predictors of mortality among colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2019.

Methods: Institution-based retrospective cohort study was conducted among 621 colorectal cancer patients selected from patients that registered between January 1st ,2013 and December 30th ,2017 and followed up to December 30th, 2018 using Census sampling. Data was collected from patient record review charts. A Kaplan Meier curve and log-rank test were used to estimate the survival curve and presence of difference in survival among explanatory variables. Cox proportional hazard model was used to determine the net effect of each explanatory variable on time to death after diagnosis.

Results: Out of the 621 colorectal cancer patients that were included in the analysis, 202(32.5%) had died. The overall mortality rate was 20.3 per 100 person-year (95% CI: 17.7-23.3). The overall survival was 18.1% with median survival time of 34.8 months (95% CI: 30.4 -36.8). Comorbidity (AHR: 1.8, CI: 1.3-2.5); stage [II (AHR=3.8, CI: 1.3-11.1), III (AHR=8.0, CI: 2.8-23.3), IV (AHR=17.6, CI: 6.1-50.7)]; smoking (AHR=1.6, CI: 1.1-2.3); alcohol consumption (AHR=1.5, CI:1.07-2.2); age>=70 (AHR=1.7, CI:1.02-2.9); and marital status [married (AHR=2.4, CI:1.5-3.8), widowed (AHR=2.4, CI:1.2-4.6), divorced (AHR=2, CI:1.1-3.7)] were significant predictors of colorectal cancer mortality.

Conclusion and recommendations: the overall survival of colorectal cancer patients was low. It is much lower than the survival rates of colorectal cancer patients in middle- and high-income countries. Hence, the study recommends early detection and screening, and giving priority to comorbid patients and patients that diagnosed at advanced stage.

Keywords: colorectal cancer**,** predictor, survival status, mortality, time to death

CHAPTER ONE

INTRODUCTION

1.1. Background

The American Cancer of Society(ACS) and American College of Gastroenterology(1) documented that colorectal cancer(CRC) starts in the colon or the rectum which originates from pre-cancerous growths or polyps that grow in the colon or rectum, but their progression to colorectal cancer could be halted if it is detected early and polyps are removed(1, 2). Globally, Colorectal cancer is the third most commonly occurring cancer and the second most common cause of cancer death next to lung cancer in men and breast cancer in women(3). According to Global Burden Cancer (GLOBOCAN) 2018, estimated that about 1.8 million new colorectal cancer cases (9.2%) whereas mortality rate was 9.0%(4).

Colorectal cancer incidence varied from 6.5 per 100,000 in the Middle East and Africa to 83.7 per 100,000 in high-income Asia-Pacific which showed that Cases were highest in lower-income Asia-Pacific (737,000) and lowest in the Middle East and Africa (103,000)(5).

In the US, the incidence rate was higher in black 56.1 per 100,000 than 45.6 per 100,000 for whites, of those males had incidence rate 53.4 per 100,000 than females 39.9 per 100,000 with overall incidence of 45.9 per 100,000 ,while the mortality rate was 14.5 per 100,000 men and women annually(6, 7).

The crude incidence of CRC in Sub-Saharan Africa(SSA) for both men and women was found to be 4.04 per 100 000 population (4.38 for men and 3.69 for women), about 24,711 new cases were estimated annually (8). In Ethiopia, It is the third most common cancer next to breast and uterine cancer, but the first most common cancer among the male population (9). In 2014, the 2011-2014 Addis Ababa cancer registry reported that the

incidence rate of colorectal cancer was 19% from all cancer have been reported among male population(10).

Increased incidence time to time has been seen in low and middle-income countries than high-income countries due to the inaccessibility of diagnostic modalities, problem in the implementation of prevention and control of the disease and absence of regular screening for the diseases, obesity and smoking (5, 11).

Systematic reviews showed that colorectal cancer survival varies due to the presence of smoking, increasing age, male gender, disease stage, primary tumor site, comorbidities and the treatment modalities given for the patient (12-17).

Colorectal cancer survival and quality of life of patients depend on surgery, chemotherapy and radiation treatments as well as the involvement of self-care management, symptom management, nursing care (palliative and hospice care) and involvement of multidisciplinary approaches(14, 18). Because of the holistic nature of nursing, nursing intervention encompasses the active involvement of the patient; reduce loss to follow up through telephone-led follow up in addition to palliative care, integrated patient care (19, 20).

Due to CRC incidence is increasing rapidly from time to time and this indicates that colorectal cancer is becoming the most factors jeopardizing the life of patients, family, and society. In general, CRC is a devastating health problem that needs utmost attention.

1.2. Statement of the problem

The global burden of colorectal cancer (CRC) increased from 1.36 million to 1.80 million within 2012-2018, of which about 881,000 mortality cases were documented (3, 21). The Global Burden of Cancer (GLOBOCAN) in 2012 estimated that incidence of males varied from less than 5 per 100,000 in African countries to greater than 40% in European, Northern American and Oceania, with the three highest rates seen in Slovakia (61.6%), Hungary (58.9%) and the Republic of Korea (58.7%). The lowest rate was seen in sub-Saharan Africa, specifically in Gambia and Mozambique (both 1.5 per 100 000)(11, 22).

Even though the incidence rate is in high-income countries compared to low-income countries, decreasing trends are seen in high-income countries while the incidence and mortality rates are still rising rapidly in many low-income and middle-income countries, which are linked to ongoing societal and economic development (4, 23).

The five-year survival rate of CRC varied from greater than 90% in patients with stage I disease to slightly greater than 10% in patients with stage IV disease in Germany (24). This variation in survival status among colorectal cancer arose due to patients' socioeconomic difference which can lead differences in early detection and timed reception of high quality treatment interventions. The same study indicated that American Pacific Islanders are most likely to survive 5 years after a CRC diagnosis, 69% versus 60% among both blacks and American Indians but lower survival rates were seen in Malay (48.5%), Chinese (39.68%) and Asian Indians (47.49%) (23, 25). Another study conducted in Iran revealed that the overall 5 years survival of CRC patients was 52% (26). However, A 5-year retrospective hospital-based study in Ghana indicated that none of the colorectal cancer patients that were diagnosed at stage IV survived (27).

Colorectal cancer has a great impact on the quality of life involving physical, psychological, and socioeconomic dimensions (28). The economic problems of colorectal cancer increases over time due to increased incidence and aging of people. For example, it caused about 5% productivity loss in Columbia from 2008 to 2012, (29). According to the US National Cancer Institute(NCI), the expenditure rate on CRC care raised from 14.1 US dollars to 16.3 US

dollars to 2016 (30). This indicates that patients couldn`t afford to pay for treatment and transportation during a long hospital stay.

It has been documented that more advanced disease stage and late presentation, age, surgery, chemotherapy and radiotherapy, nursing care, self-management and symptomatic management and comorbidity can be important predictors of colorectal cancer survival (20, 23, 31-34).

Despite cost-effective increment in treatment coverage and realization of early screening strategies in Sub Saharan Africa and South East Asia, mortality rate has been higher; whereas the US implemented early screening for CRC every 3 years (35, 36). Health education programs targeting high-risk groups and emphasizing the importance of screening and early diagnosis, as well as the recognition of symptoms and risk factors can also be important interventions which predict survival rate of colorectal cancer (37-39).

In Ethiopia, the Federal Ministry of health gives emphasis to non-communicable diseases such as cancer to reduce the incidence and mortality. However, CRC patients' survival status and associated factors have not been well studied in Ethiopia. Thus, little is known about the survival status of CRC patients and predictors of mortality in this country. That means, interventions to enhance survival and reduce mortality in colorectal cancer lack the necessary empirical evidence base. On the other hand, incidence of the diseases is increasing from time to time. Few reports done on cancer recommended that colorectal cancer-related research is highly needed due to rapid increment in the incidence and mortality rate. Hence, the purpose of this study was to assess the survival time and predictors of mortality among colorectal cancer patients in Tikur Anbessa Oncology Unit, Addis Ababa, Ethiopia.

1.3. Significance of the study

Colorectal cancer is becoming a major public health concern. Especially in Ethiopia, its prevalence is increasing but little has been done to understand survival rates and predictors of mortality. Studying survival of colorectal cancer patients has important practical implications for patients and society at large to know how their prognosis is changing over time and what their life expectancy is based on disease status, to provide an essential indicator for early detection and improvement in CRC treatment modalities and improve quality of care. Improvement in CRC survival is considered a valid indicator of the quality of care provided to the patients.

The researcher believes that the results of this study will be important for nurses to provide effective high quality based care to colorectal cancer patients. Knowing survival status and mortality predictors of colorectal cancer helps nurses to reduce treatment-related errors, to select the best care to be given for the patients, and to provide precise decision to clinicians and patients. This study also promotes nursing research, nursing education and clinical practice as it provided evidence-based nursing care based on new knowledge and estimation of prognosis based on evidence and local situations.

Moreover, the study can be an important input to policymakers, oncology program managers, and health professionals in order to implement early detection, prioritize intervention, estimate survival rate of patients, and make evidence-based decision on about colorectal cancer, to guide the national cancer control program, to support the planning systems for better cancer control and prevention program. Finally, this research can be used as a baseline for future researchers.

CHAPTER TWO

LITERATURE REVIEW

Colorectal cancer is the third common cancer and the second cause of mortality among males and females tends to be the major cause health-related problem(6). The same report documented that CRC is the third cause of cancer-related death in the US which was about 50,630 deaths. The risk of developing colorectal cancer in men was higher than women by 0.34% whereas the 5 years' overall survival rate was 60%, specifically based on the level of invasion local, regional and distant metastasis rated as 90%, 71%, and 14% respectively. Particularly, mortality rate remained high among low affluent countries and also inequality of the survival status was existed due to the presences of different determinant factors (40).

2.1. Survival status of colorectal cancer patients

The study done in Iran reveal that colorectal mortality was 96.9 person- years and 83 person-years among men and women respectively(41)which is higher than the study conducted in china indicated that, the overall mortality of colorectal patient was 49.8% in men and 39.6% in women respectively(42).

A 16 years retrospective study conducted in Saudi Arabiya revealed that the 5-year survival of colorectal cancer was 44.6% (43), which is lower than other review evidence revealed that the average 5-year overall survival rate was 52.5%. whereas, Colon, rectum, and recto-sigmoid junction accounted for 58%, 28%, and 14% of all colorectal primary sites, respectively(44). This difference was due to lack of screening, a higher proportion of advanced stage cancer at presentation, lack of specialized care outside the major cities and a higher proportion of rectal cancer cases. A study conducted in Northern Iran indicated that the 1, 3 and 5-year survival rates were 71%, 52%, and 44% respectively (95% CI: 1.30-5.40) with a median time of subjects' survival was 40.5 (24.83–56.17) months (45), which is nearly comparable with another retrospective cohort study in Southern part of Iran showed that the overall 1, 3 and 5 years survival rate of colorectal cancer were about 93.9%, 50.3% and 27.2% respectively (46). The same study bared that patients were followed for an average

of 35.4± 37.49 months with a median of 36.06±2.98 months of patients' survival time. A study done in Jordan showed that the 5 and 10 years overall survival status of a colorectal cancer patient was 58.2% and 51.8 % with 5.2 years follow up time period (47), which was almost similar with a retrospective study in New Zealand revealed that the five-year overall survival rate of colorectal cancer patients was 51%, (95% CI ;50–53) (48).

Another retrospective study from Kurdistan showed that 1, 2, 3, 4 and 5-year survival rate were 87%, 69%, 57%, 42%, and 33% respectively with the median survival time was 42.6±2.8 (95% CI: 36.1–46.2) months (49). This was fairly lower than a study in Taiwan which showed that the overall 1, 3, and 5 years CRC-specific survival rates were 95.3%, 79.4% and 68.7% respectively with the mean survival time of 71.27±1.27 months(50). In contrast, A ten-year retrospective study reveals that the mean survival time was noted at 12.8 months [95% CI], with a median survival time 9.8 months (95% CI 8.8-10.8 months(51).

A bidirectional cohort study in Malaysia divulged that the 1-, 3-, and 5-year relative survival rates ranged from 73.8 to 76.0%, 52.1 to 53.7% and 40.4 to 45.4% respectively which had the median survival of 42.00 (95% CI: 35.42–48.58) months (23). However, retrospective cohort study in Ghana revealed that the 5 years overall survival was 16% whereas the 1, 2, 3, 4, 5 years survival rate were 64% at 95% CI (56.2–71.1), 40% at 95% CI (32.2–50.1), 21% at 95% CI (11.4–30.6) 16% at 95% CI (8.9–26.9) and 16% at 95% CI (7.3–24.9 with median survival time of 15 months 95% CI (11.79–18.21) (27). Therefore, studies showed that survival rate was lower in African countries than other European, Asian and American countries.

2.2. Predictors of colorectal cancer mortality

2.2.1. Patient-related predictors

Family history had been associated with worse prognosis in individuals diagnosed at age ≤ 70 years, and in patients with distal colon cancer, suggesting a possible distinct pathogenic mechanism underlying a common genetic predisposition (52). Marital status was also an important determining factor for survival status of colorectal cancer. As showed that, widowed patients had 5% reduction cause-specific survival(CSS) compared with married

patients for stage I(89.8%), stage II (76.5%), stage III (53.9%), and at stage IV (8.2%) at P < 0.001. These results showed that unmarried patients were at greater risk of cancer-specific mortality (53). Study in Taiwan showed that married status had better survival(69.1%) than single, divorced and widowed status similarly another study in Florida designated that married patients were significantly better off than divorced/ separated (HR= 1.22), single (HR =1.29), widowed (HR =1.19) patients (54). The same study publicized that gender also determines the survival out comes of colorectal cancer patients as shown by AHR of 1.00 in male and 0.85 in females 95% CI(0.82-0.88) at p<0.001. Another follow up study in Jordan indicated that the 5 year survival rate of colorectal cancer of male and female was 54.8% and 58.1% respectively(47).

The study conducted in Malaysia revealed that patients at a younger age had better survival than the older patients (55). A study revealed that patients who were age < 50 years old had a significantly longer survival time (56). Moreover, younger age group patients had better survival compared to their older counterpart (more than 60 years) (55). The age-stratified analyses revealed that age was a statistically significant predictor of mortality risk; there was a 3% higher mortality risk with annual increase in age (54). A similar study showed that the patients in the youngest group had no increase in mortality risk with age. The study done in the Netherlands told that the 5-year survival rate of age <63.26, 63.21- 71.61, 71.61-79.49, >79.49 was 58.2%, 58.8%, 51.5%, 40.8% respectively with median survival of colon cancer patients was 5.13 years, to some extent lower median survival in rectal cancer patients which was 4.67 years. So age was a significant predictor of death(p< 0.001)(57).

Place of residence has an impact on the survival outcomes of patients. As a study from Iran revealed that rural residents have poor survival outcome than town resident patients (45). Population-based analysis study conducted in the United States showed that Insurance status determines the survival status of colorectal cancer patients as suggested by survival outcome was higher in patients with insurance than un-insurance with the 3-year survival rate of 75.6% and 61.2% respectively (58) with a HR of 1.22 95% CI(1.11- 1.35) in non-insured greater than Medicare (1.0395% CI(0.98-1.08) at p< 0.001(54).

A review study showed that smoking status determines the survival status of CRC (59) which was associated with decreased survival in stage I–III smokers with (Overall survival: AHR: 1.40), in colon cancer cases (Overall survival: AHR: 1.51) (60). Another similar prospective study in Oslo university revealed that non-smokers had lower risk to die as compared to smokers(HR=0.79, 95%CI0.64-0.99)(61). Heavy drinking also associated with poorer survival after a CRC diagnosis than light drinking. Mainly, lifetime heavy drinkers exhibited poorer overall (AHR: 1.37; 95% CI: 1.06, 1.78) and disease-free (AHR: 1.38; 95% CI: 1.09, 1.74) survival(62). A retrospective study in Japan revealed that Underweight patients had worse survival outcome than non- underweight patients with 3 years overall survival of 66.7% vs. 86.5%, HR=2.65; 95% (CI): 1.08-6.50; P=0.033) respectively, Thus, underweight status was an independent indicator of CRC mortality(63).

Comorbidity had an impact on the survival status of patients. The existence of intestinal obstruction has a significant negative effect on the survival of colorectal cancer patients. As a cross-sectional study showed that the 3-year survival rate after treatment for patients with intestinal obstruction was 48.3%, which was lower than patients after treatment without intestinal obstruction (54.9%). Similarly, the 5-year survival rate for patients with intestinal obstruction(37.3%) was lower than that of patients without intestinal obstruction (45.6%) (64). Another similar study in Japan indicated that patients with comorbid conditions were 1.2 times 1.20 (AHR=1.2; 95% CI, 1.08–1.34) at high risk to die than non-comorbid conditions(65). Moreover, study conducted in Spain found that colorectal cancer patients who had comorbid conditions experienced lower survival (56.0%) than patients with non-comorbid conditions(66).

2.2.2. Clinical and pathological related predictors

Document review analysis in South Austria showed that the five-year survival of right versus left colon including rectum right and left was 1.4% Versus 8.9% without therapy, median overall survival of 10.7 Versus 15.3 months for those treated with only chemotherapy, with overall median survival of 9.6 versus 20.3 months (P < .001) respectively (67).

The Stage of colorectal cancer creates a difference in survival status of stage I, stage II, stage III and stage IV. As the study in Malaysia told that the three and five-year survival status of stage I, II, III and IV were 77.0% and 73.4%, 78.0% and 68.3%, 54.6% and 42.6%, 33.9% and 22.1% respectively (55) which was lower than the study conducted in Jamaica for colorectal patients with stage I, II and III disease was 80%, 65%, and 33% respectively (68). From the same study, Patients with metastatic disease at the time of diagnosis had an almost six-fold increase in the risk of death than patient presented with abdominal mass 28% to 5% with median survival time was approximately two years post diagnosis (68). A study in Jordan told that the 5-year survival rate for localized, regional stage and distant metastasis cancer accounted for about 72.1%, 53.8%, and 22.6% respectively (33). A retrospective cohort study showed that the one, five and six-year survival rates by tumor stage were 100%, 80.6% and 69.2% for the localized stage and 92.4%, 51.55 and 45.85 in the regional stage. Almost all patients with distant metastases had died before the first year of follow-up. In general patients in the distant metastasis and regional stages were 55.9% and 3.43 times more likely to die during the study period, respectively (69). A 5 years' prospective cohort study in Iran revealed that the higher grade of the tumor was associated with higher mortality. The adjusted HR for stage II, III and IV were 1.79 (95% CI), 2.16 (95%CI), and 3.1 (95%CI) respectively while stage I has been taken as a reference (41).

A retrospective study in the Republic of Korea indicated that locally advanced primary tumor (high patient stage, positive regional lymph node, and local residual primary tumor) was associated with poorer outcome survival in incurable stage IV CRC patients (70). Another study in Taiwan also told that the five-year survival rate for patients with stage I, II, III and IV disease was 91.20%, 82.20%, 63.20%, and 21.70%, respectively(50). Mucinous carcinoma type of CRC had a significant indicator of outcome as shown the survival rate of 81.4% than non-mucinous (87.4%) at p (0.026) (71).

2.2.3. Treatment-related predictors

A patient who underwent surgical removal of a primary tumor and received chemotherapy had a median overall survival of 18.3 months compared with 8.4 months (95% CI) if they were treated with chemotherapy alone (P<.0001) (16). However, study in Iran revealed that

the five-year survival rate of patients who underwent resection for colorectal cancer was 73.8% with the mean survival time of 142.17 ± 21.60 months (72). A retrospective study in the Republic of Korea indicated that the primary tumor resection appeared to result in better outcome survival in patients with a primary tumor that is not locally advanced(70).

Observation of population cohort study in Scotland indicated that the five-year Cause-specific survival rate of patients cared in a multidisciplinary team was 63.1% which is higher than patients who was not cared by the multidisciplinary team (48.2%) with the adjusted hazard rate of 0.73 (0.53 to 1.00, $p = 0.047$). Therefore being cared for by the multidisciplinary team can influence the survival outcomes of the patient in different CRC stages(73). Palliative care given for advanced CRC, for symptomatic management related to treatments or tumor itself can have prolonged survival from 4 to 6 months with best supportive care to more than two years (74).

Retrospective study analysis Japan revealed that 3 years overall survival rate patients treated with adjuvant chemotherapy and surgery alone were 93.5% and 81.7%; $p<0.001$ respectively, so being treated with adjuvant therapy improves the survival outcome because of addressing the left tumor from the primary therapy and reduce relapse rate (75). Cox proportional analysis revealed that use of chemotherapy (HR=50.47, 95% CI:50.41-0.54), SRPT (HR=50.49, 95% CI:50.41-0.58), second-line Chemotherapy (HR=50.47, 95% CI:50.45-0.64), and metastasectomy (HR=50.54, 95% CI:50.45-0.64) were associated with superior survival (16). Whereas, the in five years prospective study conducted in South Africa revealed that the of CRC patients treated with surgery alone, surgery plus chemotherapy, chemotherapy alone was 60.1%, 70.8%, and 56.3% respectively which was relatively lower(76).

In general, colorectal cancer is common malignancy which increases time to time associated with the aging population and human and societal development and imposes the highest mortality. Colorectal cancer patients had different survival outcomes due to the presence of determinant variables such as age, family history, comorbidity, different lifestyle, treatment-related factors, and tumor characteristics. Few studies were conducted on colorectal cancer in developing countries as compared to developed population. All of the works of the

literatures indicated that there was poor survival among low income countries. However, a little study states the survival status and examines the predictors of colorectal cancer in Ethiopia. Hence, the aim of this research is to assess survival status of colorectal cancer and proposes concrete recommendations that could be relevant to government and patient to colorectal cancer and improve survival in Ethiopia.

2.3. Conceptual framework

This conceptual framework was developed by the researcher based on the review and synthesis of concepts from different works of literature sources (23, 27, 46, 49, 55, 60). It is the interaction between independent variables (patient related, clinicopathological, treatment variables) and outcome variable (time to death) which was taken from different works of literature operated with distal (patient-related factors) to proximate predictors (clinicopathological and treatment factors). Patient-related factors have direct effect on clinicopathological and the treatment factors which also have both direct and indirect effect on the outcome variable. Hence, the outcome variable was the cumulative effect of independent variables.

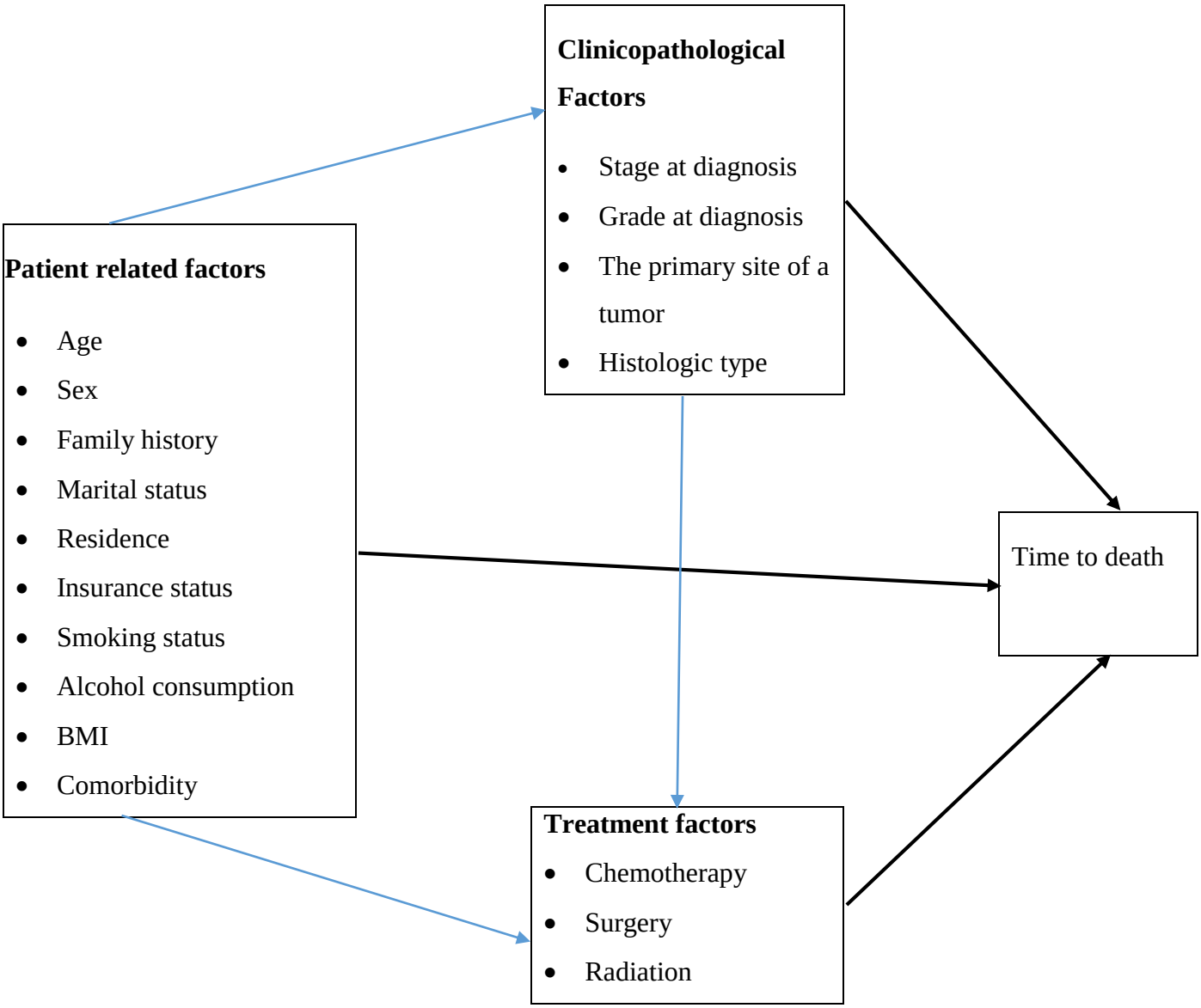

Figure 1: Conceptual framework for the assessment of survival status and its predictor among patients with colorectal cancer confirmed diagnosis enrolled from January 1st, 2013 to December 30th, 2017 in TASH, Addis Ababa, Ethiopia, 2019

CHAPTER THREE

OBJECTIVES

3.1. General objective:

To assess the survival status and predictors of mortality among colorectal cancer patients enrolled from January 1st, 2013 to December 30th, 2017 in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2019.

3.2. Specific objectives:

To determine the time to death among colorectal patients enrolled from January 1st, 2013 to December 30th, 2017 in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2019.

To identify the predictors of mortality among colorectal patients enrolled from January 1st, 2013 to December 30th, 2017 in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2019.

CHAPTER FOUR

METHODOLOGY

4.1. Study area

The study was conducted in Tikur Anbessa Specialized Hospital Oncology Unit which is found in Addis Ababa city, the capital of Ethiopia. TASH is a teaching, central tertiary generalized referral hospital with approximately 800 inpatients beds**.** It is the largest and well known public hospital which was built in the early 1960s. The hospital hosts a Cancer Treatment Center. The Center is housed in a separate, newer building on hospital grounds and consists of three floors: the clinic with three examination rooms, physicians' offices, waiting room, pharmacy, and radiation vaults; a floor for the inpatient ward; and a floor for meeting rooms. TASH Oncology Unit is the center of excellence for cancer treatment in which radiotherapy, surgery, chemotherapy treatment, and comprehensive care services are delivered for cancer patients. Colorectal, breast, cervical and sarcomas are the commonly seen cases at the Oncology Unit (77).

4.2. Study period

The actual data collection was carried out from February 15, to April 21, 2019 based on medical record review of colorectal cancer patients enrolled in TASH Oncology Unit from the 1st of January 2013 to the 30th of December 2017 time periods and who were followed up to the 30th December 2018. The starting point for retrospective follow-up was the time from first confirmed diagnosis of colorectal cancer and the endpoint was a date of death, date of loss to follow up, date of last contact or the end date of the follow-up period (30th of December 2018).

4.3. Study design

In retrospective cohort study a cohorts of single exposure can be selected and looked into, exposed and unexposed within the predictors for assessing the determinants of variations of cancer rates (78, 79). Consequently, the investigator carried out the study at the present time

and followed up among study participants done historically after the actual time follow-up has already been completed (80). This was institution-based retrospective cohort study which was conducted among eligible colorectal cancer patients in the given study period.

4.4. Population

4.4.1. Source population

All medical records of colorectal cancer patients in TASH Oncology Unit.

4.4.2. Study population

All medical records of colorectal cancer patients in TASH who were diagnosed from January 1st, 2013 to December 30th, 2017 who fulfil eligibility criteria.

4.5. Inclusion and exclusion criteria

4.5.1. Inclusion Criteria

All medical records of confirmed colorectal cancer patients at TASH during the defined period (2013–2017) were included.

4.5.2. Exclusion criteria

Incomplete patient charts

Patients` charts that were missed at the time of data collection.

Patients who had confirmed diagnosis at other hospital and were referred to TASH for advanced management.

4.6. Sampling technique and Sample size determination

4.6.1. Sample size determination

A single population proportion formula for the outcome was used to calculate the sample size by considering the following statistical assumptions: P = proportion of mortality rate

among medical record of colorectal cancer patients, 84% (27), (Z α/2 = Z score of 95% CI, d= Margin of error (5%) (81).

$n = \frac{(Z_{\frac{\alpha}{2}})^2 \times p(1-p)}{(d)^2}$, n= $(1.96)^2$ *0.84*0.16/ $(0.05)^{2=}$ 207. Then, after adding 10% contingency rate for an incomplete chart, the final sample size is 227.

The sample size for predictors was determined by using double population formula and taking into account colorectal cancer patients who had higher risk factor taken as unexposed whereas patients who had lower risk factor were considered to be exposed (41, 82). Tumor stage, smoking status, family history, sex, a primary site of the tumor, residence, presence of comorbidity and treatments were significant predictors of colorectal mortality (23, 41, 49, 69). Among those predictors, tumor stage was found to be an independent predictor having assumptions of (P1= 3.96%, P2= 48%), that gave a maximum sample size of 942 plus 10% contingency gives a total sample size of 1,037. The sample size was calculated by using Epi info version 7 statistical package (22).

$$n_1 = \frac{\left[Z_{\alpha/2}\sqrt{\left(1+\frac{1}{r}\right)P(1-P)} + Z_{\beta}\sqrt{\frac{P_1(1-P_1)+P_2(1-P_2)}{r}}\right]^2}{(P_1-P_2)^2}$$

Where:

P1: is proportion of early stage with the outcome;

P2: is proportion of late stage with the outcome;

Z α/2: is taking CI 95%;

Zβ: 80% power and, r is the ratio of exposed to non-exposed 1:1.

There were a total of 887 confirmed diagnoses of colorectal cancer registered from January 1st, 2013 to December 30th, 2017 in TASH Oncology Unit; that number was smaller than the calculated sample size (1,037). Finally, 621 study participants who fulfilled the eligibility criteria were included in the study.

4.6.2. Sampling procedure

At the beginning, all medical records of a confirmed diagnosis of colorectal cancer patients registered from January 1st, 2013 to December 30th, 2017 were assessed. Then study participants who fulfill the inclusion and exclusion criteria were identified. From the 887 medical record review of colorectal cancer patients 191 incomplete charts, 72 charts were missed at data collection time and 3 were referred for advanced treatment (radiation) were excluded from the study. Finally, all samples were selected starting from January 1st, 2013 to December 30th, 2017 using census sampling technique.

4.7. Study variables

4.7.1. Dependent (outcome) variable:

Time to death

4.7.2. Independent variables:

Patient-related factors: Age, sex, family history, marital status, residence, insurances status, smoking status, alcohol consumption, BMI and comorbidity

Clinical and pathological factors: Grade at diagnosis, stage at diagnosis, a primary site of the tumor and histologic type

Treatment factors: Chemotherapy**,** surgery, and radiation

4.8. Operational definitions

Censored: Patients whose status was unknown, patients who didn‘t develop the outcome of interest (death) at the end of the follow-up period, and patients who were lost from follow-up.

Event: Death of patients due to colorectal cancer.

Beginning date and closing date to follow-up: -The beginning date was the starting date for calculation of survival time, and this was the first date of confirmed diagnosis of colorectal cancer (January 1st, 2013 to December 30th, 2017). Closing date was the date at

the last status of the patient on the follow up, which could be death or censored (December 30th, 2018).

Follow up time period: The time from the beginning of the study period to an event, end of the study, or loss of contact or withdrawal from the study.

Survival time: In this study, survival time is the last date of contact minus first date of confirmed diagnosis of colorectal cancer.

Survival status: The status of the patients' survival to the outcome (death) or censored.

Time to death: Time from the first confirmed diagnosis date of colorectal cancer to death.

Comorbidity: According to International Classification of Disease-10, Disease from Charles comorbidity index was used during data collection. The co-occurrence of any of these diseases with colorectal cancer at the time of diagnosis labeled as "yes" response(83).

Incomplete data: When one of independent variables was not registered (stage, primary site, comorbidity).

Body Mass Index (BMI) according to disease prevention and control.

Underweight: BMI less than 18.5 Kg/m^2

Healthy weight: BMI 18.5 to 24.9 Kg/m^2

Overweight: BMI; from 25 to 29.9 Kg/m^2

Obese: - BMI 30Kg/m^2 or higher (84)

Stage at diagnosis: According to American Joint Committee of Cancer (AJCC)

Stage 0: Carcinoma *in situ*, no lymph node, and no metastasis

Stage I: Tumor invades muscularis propria, submucosa, no lymph node, and no metastasis

Stage II: Tumor invades muscularis propria, penetrates to the surface of the visceral peritoneum, adherent to other organs or structure, no lymph node and no metastasis

Stage III: Tumor metastasis in seven or more regional lymph nodes

Stage IV: Tumor metastasis into different organs(85).

4.9. Data collection tools and procedures

The information available in the eligible patients' medical records was observed and then recorded using data extraction tool prepared by adapting from different studies (23, 27, 46, 49, 55, 60), which consists of patient-related factors, Clinicopathological factors, and treatment factors. Then, all charts of colorectal cancer patients, diagnosed between 1st January 2013 to 30th December 2017 at TASH were retrieved and then reviewed (both baseline and follow up records), death certificate supplemented was identified from TASH cancer registries by their medical record number. Then, the records of all the study participants were selected according to the eligibility criteria. Five BSc nurses, two supervisors, and one MSc student were involved in the data collection.

4.10. Data quality Assurances

Data quality was assured by designing appropriate data extraction tool. The adapted data extraction tool was evaluated by experienced researchers. Pretest on 5% of medical record review was done on a confirmed diagnosis of patients enrolled in 2012 and 2018 two weeks prior to the actual data collection time at TASH cancer registries. That was done to check the recorded variables. As a result, some unrecorded variables were reduced from the data extraction tool.

Training on data extraction was given to data collectors and supervisors for two days before data collection task and training guide was prepared to facilitate the training. Furthermore, the investigator supervised every aspect of the review and other supervisors (MSc student and data clerk) handled the task in the absence of the investigator. Random evaluation of the recording data extraction tool was done by the principal investigator. Review of data extraction tool filled was gathered and checked for completeness by the principal investigator and supervisors on daily basis. Double data entry using epi data 4.2 was carried out to assure the quality.

4.11. Data processing and analysis

Data was cleaned, edited, coded and then entered using epi data 4.2 and then transferred into STATA 14 for analysis. Basic descriptive analyses were done in terms of central tendency and dispersion value for continuous data and frequency distribution for categorical data based on the nature distribution. The incidence density and cumulative incidence density were calculated for the entire study period. The independent variables were dichotomized into death and censored. Survival table was used to estimate probabilities of survival after diagnosis of colorectal cancer at different time intervals. Kaplan Meier survival curve, together with the log-rank test, was used to estimate the survival curve and the presence of a difference in survival among explanatory variables.

Before running the Cox Proportional hazard regression model, multi-collinearity was checked. Cox regression was tested to find out predictors of survival time. The necessary assumptions for the model were checked using goodness-of –fit test by Schoenfeld residual and variables having P-value >0.05 were considered as fulfilling the assumption. Residuals tested by goodness-of-fit fulfilled the model assumptions. Bivariable Cox regression was fitted and those independent variables which fitted on the bivariable regression less than or equal to 0.25 level of significance were included in the multivariable analysis (86, 87). Multiple Cox regression was done at 0.05 level of significance to determine the net effect of each explanatory variable on time to death of colorectal cancer. The P value less than 0.05 in the multivariable analysis was considered as statically significant. The results of these models were expressed as hazard ratios (HRs) with 95% confidence interval and p-values are used to measure the strength of association and to identify statistically significant factors. Finally, the result of the study was presented using text, tables and graphs.

4.12. Ethical consideration

Ethical clearance for the proposed study was obtained from Addis Ababa University, School of Nursing and Midwifery research ethical committee. Letter of cooperation was written to the TASH and concerned bodies. Consent was obtained from medical director and cancer treatment center focal person of Tikur Anbessa Specialized Hospital. Confidentiality of the

information was kept throughout the study by excluding names and patient record numbers as identification in the data extraction form and the data was used only for the purpose of the proposed study. To keep the confidentiality all collected data was coded and locked in a separate room before entered into the computer. After entering to the computer the data was locked by password, and the data didn`t disclose to any person other than principal investigator.

4.13. Dissemination of the study

The result of the study will be presented and submitted to School of Nursing and Midwifery College of Health Science, Addis Ababa University in partial fulfillment of the requirements for the degree of Master of Science in Adult Health Nursing. The result will be submitted also to TASH Oncology Unit. The result will also be presented on scientific workshops and conferences. Efforts will be made to publish the findings on peer-reviewed scientific journals.

CHAPTER FIVE

RESULTS

5.1. Patient-related characteristics of the study participants

Out of the 621 study participants, 419 were censored and 202 were died. About 360 (57.9%) of study participants were males and 64.9% came from urban areas. A little more than two-fifths of them were from Addis Ababa (43%). The mean age of the study participants was 46.9 $\pm$ 13.9SD years; of those, two hundred forty-nine (40.1%) were less than 40 years old. BMI of more than two-thirds (71.3) of the participants was in the 18.5 – 24.9 Kg/m^2 range. About half were paid (50.4); slightly more than one-quarter (27.1%) had comorbid conditions, of which 58.3% died. Among the comorbid conditions, hypertension (25.6%) and diabetes (20.2%) were the frequent medical conditions among more than half (58.3%) of the died. Further details on patient-related characteristics are presented in Table 1.

Table 1:- Patient-related characteristics of colorectal cancer patients in TASH oncology department, Addis Ababa, Ethiopia from January 1st, 2013 to December 30th, 2018(n=621)

Variable	Category	Status at last contact		Total
		Death No. (%)	Censored No. (%)	No. (%)
Sex	Male	130(36.1)	230(63.9)	360(57.9)
	Female	72(27.6)	189(72.4)	261(42.1)
Age of patient	<40	79(31.8)	170(68.2)	249(40.1)
	40-49	27(27.6)	71(72.4)	98(15.8)
	50-59	34(24.3)	106(75.7)	140(22.5)
	60-69	36(40.5)	53(59.5)	89(14.3)
	>=70	26(57.8)	19(42.2)	45(7.3)
Family history	Yes	19(44.2)	24(55.8)	43(6.9)
	No	183(31.7)	395(68.3)	578(93.1)
Region	Amhara	19(25.7)	55(74.3)	74(11.9)
	Oromia	51(29.5)	122(70.5)	173(27.9)
	Tigray	7(23.3)	23(76.7)	30(4.8)
	SNNP	20(34.5)	38(65.5)	58(9.3)
	Addis ababa	98(36.7)	169(63.3)	267(43)
	Others	7(36.8)	12(63.2)	19(3.1)
Residence of patients	Urban	140(34.7)	263(65.3)	403(64.9)
	Rural	62(28.4)	156(71.6)	218(35.1)
Marital status	Single	32(30.8)	72(69.2)	104(16.7)
	Married	118(29.4)	284(70.6)	402(64.8)
	Widowed	22(37.3)	37(62.7)	59(9.5)
	Divorced	30(53.6)	26(46.4)	56(9.0)
Insurance status	Free paid	86(27.9)	222(72.1)	308(49.6)
	Paid	116(37.1)	197(62.9)	313(50.4)
Smoking status	Smoker	77(52.4)	70(47.6)	147(23.7)
	not smoker	125(26.4)	349(73.6)	474(76.3)
Alcohol consumption	Yes	107(42.1)	147(57.9)	254(40.9)
	No	95(25.9)	272(74.1)	367(59.1)
Body mass index	≤18.5	53(32.3)	111(67.7)	164(26.4)
	18.5-24.9	145(32.7)	298(67.3)	443(71.3)
	25-29.9	4(28.6)	10(71.4)	14(2.3)
	≥ 30.0	0	0	0
Comorbidity	Yes	98(58.3)	70(41.7)	168(27.1)
	No	104(22.9)	349(77.1)	453(72.9)

N.B: *Others (Harari, Somalia, Drie Dawa, Afar, Gambela)

5.2. Clinicopathological and treatment-related characteristics

More than half (56.4%) of the primary site of tumor was found to be colon. Of those patients, 34.9% died. A large percentage (65.7%) of the patients were diagnosed at late stages (39.3% at stage III, and 26.4% at stage IV). Three-fifth (60.4%) of the patients that had diagnosed at stage IV died. Nearly half (47.7%) of the tumor grade was differentiated; about 488 (78.6%) was adenocarcinoma type. Concerning the type of treatment given, 30.0% of the cases were given surgery plus chemotherapy and 28.2% of the cases were served radiation plus surgery plus chemotherapy. Further Clinicopathological and treatment-related characteristics of the patients are summarized in Table 2.

Table 2:- Clinicopathological and treatment related characteristics of colorectal cancer patients in TASH oncology department, Addis Ababa, Ethiopia from January 1st, 2013 to December 30th, 2018(n=621).

Variables	Category	Status at last contact		Total No. (%)
		Death No. (%)	Censored No.(%)	
primary site of tumor	Colon	122(34.9)	228(65.1)	350(56.4)
	Rectum	80(29.5)	191(70.5)	271(43.6)
Stage of the diseases	Stage I	4(8.0)	46(92.0)	50(8.1)
	Stage II	33(20.2)	130(79.8)	163(26.2)
	Stage III	66(27.1)	178(72.9)	244(39.3)
	Stage IV	99(60.4)	65(39.6)	164(26.4)
Grade	Differentiated	70(23.6)	226(76.4)	296(47.7)
	Moderately differentiated	51(29.7)	121(70.3)	172(27.7)
	Undifferentiated	81(52.9)	72(47.1)	153(24.6)
Histology type	Adenocarcinoma	148(30.3)	340(69.7)	488(78.6)
	mucinous carcinoma	36(38.7)	57(61.3)	93(15.0)
	Signet ring-cell carcinoma	18(45.0)	22(55.0)	40(6.4)
Treatment modality	radiotherapy alone	11(31.4)	24(68.6)	35(5.6)
	surgical treatment alone	10(24.4)	31(75.6)	41(6.6)
	chemotherapy alone	41(34.2)	79(65.8)	120(19.3)
	surgery plus chemo	53(28.5)	133(71.5)	186(30.0)
	radiation as neo-adjuvant to surgery	19(31.1)	42(68.9)	61(9.8)
	radiation + surgery chemo	67(38.3)	108(61.7)	175(28.2)
	didn`t receive treatment	1	2	3(0.5)

5.3. Survival status of colorectal cancer patients

A total of 621 colorectal cancer patients were followed for 72 months. The overall mortality rate for diagnosed colorectal cancer patients registered at TASH during 995 person- year observations was 20.3 per 100 (95% CI:17.7-23.3) person year follow up. The cumulative incidence of death of colorectal cancer patients over the six year follow up period was 202(32.5%), with the confidence interval of (95%CI: 19.0-36.4) while 419(67.5%) were censored up to the end of the study.

5.4. Overall survival rate of colorectal cancer patients

As Kaplan- Meier survival estimate curve showed that the overall survival rate was 18.1% at 72 months follow up (Figure 2). The estimated cumulative survival rates of colorectal cancer patients at 12, 24, 36, 48, and 60 months were 90.7%, 67.4%, 47.0 %, 31.8%, and 21.7%, respectively. The overall median survival time of colorectal cancer patients was found to be 34.8 months (95% CI: 30.4 -36.8). The probability of survival as the highest at the first day of diagnosis of colorectal cancer, but it relatively fell later as follow up time increases. In this study, the highest mortality rate was found between 40 months and 60 months of confirmed diagnosis of colorectal cancer.

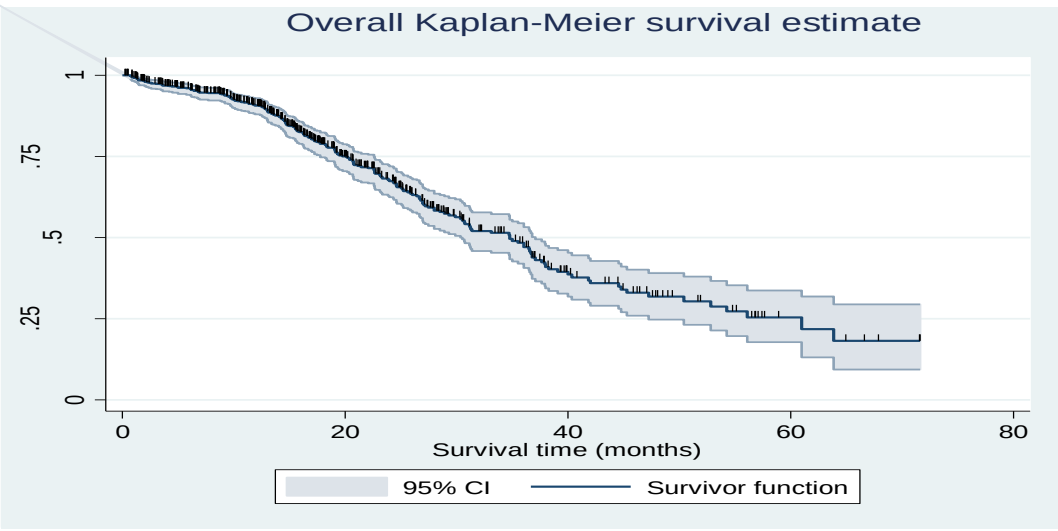

Figure 2:- Overall Kaplan-Meier estimation of survival functions of colorectal cancer patients diagnosed in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, from January 1st, 2013 to December 30th, 2018.

5.5. Survival estimate among predictor variables

The Kaplan-Meier estimator survival curve provides the estimate of survivor function among different groups of covariates to make comparisons. Separate graphs of the estimates of the Kaplan-Meier survivor functions were constructed for different predictors. The pattern that one survivorship function lying above another group means that the group demarcated by the upper curve has a better survival than the group demarcated by the lower curve. It signifies that the group demarcated by the upper curve had a more favorable survival capability than the group demarcated by the lower curve. This difference was explained statically by log rank test. Hence, the presence of any significant difference in survival time was considered in this study. The test statistics which is obtained from log rank test clearly showed that there was a significant difference in survival curve for different categorical variables.

The study found that median survival time of colorectal cancer having comorbid condition had lower survival than non- comorbid conditions (23.2 months CI: 18.3-25.9) as shown by statistical significance with p- value=0.000. Those colorectal cancer patients whose marital status was ‘divorced’ had the lowest median survival (24.4 months CI: 18.5-31.2) with statically difference of (p=0.000). The median survival time of colorectal cancer patients who were clinically diagnosed as stage I, II, and IV at baseline survived longer than clinically diagnosed stage IV at base line (22.7 months CI;19.1-25.9). This difference was significant at p value= 0.000. The overall four years’ survival rates of clinically stage I, II, III and IV were 83.2%, 45.4%, 22.4%, and 8.6%, respectively; but, the five and six year overall survival rates of stage III and IV were found to be zero. The median survival time of age greater than 70 years old (22.3months) was the lowest relative to age <40,40-49, 50-59 and 60-69 38 months, 36.1 months, 41.8 months and 24.4 months, respectively (Table 3 and 4).

Table 3:- Survival time, cumulative survival probability and log-rank test for the study population according to patient related characteristics during six-year of follow-up (Kaplan-Meier method) of colorectal cancer patients in TASH oncologic unit, 2019(n=621).

Variable	Category	Median survival in month (95% CI)	1 year survival(%)	2 year survival(%)	3 year survival(%)	4 year survival(%)	5 year survival(%)	Overall survival (%)	Log-rank test (p-value)
Sex	1. Male	30.4(26.1-34.8)	91.7	62.8	38.5	26.9	20.6	13.7	0.023
	2. Female	38.3(36.5-52.8)	89.3	72.7	60.2	39.2	25.2	25.2	
Age	<40	38(30.5-54.3)	91.5	71.5	54.1	44.7	27.4	22.0	0.000
	40-49	36.1(26.7-39.1)	95.1	74.5	44.5	20.9	-	-	
	50-59	41.8 (33.1-47.2)	93.2	73.5	60.3	28.7	28.7	-	
	60-69	24.4(19.0-28.5)	85.1	48.9	22.8	22.8	-	-	
	>=70	22.3(15.5-30.7)	81.0	34.2	11.4	-	-	-	
Family history	1. Yes	30.7(23.8-52.8)	92.2	66.8	39.7	31.7	23.8	-	0.86
	2. No	35.5(30.4-37.6)	90.5	67.5	48.0	30.6	22.5	18.7	
Residence	1. Urban	34.7(26.9-36.8)	90.0	63.1	45.0	28.1	19.3	19.3	0.073
	2. Rural	36.7 (31.2-37.1)	92.1	75.8	51.4	34.6	25.9	17.3	
Marital status	1.Single	42(36.5-54.3)	95.6	81.9	67.2	45.2	9%	-	0.0002
	2. Married	36.1(28.9-40.3)	91.2	68.1	45.0	33.0	26.4	26.1	
	3. Widowed	29.3(17.0-37.6)	80.3	53.6	28.7	19.2	-	-	
	4. Divorced	24.4(18.5-31.2)	86.7	47.7	10.5	-	-	-	
Insurance	1. Free paid	36.5(29.8-44.6)	92.2	71.7	50.5	33.2	14.2	-	0.187
	2. Paid	31.3(27.0-36.8)	89.2	63.5	43.9	30.0	18.9	18.9	
Smoking status	1.Yes	23.3(20.4-25.9)	86.7	47.6	19.9	13.4	-	-	0.000
	2.No	38.3(36.1-45.3)	92.0	74.2	57.4	38.5	23.1	27.7	
Alcohol consumption	1.Yes	25.6(22.6-30.7)	89.5	54.1	32.1	17.7	6.3	-	0.000
	2. No	40.3(36.1-52.8)	91.5	76.1	57.3	41.8	28.1	28.1	
Body mass index	<18.5	31.3(25.2-45.3)	92.9	64.3	47.4	14.8	-		0.99
	18.5-24.9	34.8 (29.3-37.1)	90.7	68.5	46.5	30.9	19.2	19.2	
	25-29.9	36.6(17.8- …)	84.4	72.4	30.9	-	-	-	
	≥ 30.0								
Comorbidity	1. Yes	23.2(18.3-25.9)	87.0	45.3	21.7	8.2	2.7	-	0.000
	2. No	44.6(36.8-52.8)	92.2	77.3	60.9	43.7	30.8	30.8	

CI; confidence interval

Table 4:- 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 TASH(n=621).

Variable	Category	Median survival in month (95% CI)	1 year survival(%)	2 year survival(%)	3 year survival(%)	4 year survival(%)	5 year survival(%)	Overall survival (%)	Log-rank test (p-value)
primary site	1. Colon	35.5(28.5-37.6)	88.7	67.7	48.8	30.8	17.5	21.5	0.68
	2. rectum	33.1(28.0-44.6)	93.2	66.8	44.2	33.7	23.1	-	
Stage of cancer at diagnosis	1. Stage I	-	98.0	94.6	89.6	83.2	8.3	8.3	0.000
	2. Stage II	37.6(35.0- …)	97.2	82.3	60.8	45.4	22.7	22.7	
	3. Stage III	34.8(27.2-38.0)	91.2	67.2	44.5	22.4	-	-	
	4. Stage IV	22.7(19.1-25.9)	81.6	46.6	20.9	8.6	-	-	
Grades of cancer	1. Differentiated	45.3(38.3-61.0)	93.5	79.6	64.3	46.5	30.7	23.3	0.000
	2.Moderately differentiated	33.1(27-36.6)	92.4	66.8	36.5	22.8	-	-	
	3. Undifferentiated	23.1(19.4-27.0)	83.5	47.1	24.2	11.7	8.7	8.7	
Histologic	1.Adenocarcinoma	36.7(31.2-41.8)	91.5	68.0	51.8	37.1	26.2	21.8	0.020
	2.mucinous carcinoma	29.3(24.4-36.8)	86.4	65.7	38.2	9.3	-	-	
	3.Signet-ring-cell carcinoma	30.7(23.3-36.1)	85.3	64.5	21.5	7.2	-	-	
Treatment	1. radiotherapy alone	37.9(34.8-…)	84.4	71.7	47.5	46.5	46.5	46.5	0.00
	2. surgical treatment alone	-	89.0	71.9	50.3	50.3	50.3	50.3	
	3.chemotherapy alone	27.2(23.2-26.1)	87.3	60.7	30.3	24.3	-	-	
	4. surgery plus chemo	37.6(34.7-45.3)	91.6	70.4	55.0	36.4	18.2	-	
	5. radiation as neo-adjuvant to surgery	36.8(18.33-…)	96.4	60.0	46.8	37.4	-	-	
	6.radiation + surgery + chemo	30.4(25.9-36.6)	90.8	67.3	40.3	17.4	8.7	-	
	7.didn`treceiv RX	--	-	-	-	-	-	-	

CI; confidence interval

The Kaplan Meier graph indicated that the median survival for those patients who had comorbid condition was (23.2 months, CI: 18.3-25.9) which was lower than median survival time of those who hadn`t comorbid conditions (44.6 months, CI: 36.8-52.8)with statically difference of p value=0.000(AS shown figure 3 below).

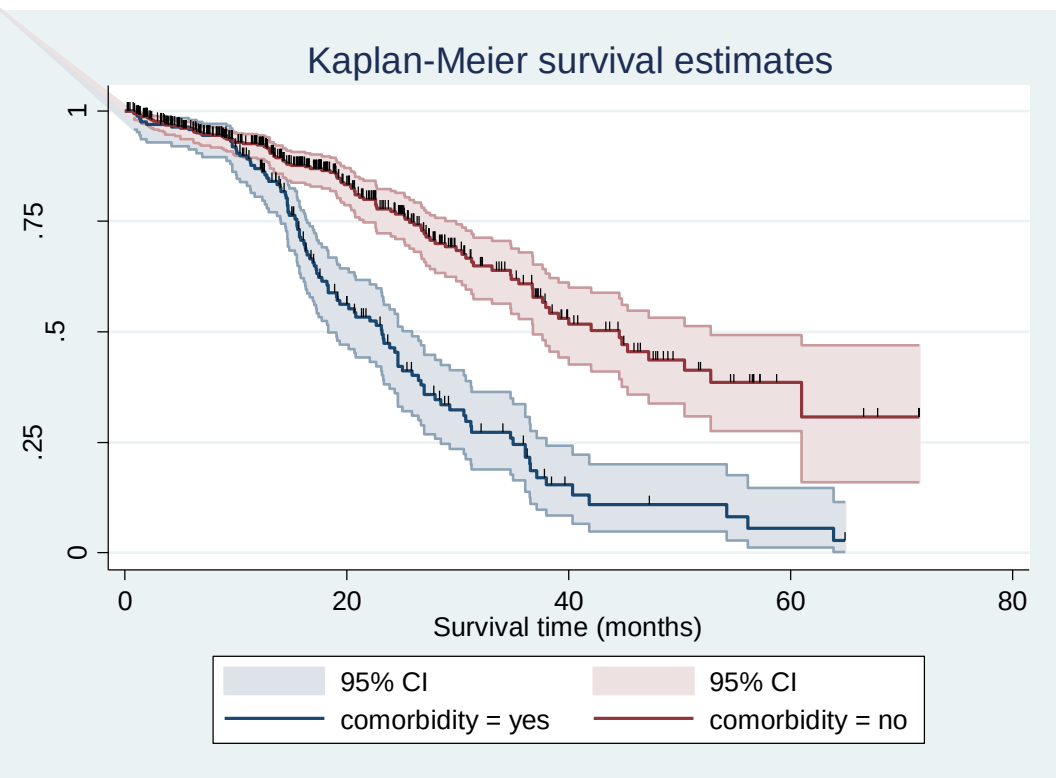

Figure 3:- The Kaplan-Meier failure function compare failure time of colorectal cancer patients with different categories of baseline comorbid conditions in Tikur Anbessa specialized hospital , Addis Ababa ,Ethiopia from January 1st ,2013 to December 30th , 2018

The median survival time for clinical stage II at baseline (37.6 months (35.0- …) higher than stage III, (34.8 months (27.2-38.0) and stage IV (22.7 months, 19.1-25.9). Whereas stage I was above the median. This difference is statically significant at p value=0.000 (As shown figure 4 below).

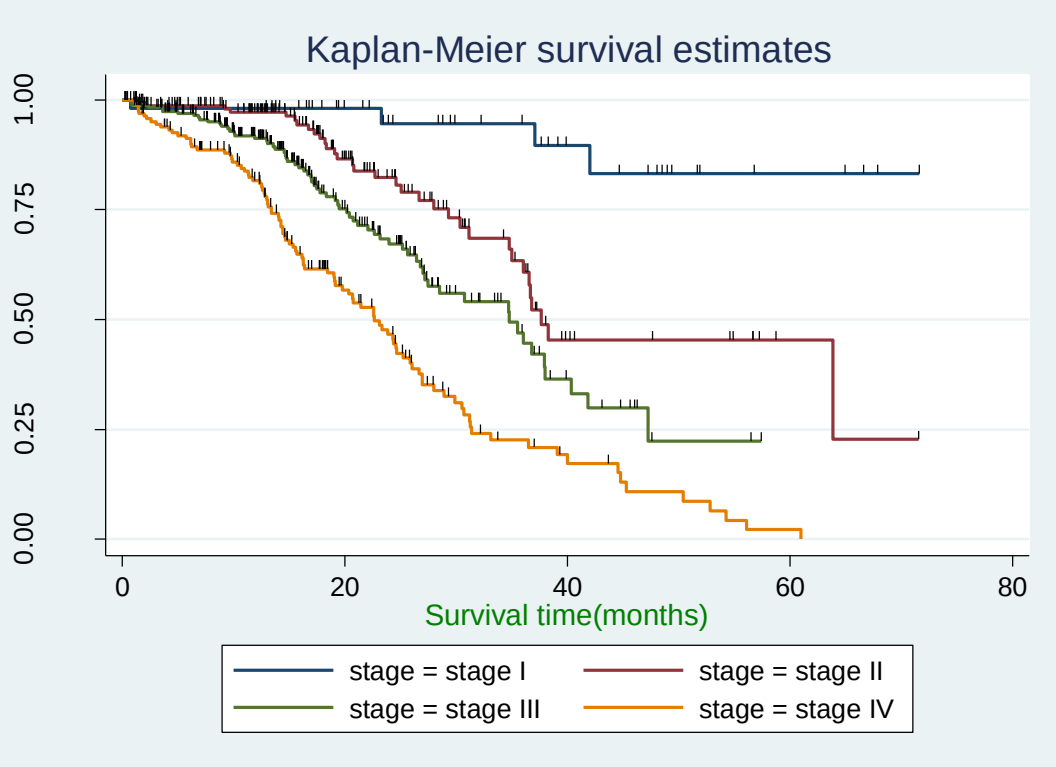

Figure 4:- The Kaplan-Meier survival curves compare survival time of colorectal cancer patients with different categories of baseline clinical stage in Tikur Anbessa specialized hospital , Addis Ababa ,Ethiopia from January 1st, 2013 to December 30th, 2018.

The Kaplan- Meier survival curve showed that the median survival time of those patient who smokes cigarettes had 23.3(20.4-25.9) lower than median survival time of non-smokers 38.3(36.1-45.3). This difference was statically significant with p- value=0.000 (As shown figure 5 below).

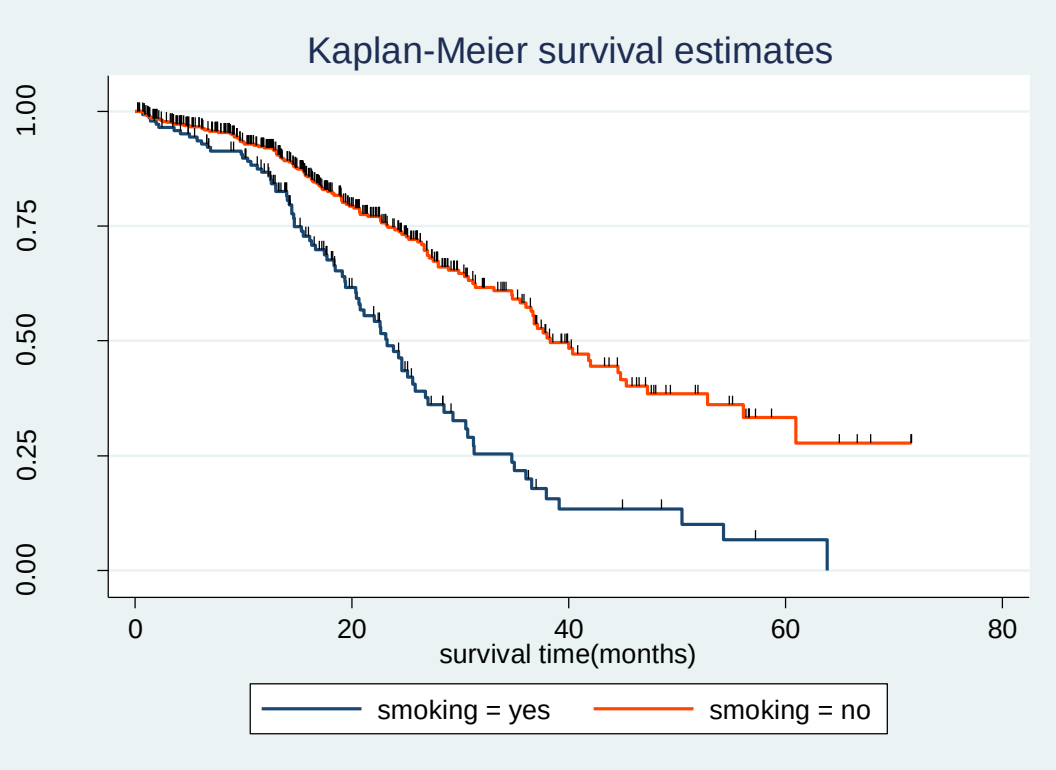

Figure 5:- The Kaplan-Meier survival curves compare survival time of colorectal cancer patients with different categories of baseline smoking status in Tikur Anbessa specialized hospital , Addis Ababa ,Ethiopia from January 1st ,2013 to December 30th , 2018.

As figure six below shown that, the median survival time of differentiated type at baseline had higher (45.3, CI: 38.3-61.0) than median survival time of moderately differentiated (33.1months CI: 27,0-36.6) and undifferentiated (23.1 months CI: 19.4-27.0). This difference was statically significant with p-value=0.000.

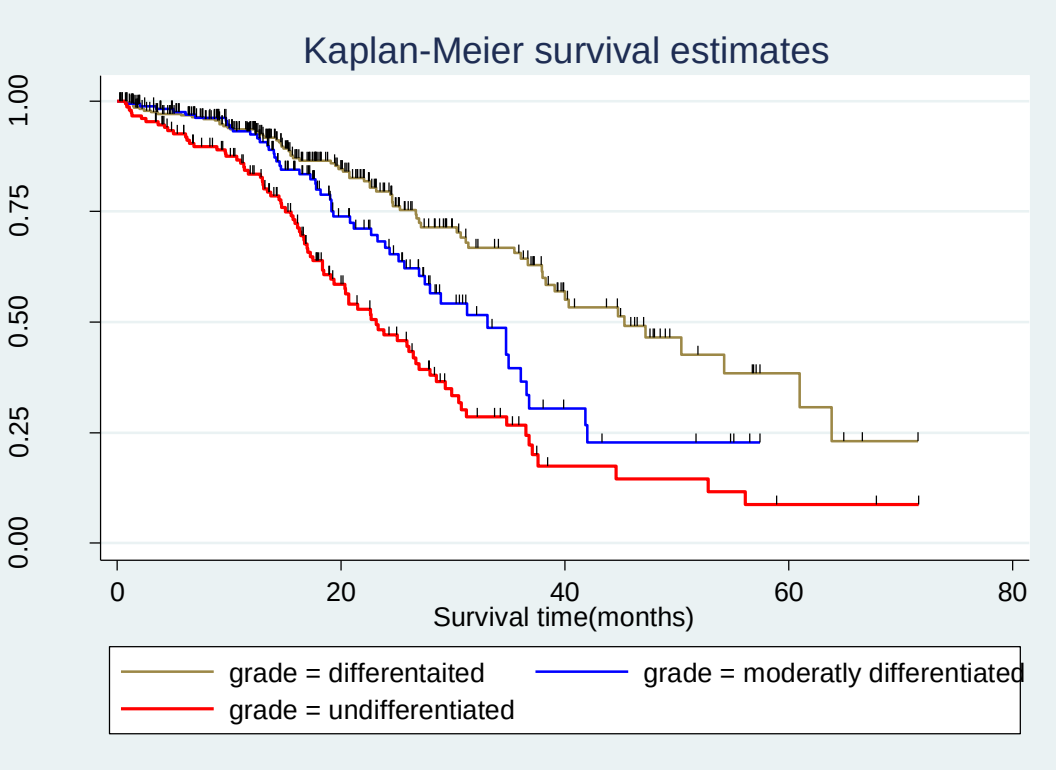

Figure 6:-The Kaplan-Meier survival curves compare survival time of colorectal cancer patients with different categories of baseline tumor grade in Tikur Anbessa specialized hospital , Addis Ababa ,Ethiopia from January 1st, 2013 to December 30th, 2018.

The median survival time of those colorectal cancer patients who intakes alcohol Lower (29.7 months, CI: 26.4-33.1) than non- drinkers (43.5 months, CI: 39.4- 47.5). The curve revealed that estimated 60 months' survival function for alcohol consumers found to be 6.3% (As shown figure 7).

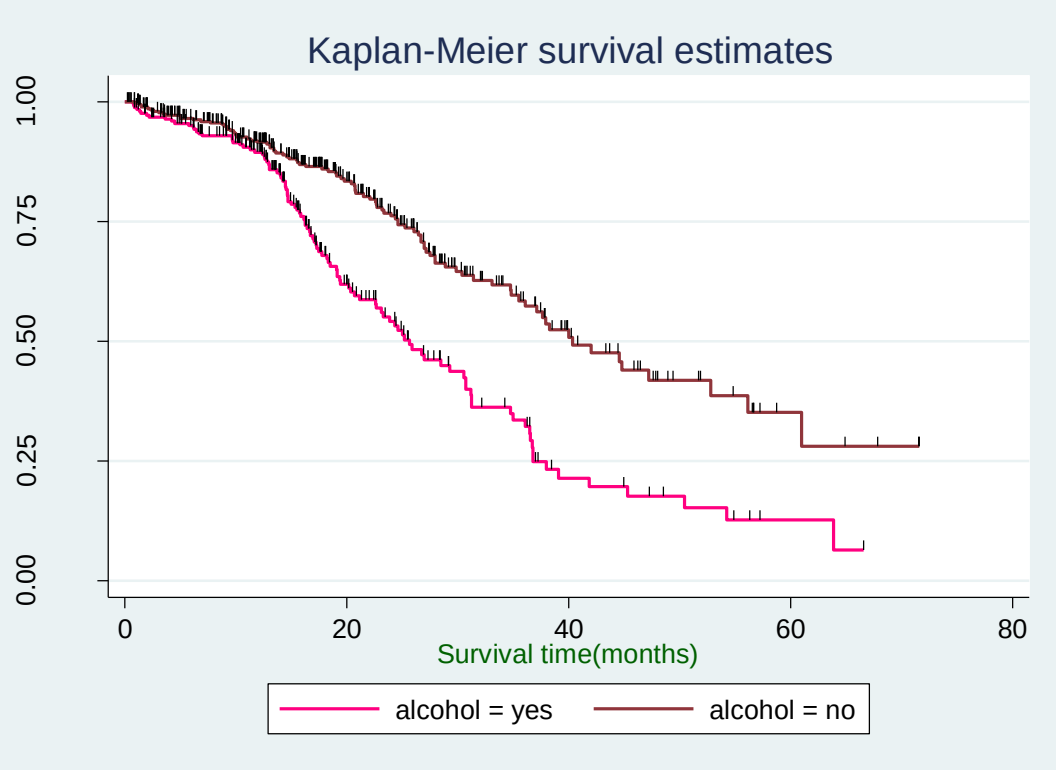

Figure 7:- The Kaplan-Meier survival curves compare survival time of colorectal cancer patients with different categories of baseline alcohol consumption in Tikur Anbessa specialized hospital , Addis Ababa ,Ethiopia from January 1st, 2013 to December 30th, 2018.

5.6. Predictors of colorectal cancer mortality

The relationship between base line variables and hazard of mortality was analyzed using cox proportional hazard regression model. In bivariable cox proportional hazard regression sex, age (60-69 and ≥ 70years), residence, marital status, insurance status, smoking, alcohol consumption, comorbidity, stage, grade, histology and treatment given were fitted in bivariable analysis at ($p < 0.25$). Those variables with p-value <0.25 in the bivariable analysis and non-collinear independent variables were included in multivariable analysis. In multivariable cox proportional hazards model; age, marital status, smoking, alcohol consumption, comorbidity, stage and grade were significant predictors of colorectal cancer mortality (P-value<0.005).

As the multivariable analysis showed that age group >= 70 years were 1.7 times at high hazard to die (AHR: 1.7, CI: 1.02-2.9) than age below 40 years old as a reference. Colorectal cancer patients whose marital status were married 2.4 times (AHR 2.4, CI: 1.02-2.9), widowed 2.4 times (AHR=2.4, CI: 1.5-3.8) and divorced 2 times (AHR=2, CI: 1.1-3.7) at high hazard to die than single marital status. Colorectal cancer Patients having comorbid condition were 1.8 times at high hazard to die than patients with non-comorbid conditions (AHR: 1.8, CI: 1.3-2.5). Those colorectal cancer patient who smokes cigarettes' and alcohol user were 1.6 verses 1.5 times at high hazard to die than non-smokers (AHR: 1.6, CI: 1.1-2.3) alcohol users (AHR: 1.5, CI: 1.07 -2.2) respectively. Patient who were diagnosed at clinical stage IV were 17.6 times at high hazard to die than those who were diagnosed as clinical stage I (AHR: 17.6, CI: 6.1-50.0). Among colorectal cancer patients diagnosed as undifferentiated tumor grade were 1.7 times at high hazard to die than those who were differentiated type of tumor (AHR:1.7, CI:1.17-2.4).

Table 5:- Results of the bivariable and multivariable cox regression analysis of colorectal cancer patients in Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia, January 1st, 2013 to December 31st, 2018 (n=621).

Variable	Bivariable cHR(95%CI)	Multivariable aHR(95%CI)
Sex		
Female	1	1
Male	1.4(1.047-1.86)*	0.89(0.64-1.24)
Age of patient		
<40	1	1
40-49	1.1(0.71-1.73)	0.97(0.60-1.55)
50-59	0.93(0.62-1.39)	8.6(0.5-1.34)
60-69	2.2(1.46-3.28) ***	1.5(0.98-2.4)
>=70	2.9(1.89-4.66) ***	1.7(1.02-2.9)*
Residence of patients		
Rural	1	1
Urban	1.3(0.97-1.77)	1.3(0.93-1.8)
Marital status		
Single	1	1
Married	1.4(0.96-2.105)	2.4(1.5-3.8) ***
Widowed	2.3(1.31-3.9) **	2.4(1.2-4.6) **
Divorced	2.7(1.62-4.4)***	2(1.1-3.7)*
Smoking status		
No	1	1
Yes	2.4(1.80- 3.19)***	1.6(1.1-2.3)*
Alcohol consumption		
No	1	1
Yes	2.1(1.59- 2.76)***	1.5(1.07-2.2)*
Comorbidity		
No	1	1
Yes	2.7(2.10-5.66)***	1.8(1.3-2.5)***
Stage at diagnosis		
1. Stage I	1	1
2. Stage II	4.8(1.7-13.9) **	3.8(1.3-11.1) *
3. Stage III	8.9(3.2-24.7) ***	8.0(2.8-23.3) ***
4. Stage IV	18.1(6.6-50.1) ***	17.6(6.1-50.7)***

Grades of cancer		
1. Differentiated	1	1
2.Moderately differentiated	1.6(1.14-2.4) **	1.4(0.94-2.03)
3. Undifferentiated	2.8(2.04-3.89)***	1.7(1.17-2.4)**
Histologic		
Adenocarcinoma	1	1
Mucinous carcinoma	1.4(0.97-2.02)	1.2(0.80-1.75)
Signet-ring-cell carcinoma	1.8(1.1-2.9)*	1.3(0.71-2.19)
Treatment modality		
Radiation alone	1	1
surgical treatment alone	0.89(0.37-2.07)	0.85(0.35- 2.1)
chemotherapy alone	1.8(0.92-3.5)	0.82(0.40-1.7)
surgery plus chemo	1.2(0.61-2.2)	0.67(0.34-1.3)
radiation as neo-adjuvant to surgery	1.2(0.58-2.6)	0.82(0.37-1.8)
radiation + surgery +chemo	1.5(0.80-2.89)	0.69(0.34-1.4)
didn`t receive treatment	0.83(0.10-6.47)	0.6(0.07-5.4)

NB: * Significant (P-value < 0.05), **significant (p-value<0.01), * significant (p<0.001)**

5.7. Test of proportional hazard assumption

Testing the proportional hazard assumption is vital for interpretation and use of fitted proportional hazard models. Therefore, in this study goodness-of-fit (GOF) particularly the Schoenfeld residuals proportional hazard assumption test for the individual covariates and global tests was used. If P-Value < 0.05, then the proportional hazard assumption is rejected. From Table below, each covariate (P-Value > 0.05) and all of covariates simultaneously (Global test for Cox proportional hazard P-Value=0.8616 > 0.05) met the proportional hazard assumption.

Table 6:- Goodness-of-fit test for assessing proportional hazards Assumption of each covariates and overall colorectal survival model, TASH, Addis Ababa, Ethiopia, 2019.

Predictors	rho*	chi2	df**	P- value
Sex	-0.00181	0.00	1	0.9793
Residence	0.01940	0.08	1	0.7806
Insurance	-0.07505	1.19	1	0.2750
Marital status	0.04878	0.49	1	0.4851
Smoking	0.01345	0.04	1	0.8401
Alcohol	-0.02711	0.15	1	0.6955
Comorbidity	-0.07228	1.07	1	0.3020
Stage	0.01864	0.07	1	0.7863
Grade	-0.05510	0.67	1	0.4123
Histology	0.08371	1.55	1	0.2130
Treatment	0.11054	2.82	1	0.0932
Age group	0.02730	0.18	1	0.6741
Family Hx	-0.00151	0.00	1	0.9825
Site	0.05536	0.66	1	0.4175
Body mass	0.02376	0.12	1	0.7300
Global test		9.29	15	0.8616

*The correlation coefficient between the residuals and time.
**Degree of freedom

CHAPTER SIX

DISCUSSION

This retrospective follow up study aimed to assess the survival status and predictors of mortality among confirmed diagnosis of colorectal cancer TASH oncology unit. Large percentage (65.7%) of the patients are diagnosed at late stage which is almost similar with the 2015 national cancer control programme report in Ethiopia [80%](88). Perhaps due to low awareness of signs and symptoms, inadequate screening and early detection and treatment services, inadequate diagnostic facilities and poorly structured referral. This study revealed that the cumulative incidence found to be 32.5 %(95%CI: 29.0-36.4) and mortality rate of 20.3 per 100 person- years. This finding is lower than study conducted in Iran(41) and china(42). The difference could be due to follow up time variation, absence of early screening and detection. In addition, the presence of alcohol, Tobacco smoking, and physical inactivity attributes.

This study showed that the overall of 1,3 and 5-year survival rate of colorectal cancer patients was found to be 90.7%, 47.0 %, and 21.7% respectively. This finding is inline with other previous studies which have been conducted in South Iran [93.9%, 50.3%, and 27.2%](46). However, this finding was lower than Taiwan [95.3%, 79.4, 68.7](50), Kurdistan[87%,57%, 33%](49), North Iran[71%,52%.44%](45), Malaysia [73.8-76%,52.1-51.7%, 40.4-45.4%](23) and New Zealand [51%](48), Jordan[58.2](47), Saudi Arabiya [44.6%](43) at 5 years. In addition, this finding is higher the study conducted in Ghana [64%, 21%, 16%] at 1, 3 and 5 years respectively(27).

This discrepancy may be due to lack of early screening program, a higher proportion of advanced stage cancer at time of diagnosis, lack of specialized care, and delay in receiving care. Other possible explanation may be health facilities are existing at the city centers, but patient from country side can`t access easily. As a result of economical constraint and far from health facility patients may delay in diagnosis and treatment. In Addition, the discrepancy might be due to difference in methodology, the study period, individual difference and difference in clinical presentation.

In this retrospective follow up study, the overall median survival time of confirmed diagnosis of colorectal cancer patients was 34.8 months (95%CI: 30.4-36.8). This result is inline with the study conducted in South Iran [36.06 months] (46). On the contrast, it is lower than other studies which was conducted in Malaysia[42 months](23), North Iran [40.5 months](45)and Greece[98 months] (51). However, median survival was higher than study conducted in Ghana was 15 months(27). The lower median survival time compared with study in Ghana may possibly due to difference in follow up study, early detection, health seeking behavior and treatment adherence.

Survival time of confirmed diagnosis of colorectal cancer patients based on age lower than other study done in Netherlands [<63.26, 63.2-71.6, 71.6-79.49, 79.5] was 58.2%, 58.8%, 51.5%,40.8% respectively(57). Moreover, the survival times of patients were lower among patient diagnosed at late stages. The survival difference between young and older colorectal patients arises from different attributes survival such as: difference in treatment modalities, the unfavorable effects of medication and intoxication, comorbidity in older patients, low progression of disease in younger patients(89).This could be due lack of health awareness in receiving medical care, adherence to treatment during outpatient treatment and frequent follow up constraint.

In this study, the survival rate of married colorectal cancer patients had better survival rate(26.1%) than single, divorced and widowed status using log rank test at p value= 0.002 which is similar with the study conducted in Taiwan, but higher in survival rate[69.1%](90). In addition, marital status found to be statically significant predictors of CRC mortality taking single marital status as a reference correspond to the study conducted in Florida(54). However, in the current study married status found to be statically significant could be owing to relatively large number of older participants who were probably had spouse. On the other hand, divorced and widowed status may lack stimulator to seek early cancer detection, treatment, and regular follow-up, social support, health related behavior.

The overall three years and four years' survival of confirmed diagnosis of stage I, II, III, IV was 89.6%,60.8%, 44.5% ,20.9% and 83.2%,45.4%,22.4%,8.6% respectively. This finding is lower than other studies conducted Malaysia at three year survival [77%, 73.4%, 78%,

68.3% and 54.6%](55). The overall four year survival of stage I in this study in line with 5 overall survival study in Jamaica at stage I, and 5year overall survival in Taiwan at stage II, whereas the overall four year survival is lower than studies conducted in Taiwan at 5 years at stage I,II,III,IV[91.2%, 82.2%,63.2%,21.7%], in Jamaica at five year[80% stage I,65% stage II, 33% stage III](50, 68). Furthermore, the overall five and six year survival of the this study for both stage III and stage IV was similar with the five 5 year overall survival of stage IV[0.0%] which was conducted in Ghana(27).

This discrepancy could be due to late presentation of cancer stage, early screening and detection, early initiation of different treatment modalities and inadequate health information regarding the nature of the disease. In addition, it might also be due to poor adherences to treatment and discontinuing the medical outpatient follow up.

The overall 3 and 5-year survival for confirmed diagnosis of CRC having comorbid condition was 21.7% and 2.7%, which is lower than previous study conducted in Malaysia [48.3% and 37.3%](64)and Spain [56.0%](66).This difference could due to early implementation and advanced treatment modality and adherence to treatment. Furthermore, colorectal cancer patient having comorbid condition were statically significant increased hazard to die than non-comorbid patient likewise study conducted in Japan(65) because comorbidity is associated with alterations in morphology, histology, differentiation, and proliferation of tumor status. For example, patients with Diabetes mellitus hyperinsulinemia involves in carcinogenesis(91). Colorectal cancer patients with comorbid conditions are less capable to receive standard treatments due to treatment related increased side effect and toxicity; increased disabilities and geriatric syndromes. Furthermore, comorbid condition cause the early sign and symptoms of the CRC indistinguishable which leading to late diagnosis, results accelerate disease progression and increasing mortality risk (12).

The current study showed that colorectal cancer patients diagnosed as undifferentiated tumor grade were 1.7 times at high hazard to die than those who were well differentiated type of tumor (AHR=1.7, CI:1.17-2.4) due to the aggressive nature of undifferentiated type of tumor tend to have poor survival outcome. Being clinically diagnosis of stage IV, stage III, and stage II at base line has 17.6 times ($p< 0.001$), 8.0 times($p< 0.001$) and 3.8 times ($p<0.05$)

at high hazard to die than stage I, This finding is similar with other previous studies in terms of increased hazard to die, but the rate of hazard to die varies than other previous the studies conducted in Iran who were clinically diagnosed stage [II, AHR=3.1, III, AHR=2.16, IV AHR=1.79 at base line respectively] (69). Similarly, study in Iran revealed that stage was significant factor for colorectal cancer mortality for patents diagnosed as early stage at baseline had lower hazard to die than late stage at base line[AHR=3.43] (41). The possible explanation might be delay in timely recipient of treatment, the presence of comorbidities, and most of the patients are clinically diagnosed at late stage in which multiple lymph node involvement and distant metastasis occur by shading cells into blood stream that settle in another part of body leads to invasion of all body systems.

In the current study, statically significant increased hazard found in cigarette smokers (AHR; 1.6; 95%CI: 1.1-2.3 at $p < 0.05$). This finding is similar with other previous studies conducted in Germany [AHR=1.4](60) and United states[AHR=1.32 and 1.41 among men and women respectively]. Alcohol consumption also found to be significant increased hazard to die (AHR:1.5, 95%CI: 1.07-2.2 at $p< 0.05$) than non-alcohol consumers likewise other study done in Germany[AHR=1.37](62). This is possibly related to carcinogenic effect of alcohol and smoking. Indeed, being diagnosed with colorectal cancer creates negative illness perception leads behavioral changes ends poor outcome survival(92). Another explanation could be smoking has effect on carcinogenesis as evidenced that the nicotine stimulates the tumor growth; increase survival pathway of tumor, increased proliferation of tumor and decreases the effectiveness of chemotherapy. Moreover, biological biomarkers also associated with CRC prognosis, for example, patients with micro satellite instability had more hazard to die in patient who smokes cigarettes (15).

Strength and limitation of the study

Strength

The study has the following strengths:

The follow up study conducted was fairly longer, this make the possibility of developing an event and identifying the confirmed diagnosis of colorectal cancer stage, grade and histology has an advantageous on giving good quality data.

Data were collected by oncologic nurses which had an important role in the quality of the data.

It was easy to establish temporal relationship of outcome death with predictor variables.

Limitations

Despite the above strength this study has the following potential limitations:

Selection bias was possibly introduced during secondary data collection because patients with incomplete records were excluded so that, the incidence of death may be under or over estimated.

Cause specific (relative) survival was not determined due to lack of data on specific cause of death, this may over estimates colorectal cancer related mortality rate.

Since the data collected from secondary source; some important predictors such as biological biomarkers, treatment adherence, physical exercise, cycle of chemo, aim of treatment, educational status and multidisciplinary care were missed which might have significant prediction for colorectal cancer mortality.

Conclusion

The overall survival probability of confirmed diagnosis of colorectal cancer was 18.1% at 72 months of follow up. The findings revealed that lower survival probability of confirmed colorectal cancer patients in Tikur Anbessa Specialized Hospital as compared with those of high and middle income countries. Age >=70 years old, marital status, comorbidity, smoking, alcohol consumption, stage and grade of tumor found to be significant predictors of mortality among confirmed diagnosis of colorectal cancer.

Recommendations

According to the study finding, the following recommendations could be forwarded to:

To Federal Minister of Health

- Better if implement colorectal cancer early screening and detection programme to improve treatment results and survival outcomes
- Better if strengthen awareness in collaboration with public medias about colorectal cancer prevention, screening and treatment is vital.
- Better if give especial emphasis on the silently rising colorectal cancer

To Tikur Anbessa Specialized Hospital and health care providers

- Could give especial attention to those who came from country side and patient with comorbid conditions
- The health care providers could enhance the awareness on treatment adherences
- Could enhance effective and feasible treatment regimens
- The health care providers could emphasis on health information dissemination on early detection and encourage seeking clinical support.

To Future researchers

- Further prospective follow up study could be conducted by including important predictors of mortality like financial problems, laboratory findings, societal and health system related factors.
- Could carry out molecular studies should be done to identify potential molecular bio-markers for an improved and effective treatment.
- Could address the limitation of this study

REFERENCES

1. ACG. National Colorectal Cancer Awareness Month Media Outreach. 2018.

2. ACS. About Colorectal Cancer. 2018.

3. WHO. International agency research on cancer. Latest Global Cancer Data. 2018.

4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2018;68(6):394-424.

5. Olabisi J, Parihar N, Isherwood A, Hughes M. World wide incidence of colorectal cancer; A 10 year forecast (2017-2027). 2017.

6. ACS. Cancer Facts & Figures 2018. Atlanta, Ga: American Cancer Society. Atlanta. 2018.

7. Ansa BE, Coughlin SS, Alema-Mensah E, Smith SA. Evaluation of Colorectal Cancer Incidence Trends in the United States (2000–2014). Journal of Clinical Medicine. 2018;7(2):22.

8. Graham A, Davies Adeloye LG, Theodoratou E, Campbell H. Estimating the incidence of colorectal cancer in Sub–Saharan Africa: A Systematic Analysis. Journal of Global Health. 2012;2(2).

9. Woldu M, Legese D, Abamecha F, Berha A. The Prevalence of Cancer and its Associated Risk Factors among Patients Visiting Oncology Unit, Tikur Anbessa Specialized Hospital, Addis Ababa-Ethiopia. J Cancer Sci Ther. 2017;9:414-21.

10. Timotewos G, Matewos A, Solomon A, Bireda W, Ayalnesh B. Addis Ababa City Cancer Registry. 2014.

11. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-91.

12. Boakye D, Rillmann B, Walter V, Jansen L, Hoffmeister M, Brenner H. Impact of comorbidity and frailty on prognosis in colorectal cancer patients: A systematic review and meta-analysis. Cancer Treatment Reviews. 2018;64:30-9.

13. Galvin A, Delva F, Helmer C, Rainfray M, Bellera C, Rondeau V, et al. Sociodemographic, socioeconomic, and clinical determinants of survival in patients with

cancer: A systematic review of the literature focused on the elderly. Journal of Geriatric Oncology. 2017.

14. Heervä E, Carpelan A, Kurki S, Sundström J, Huhtinen H, Rantala A, et al. Trends in presentation, treatment and survival of 1777 patients with colorectal cancer over a decade: a Biobank study. Acta Oncologica. 2018:1-8.

15. Walter V, Jansen L, Hoffmeister M, Ulrich A, Chang -Claude J, Brenner H. Smoking and survival of colorectal cancer patients: Population ‐ based study from Germany. International Journal of Cancer. 2015;137(6):1433-45.

16. Bekaii-Saab T, Kim R, Kim TW, O'Connor JM, Strickler JH, Malka D, et al. Third-or Later-line Therapy for Metastatic Colorectal Cancer: Reviewing Best Practice. Clinical Colorectal Cancer. 2018.

17. Hamza AH, Aglan HA, Ahmed HH. Recent Concepts in the Pathogenesis and Management of Colorectal Cancer. Recent Advances in Colon Cancer. 2017:3-58.

18. Granados-Romero JJ, Valderrama-Treviño AI, Contreras-Flores EH, Barrera-Mera B, Enríquez MH, Uriarte-Ruíz K, et al. Colorectal cancer: A Review. International Journal of Research in Medical Sciences. 2017;5(11):4667-76.

19. Williamson S, Chalmers K, Beaver K. Patient experiences of nurse-led telephone follow-up following treatment for colorectal cancer. European Journal of Oncology Nursing. 2015;19(3):237-43.

20. Ose D, Winkler EC, Berger S, Baudendistel I, Kamradt M, Eckrich F, et al. Complexity of care and strategies of self-management in patients with colorectal cancer. Patient Preference and Adherence. 2017;11:731.

21. Ferlay J, Soerjomataram I, Ervik M. Cancer incidence and mortality worldwide: IARC Cancer Base. 2012;11.

22. Sadeghi Gandomani H, Aghajani M, Mohammadian-Hafshejani A, Asgari Tarazoj A, Pouyesh V, Salehiniya H. Colorectal cancer in the world: Incidence, mortality and risk factors. Biomedical Research and Therapy:. 2017;4(10).

23. Magaji BA, Moy FM, Roslani AC, Law CW. Survival rates and predictors of survival among colorectal cancer patients in a Malaysian Tertiary Hospital. BMC Cancer. 2017;17(1):339.

24. Hermannn bernner Mc, Christian peter colorectal cancer. 2014.
25. American Cancer Society. Colorectal Cancer Facts & Figures 2017-2019. Atlanta: American Cancer Society; 2017.
26. Tahmasbi B, Abedi G, Moosazadeh M, Janbabai G, Farshidi F, Mansori K, et al. Determining the Survival Rate of Colorectal Cancer in Iran: A Systematic Review and Meta-Analysis. Asian Pac J Cancer Prev. 2018;19 (11),:3009-18.
27. Agyemang-Yeboah F, Yorke J, Obirikorang C, Batu EN, Acheampong E, Frimpong EA, et al. Colorectal cancer survival rates in Ghana: A retrospective Hospital-Based Study. PloS one. 2018;13(12):e0209307.
28. Quach C, Sanoff HK, Williams GR, Lyons JC, Reeve BB. Impact of colorectal cancer diagnosis and treatment on health‐related quality of life among older Americans: A Population‐based, case‐control study. Cancer. 2015;121(6):943-50.
29. Weir HK, Li C, Henley SJ, Joseph D. Years of life and productivity loss from potentially avoidable colorectal cancer deaths in US counties with lower educational attainment (2008–2012). Cancer Epidemiology and Prevention Biomarkers. 2017;26(5):736-42.
30. NCI. Financial Burden of Cancer Care. 2017 Last updated, 2018.
31. Ribarov R, Ivanov A, Ivanova N. Necessity of self-management support following colorectal cancer treatment. Archives of the Balkan Medical Union. 2017;52(3):285-91.
32. Quintana JM, González N, Lázaro S, Baré M, Fernandez de Larrea N, Redondo M, et al. Predictors of one and two year mortality in patients with rectal cancer. Colorectal Disease. 2018;13(6).
33. Sharkas GF, Arqoub KH, Khader YS, Tarawneh MR, Nimri OF, Al-zaghal MJ, et al. Colorectal cancer in Jordan: Survival rate and its related factors. Journal of Oncology. 2017;2017.
34. Cotton P, Eastman P, Le BH. Palliative Care and Colorectal Cancer. Department of Palliative Care, Royal Melbourne Hospital, Parkville, Victoria, Australia. 2014.
35. Ginsberg GM, Lauer JA, Zelle S, Baeten S, Baltussen R. Cost effectiveness of strategies to combat breast, cervical, and colorectal cancer in sub-Saharan Africa and South East Asia: Mathematical modelling study. BMJ. 2012;344:e614.

36. Siegel RL, Miller KD, Fedewa SA, Ahnen DJ, Meester RG, Barzi A, et al. Colorectal cancer statistics, 2017. CA: a Cancer Journal for Clinicians. 2017;67(3):177-93.
37. Bello A., Foong Mi., April C., Chee W. Survival rates and predictors of survival among colorectal cancer patients in a Malaysian tertiary hospital. 2017.
38. Gupta S, Sussman DA, Doubeni CA, Anderson DS, Day L, Deshpande AR, et al. Challenges and possible solutions to colorectal cancer screening for the underserved. JNCI: Journal of the National Cancer Institute. 2014;106(4).
39. Dharni N, Armstrong D, Chung‐Faye G, Wright AJ. Factors influencing participation in colorectal cancer screening a qualitative study in an ethnic and socio‐economically diverse inner city population. Health Expectations. 2017;20(4):608-17.
40. Feller A, Schmidlin K, Bordoni A, Bouchardy C, Bulliard JL, Camey B, et al. Socioeconomic and demographic inequalities in stage at diagnosis and survival among colorectal cancer patients: Evidence from a Swiss population‐based study. Cancer Medicine. 2018;7(4):1498-510.
41. Ahmadi A, Mosavi-Jarrahi A, Pourhoseingholi MA. Mortality determinants in colorectal cancer patients at different grades: A prospective, cohort study in Iran. Asian Pacific Journal of Cancer Prevention. 2015;16(3):1069-72.
42. Gu M-J, Huang Q-C, Bao C-Z, Li Y-J, Li X-Q, Ye D, et al. Attributable causes of colorectal cancer in China. BMC cancer. 2018;18(1):38.
43. Alsanea N, Abduljabbar AS, Alhomoud S, Ashari LH, Hibbert D, Bazarbashi S. Colorectal Cancer in Saudi Arabia: Incidence, Survival, Demographics and Implications for National Policies. Annals of Saudi Medicine. 2015;35(3):196-202.
44. Hoseini S, Moaddabshoar L, Hemati S, Mohammadianpanah M. An overview of clinical and pathological characteristics and survival rate of colorectal cancer in Iran. Ann Colorectal Res. 2014;2(1):e17264.
45. Semnani S, Noorafkan Z, Aryaie M, Sedaghat SM, Moghaddami A, Kazemnejhad V, et al. Determinants of healthcare utilisation and predictors of outcome in colorectal cancer patients from Northern Iran. European Journal of Cancer Care. 2016;25(2):318-23.

46. Mehrabani D, Almasi-Hashiani A, Moshfeghi K, Khedmati E. Survival rate and its predictors in colorectal cancer patients, Southern Iran. Middle East J Sci Res. 2012;12(8):1072-7.
47. Sharkas GF, Arqoub KH, Khader YS, Tarawneh MR, Nimri OF, Al-zaghal MJ, et al. Colorectal cancer in Jordan: Survival rate and its related factors. Journal of Oncology. 2017:6.
48. Sharples K, Firth M, Hinder V, Hill A, Jeffery M, Sarfati D, et al. The New Zealand PIPER Project: Colorectal cancer survival according to rurality, ethnicity and socioeconomic deprivation results from a retrospective cohort study. The New Zealand Medical Journal. 2018;131(1476):24-39.
49. Rasouli MA, Moradi G, Roshani D, Nikkhoo B, Ghaderi E, Ghaytasi B. Prognostic factors and survival of colorectal cancer in Kurdistan province, Iran: A Population-based study (2009–2014). Medicine. 2017;96(6).
50. Chao-Hsien L, Cheng S-C, Hong-Yi T, Chang S-C, Ching C-Y, Shu-Fen W. The Risk Factors Affecting Survival in Colorectal Cancer in Taiwan. Iranian Journal of Public Health. 2018;47(4):519.
51. Zacharakis M, Xynos ID, Lazaris A, Smaro T, Kosmas C, Dokou A, et al. Predictors of survival in stage IV metastatic Colorectal Cancer. Anticancer Research. 2010;30(2):653-60.
52. Chong DQ, Banbury BL, Phipps AI, Hua X, Kocarnik J, Peters U, et al. Association of family history and survival in patients with colorectal cancer: A pooled analysis of eight epidemiologic studies. Cancer Medicine. 2018;7(5):2192-9.
53. Qingguo L, Gan L, Liang L, Li X, Cai S. The influence of marital status on stage at diagnosis and survival of patients with colorectal cancer. Oncotarget. 2015;6(9):7339.
54. Tannenbaum SL, Hernandez M, Zheng DD, Sussman DA, Lee DJ. Individual-and neighborhood-level predictors of mortality in Florida colorectal cancer patients. PloS One. 2014;9(8):e106322.
55. Hassan M, Suan M, Soelar SA, Mohammed NS, Ismail I, Ahmad F. Survival analysis and Prognostic factors for colorectal cancer patients in Malaysia. Asian Pac J Cancer Prev. 2016;17(7):3575-81.

56. Fiorot A, Pozza A, Ruffolo C, Caratozzolo E, Bonariol L, D'Amico FE, et al. Colorectal cancer in the young: A possible role for immune surveillance? Acta Chirurgica Belgica. 2018;118(1):7-14.
57. van Eeghen, E E, Bakker SD, van Bochove A, Loffeld RJ. Impact of age and comorbidity on survival in colorectal cancer. Journal of Gastrointestinal Oncology. 2015;6(6):605.
58. Pulte D, Jansen L, Brenner H. Disparities in Colon Cancer Survival by Insurance Type: A Population-Based Analysis. Diseases of the Colon & Rectum. 2018;61(5):538-46.
59. Walter V, Jansen L, Hoffmeister M, Brenner H. Smoking and survival of colorectal cancer patients: systematic review and meta-analysis. Annals of Oncology. 2014; 25(8):1517-25.
60. Walter V, Jansen L, Ulrich A, Roth W, Bläker H, Chang-Claude J, et al. Alcohol consumption and survival of colorectal cancer patients: A population-based study from Germany, 2. The American Journal of Clinical Nutrition. 2016;103(6):1497-506.
61. Japuntich SJ, Kumar P, Pendergast JF, Caballero GYJ, Malin JL, Wallace RB, et al. Smoking Status and Survival Among a National Cohort of Lung and Colorectal Cancer Patients, Nicotine & Tobacco Research. April 2019;21(4):97-504.
62. Walter V, Jansen L, Knebel P, Chang‐Claude J, Hoffmeister M, Brenner H. Physical activity and survival of colorectal cancer patients: Population‐based study from Germany. International Journal of Cancer. 2017;140(9):1985-97.
63. Kaneko M, Sasaki S, Ozaki K, Ishimaru K, Terai E, Nakayama H, et al. Underweight status predicts a poor prognosis in elderly patients with colorectal cancer. Molecular and Clinical Oncology. 2016;5(3):289-94.
64. Suan MAM, Tan WL, Soelar SA, Ismail I, Hassan MRA. Intestinal obstruction: Predictor of poor prognosis in colorectal carcinoma? Epidemiology and Health. 2015;37.
65. Morishima T, Matsumoto Y, Koeda N, Shimada H, Maruhama T, Matsuki D, et al. Impact of Comorbidities on Survival in Gastric, Colorectal, and Lung Cancer Patients. J Epidemiol. 2019;29(3):110-5.
66. Parés-Badell O, Banqué M, Macià F, Castells X, Sala M. Impact of comorbidity on survival by tumour location: Breast, colorectal and lung cancer (2000–2014). Cancer Epidemiology. 2017;49:66-74.

67. Price TJ, Beeke C, Ullah S, Padbury R, Maddern G, Roder D, et al. Does the primary site of colorectal cancer impact outcomes for patients with metastatic disease? Cancer. 2015;121(6):830-5.
68. Plummer JM, Leake P-A, Ferron-Boothe D, Roberts PO, Mitchell DI, McFarlane ME. Colorectal cancer survival in Jamaica. Annals of Medicine and Surgery. 2016;6:26-9.
69. Aryaie M, Roshandel G, Semnani S, Asadi-Lari M, Aarabi M, Vakili MA, et al. Predictors of colorectal cancer survival in Golestan, Iran: A population-Based Study. Epidemiology and Health. 2013;35.
70. Kim MS, Park EJ, Kang J, Min BS, Lee KY, Kim NK, et al. Prognostic factors predicting survival in incurable stage IV colorectal cancer patients who underwent palliative primary tumor resection. Retrospective cohort study. International Journal of Surgery. 2018;49:10-5.
71. Park JS, Huh JW, Park YA, Cho YB, Yun SH, Kim HC, et al. Prognostic comparison between mucinous and nonmucinous adenocarcinoma in colorectal cancer. Medicine. 2015;94(15).
72. Fatemi SR, Pourhoseingholi MA, Asadi F, Vahedi M, Pasha S, Alizadeh L, et al. Recurrence and five-year survival in colorectal cancer patients after surgery. Iranian Journal of Cancer Prevention. 2015;8(4).
73. Munro A, Brown M, Niblock P, Steele R, Carey F. Do Multidisciplinary Team (MDT) processes influence survival in patients with colorectal cancer? A Population-based experience. BMC cancer. 2015;15(1):686.
74. Costi R, Leonardi F, Zanoni D, Violi V, Roncoroni L. Palliative care and end-stage colorectal cancer management: the surgeon meets the oncologist. World Journal of Gastroenterology: WJG. 2014;20(24):7602.
75. Tashiro J, Yamaguchi S, Ishii T, Suzuki A, Kondo H, Morita Y, et al. Inferior oncological prognosis of surgery without oral chemotherapy for stage III colon cancer in clinical settings. World Journal of Surgical Oncology. 2014;12(1):145.
76. Brand M, Gaylard P, Ramos J, BCh M. Colorectal cancer in South Africa : An assessment of disease presentation, treatment pathways and 5-year survival. S Afr Med. 2018;108(2):118-22.
77. Tikur Anbessa Specialized Hospital Oncology Unit manager office. 2018.

78. Euser AM, Zoccali C, Jager KJ, Dekker FW. Cohort studies: prospective versus retrospective. Nephron Clinical Practice. 2009;113(3):c214-c7.
79. Setia MS. Methodology series module 1: Cohort studies. Indian Journal of Dermatology. 2016;61(1):21.
80. Song JW, Chung KC. Observational studies: Cohort and case-control studies. Plastic and Reconstructive Surgery. 2010;126(6):2234.
81. DANIEL WW. Biostatstics. A Foundation for Analysis in the Health Sciences. 13th edition. 2010. p.167.
82. Hsu Y-H, Kung P-T, Wang S-T, Fang C-Y, Tsai W-C. Improved patient survivals with colorectal cancer under multidisciplinary team care: a nation wide cohort study of 25,766 patients in Taiwan. Health Policy. 2016;120(6):674-81.
83. Diseases. International Classification of disaeases. Comorbidity scores. Charlson comorbidity score. 2012; Last updated on April 17, 2019.
84. Center of Disease Control and Prevention. About Adult BMI. Clifton Road Atlanta, GA 30329-4027 USA: 2018.
85. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population‐based to a more "personalized" approach to cancer staging. CA: Cancer Journal for Clinicians. 2017;67(2):93-9.
86. Zhongheng Z. Model building strategy for logistic regression: purposeful selection. Annals of Translational Medicine. 2016;4(6):111.
87. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. BioMed Central. 2008;3: 17.
88. Health FMo. Disease Prevention And Control Directorate. Ethiopia National Cancer Control Plan 2016-2020. 2015: P.14.
89. Jorgensen M, Young J, Solomon M. Adjuvant chemotherapy for colorectal cancer: Age differences in factors influencing patients' treatment decisions. Patient Prefer Adherence. 2013; 7:827-34.

90. Yang C-C, Cheng L-C, Lin Y-W, Wang S-C, Ke T-M, Huang C-I, et al. The impact of marital status on survival in patients with surgically treated colon cancer. Medicine. 2019;98(11):e14856.
91. Søgaard M, Thomsen RW, Bossen KS, Sørensen HT, Nørgaard M. The impact of comorbidity on cancer survival: A Review. Clinical Epidemiology. 2013;5(1):p.3.
92. Thong MS, Kaptein AA, Vissers PA, Vreugdenhil G, van de Poll-Franse LV. Illness perceptions are associated with mortality among 1552 colorectal cancer survivors: A study from the population-based PROFILES registry. Journal of Cancer Survivorship. 2016;10(5):898-905.

ANNEXES

Annex 1: Information Sheet English Version

Title of the Research proposal: Survival status and predictors of mortality among colorectal cancer patients from 2013- 2017 followed up to 2018 in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2019: retrospective follow up study

Name of Investigator: Bantalem Tilaye, BSc

Name of the Organization: Addis Ababa University, College of Health Science, School of Nursing and Midwifery, Department of Adult health nursing

Name of the Sponsor: Addis Ababa University

Purpose of the Research Project: To determine Survival status and predictor of mortality among colorectal cancer patients from 2013-2017 followed up to 2018 in TASH, Addis Ababa, Ethiopia, 2019

Procedure: In order to achieve the above objective, information which was necessary for the study was taken from medical record forms by the aid of data extraction tool and patients enrolled during January 1st, 2013 to December 30th, 2017 have been selected and followed up to December 30th, 2018.

Risk and /or Discomfort: Since the study was conducted by taking appropriate information from the medical chart, it will not inflict any harm on the patients. The name or any other identifying information was not be recorded on the questionnaire and all information was taken from the chart was kept strictly confidential and in a safe place. The information retrieved would only be used for the study purpose.

Benefits: The research had no direct benefit for those whose document/ record was included in this research. However, the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing a predicted plan, there is a benefit for clients in the program of getting appropriate care and treatment

services for the colorectal cancer patients. Of all, the research work has a paramount direct benefit for health care planners and managers, especially for those on colorectal cancer program planning and management**.**

Confidentiality: To reassure confidentiality the data on the chart was collected without the name of the clients and the information collected from this research project was kept confidential and will be stored in a file cabinet. In addition, it hasn`t been revealed to anyone except the investigator and it was kept in a key and locked system with computer pass ward.

Person to contact: This research project was reviewed and approved by the institutional review board of school of nursing and midwifery, college of health sciences, Addis Ababa University. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you might ask at any the time you want.

Fekadu Aga, MSc, Assistant. Professor, PhD Fellow: Addis Ababa University, College of Health Sciences, School of Nursing and Midwifery

Tefera Mulugeta, MSc, PhD Fellow: Addis Ababa University, College of Health Sciences, School of Nursing and Midwifery.

Bantalem Tilaye, BSc: Addis Ababa University, College of Health Sciences, School of Nursing and Midwifery

Cell phone: +251928557815, E-mail: bantalemtilaye@gmail.com

Annex 2: Information Sheet Amharic Version

አባሪ 1: የመረጃ ዝርዝር

የጥናቱ ርዕስ፡ የትልቅ አንጀት ካንሰር ሕመምተኞች የመትረፍ ሁኔታ እና ሚችነትን አመላካቾች ከ2013 እስከ 2017እ.ኤ.አ. ባሉት ጊዚያት ዉስጥ የተመዘገቡ ታካሚዎች በጥቁር አንበሳ እስፔሳላይዝድ ሆስፒታል, አዲስ አበባ, ኢትዮጲያ, 2019 ፡ የኋልዮስ ምልከታ

የአጥኚው ስም: ባንታለም ጥላዬ, ቢኤስሲ

የድርጅቱ ስም: የአዲስ አበባ ዩኒቨርሲቲ, ጤና ሳይንስ ኮሌጅ, የነርስ እና የአዋላጂ ነርስ ትምህርት ቤት, የአዋቂዎች ነርስ ትምህርት ክፍል

የድጋፍ አድራጊ ስም፡ አዲስ አበባ ዩኒቨርስቲ

የጥናቱ ዓላማ፡ ከ2013 መጀመሪያ እስከ 2017 መጨረሻ ባሉት ዓመታት የተመዘገቡትን የትልቅ አንጀት ካንሰር ታካሚዎችን በመዉሰድ እስከ ታህሳስ መጨረሻ 2018 የኋልዮስ ምልከታ በማድረግ የቆይታ ሁኔታ እና ሚችነትን አመላካቾች ለማወቅ አዲስ አበባ፣ኢትዮጵያ፣2019

የአሠራር ሂደት: ከላይ የተጠቀሰውን ግብ ለመምታት ለጥናቱ አስፈላጊ መረጃዎች ለማግኘት የመረጃ መሰብሰቢያ መሳሪያ በመጠቀም ከመዝገብ ፋይል ከጥር መጀመሪያ 2013 እስከ ታህሳስ መጨረሻ 2017 ድረስ የተመዘገቡ ታካሚዎችን በመዉሰድ እስከ ታህሳስ መጨረሻ 2018 የኋልዮስ ምልከታ ይደረጋል

አደጋ እና ወይም አለመረጋጋት: ጥናቱ የሚካሄደው ከሕክምና ሰነድ ላይ ተገቢውን መረጃ በመውሰድ በታካሚው ላይ ምንም ዓይነት ጉዳት አያስከትልም ስሙ ወይም ሌላ ማንነትን የሚለይ መረጃ በእጩ መጠይቅ ላይ አይመዘገብም እና ሁሉም መረጃ በጥብቅ ሚስጥራዊ እና ደህንነቱ በተጠበቀ ሁኔታ ይወሰድና በሚያስተማምን ቦታ ይቀመጣል የተወሰደው መረጃ ለጥናት ዓላማ ብቻ የሚዉ ይሆናል።

ጥቅማ ጥቅሞች: ጥናቱ ሰነዱ ወይም መዝገቡ ውስጥ ለተካተቱት ታካሚዎች ቀጥተኛ የሆነ ጥቅም የለዉም።ይሁን እንጂ በፕሮግራሙ ውስጥ ለተሳተፉ እና ለሌሎች ደንበኞች ምርምር ማድረግ ቀጥተኛ ያልሆነ ጥቅም ግልጽ ነው። ይህ ምክንያቱ የፕሮግራም ዕቅድ አውጪዎች የታቀደውን እቅድ እያዘጋጁ ከሆነ የትልቅ አንጀት ካንሰር ታካሚዎችን ተገቢ የሆነ እንክብካቤ እና ህክምና አገልግሎት ለማግኘት ለደንበኞች የሚሰጠው ጥቅም አለው።ከሁሉም በላይ የምርምር ሥራ ለጤና አጠባበቅ እቅድ አውጪዎች እና አስተዳዳሪዎች በተለይም የትልቅ አንጀት ካንሰር መርሃ ግብር እቅድ እና አስተዳደር ላይ ለታለመላቸው ቀጥተኛ ጥቅሞች አሉት።

ሚስጢራዊነት፡ሚስጢራዊነት ለማረጋገጥ በምርጫው ላይ ያለው መረጃ ደንበኞቹን ስም ሳይገልጽ ይሰበሰባል፣ከዚህ የምርምር ፕሮጀክት የተሰበሰበው መረጃ በምስጢር የሚጠበቅ በተጨማሪ, ከአጥኚው በቀር ለማንም አይገለጽም እና በቁልፍ ከተዘጋ በኋላ በተቆለፈ ስርአት አማካኝነት በኮምፕዩተር ማቆሚያ ክፍል ውስጥ እንዲቀመጥ ይደረጋል።

መገናኘት ያለበት ግለሰብ፡ ይህ የምርምር ፕሮጀክት በነርስ እና በአዋላጂ ነርስ ትምህርት፣ በጤና ሳይንስ ኮሌጅ፣ በአዲስ አበባ ዩኒቨርሲቲ ቦርድ ተገምግሞ የሚጸድቅ ይሆናል።ማናቸውም ጥያቄ ካልዎት ከሚከተሉት ግለሰቦች ጋር መገናኘት ይችላሉ (መርማሪና አማካሪዎች)እና በፈለጉት ጊዜ መጠየቅ ይችላሉ.

ፍቃዱ አጋ፣ ኤምሲ፣ ረዳት ፕሮፌሰር እና ፒኤችዲ ተማሪ፡-የአዲስ አበባ ዩኒቨርስቲ, የጤና ሳይንስ ኮሌጅ, የነርሶች እና የአዋላጅ ነርሶች ትምህርት ቤት

ተፈራ ሙሉጌታ፣ ኤምሲ፣ ማከስ እና ፒኤችዲ ተማሪ፡- የአዲስ አበባ ዩኒቨርስቲ, የጤና ሳይንስ ኮሌጅ, የነርሶች እና የአዋላጅ ነርሶች ትምህርት ቤት

ባንታለም ጥላዬ, ቢኤስሲ: - የአዲስ አበባ ዩኒቨርስቲ, የጤና ሳይንስ ኮሌጅ, የነርሶች እና የአዋላጅ ነርሶች ትምህርት ቤት

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Annex 3: Data Extraction tool

This checklist was used for the collection of patient related and Clinicopathological and treatment related factors to colorectal cancer. All this information were retrieved from the client's registration book and from an individual patient card without mentioning the name of the clients from (2013-2017).

	Code	
	Date of confirmed diagnosis	
Patient-related factors		
1	Age	---------- years
2	Sex	1. Male 2. Female
3	Family history	1. Yes 2. No
4	Region	1. Amhara 2. Oromiya 3. Tigray 4. SNNP 5. Others
5	Place of residence	1. Urban 2. Rural
6	Marital status	1.Single 2. Married 3. Widowed 4. Divorced
7	Insurance	1. Insured 2. Uninsured
8	Smoking status	1.Yes 2.No
9	Alcohol consumption	1.Yes 2. No
10	Body mass index	Weight ----------Kg Height ----------m ----------Kg/m^2
11	Comorbidity	1. Yes 2. No

12	If `yes` specify	----------
	Clinicopathological factors	
13	The primary site of the tumor	1. Colon 2. rectum
14	Stage of cancer at diagnosis	1. Stage I 2. Stage II 3. Stage III 4. Stage IV 5. Unknown
15	Grades of cancer	1. Local 2. Regional 3. Advanced
16	Histologic type	1.Adenocarcinoma 2. mucinous carcinoma 3. Signet-ring-cell carcinoma 4. Unknown
	Treatment factors	
17	Radiotherapy alone	1. Yes 2. No
18	Surgical treatment alone	1. Yes 2. No
19	Chemotherapy alone	1. Yes 2. No
20	Surgery plus chemotherapy as adjuvant	1. Yes 2. No
21	Radiation as neo-adjuvant to surgery	1. Yes 2. No
22	Surgery plus chemotherapy plus radiation	1. Yes 2. No
23	Status of the patient during the last contact	1. Censored 2. Dead
24	Date of the last contact	

Annex 4: Charles comorbidity index

Based on the International Classification of Diseases code 10, each condition is assigned with a score of 1, 2, 3 or 6 associated with risk of dying.

Conditions

Acute Myocardial Infarction

Congestive Heart Failure

Peripheral Vascular Disease

Cerebrovascular Disease

Dementia

Chronic Obstructive Pulmonary Disease or other Respiratory diseases

Rheumatic-like Diseases

Ulcers of the Digestive System

Liver Disease – Mild

Diabetes - No Chronic Complications

Diabetes with Chronic Complications

Hemiplegia or Paraplegia

Renal (Kidney) Disease

Any malignancy including lymphoma and leukemia

Moderate to Severe Liver Disease

Cancer (Metastatic - secondary)

HIV / AIDS

DECLARATION

I the undersigned declare and affirm that this thesis entitled, **"Survival status and predictors of mortality among colorectal cancer patients in Tikur Anbessa Specialized Hospital: a retrospective cohort study"** is my own work. I have followed all ethical principles of scholarship in the preparation of this thesis; all scholarly matter that is included in the proposal has been given recognition through citation. I affirm that I have cited and referenced all sources used in this document. Every effort has been made to avoid plagiarism in the preparation of this thesis.

INVESTIGATOR

NAME	SIGNATURE	DATE
Bantalem Tilaye	_____	_____

This research thesis has been submitted for examination with my/our approval as:

RESEARCH ADVISORS:

NAME	SIGNATURE	DATE
Mr. Fekadu Aga	_____	_____
Mr. Tefera Mulugeta	_____	_____