ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

DETERMINANTS OF SURVIVAL, SURVIVAL TIME AND RECURRENCE AFTER SURGERY AMONG COLON CANCER PATIENTS AT TIKUR ANBESSA HOSPITAL, ADDIS ABABA , ETHIOPIA , RETROSPECTIVE COHORT STUDY

BY- SARA TEKLEWOLD (BSc)

ADVISORS- Dr. MULUKEN GIZAW (Ph.D.)

Mr. AWGICHEW KIFLE (Ph.D. CANDIDATE)

Dr. EDOM SEIFE (MD, ONCOLOGIST)

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Acronyms

AAPBCP- Addis Ababa Population- Based Cancer Registry

AHR- Adjusted Hazard Ratio

APC- Adenomatous Polyposis Coli

BLH- Black Lion Hospital

BMI- Body Mass Index

BSc- Bachelor of Science

CHR- Crude Hazard Ratio

CRC- Colorectal Cancer

DALYs- Disability Adjusted Life Years

GLOBOCAN- Global Organization Board of Cancer Association Network

IBD- Inflammation of Bowel Disease

INCT- International Network on Cancer Treatment

PH- Proportional Hazard

SIR-Standardized Incidence Ratio

SPSS - Statistical Package for Social Science

TASH- Tikur Anbessa Specialized Hospital

WHO- World Health Organization

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Abstract

Background: Colon cancer is cancer of the large intestine that originates from the colonic epithelial cells that line the lumen of the intestine. It is the fourth most common and fatal cancer worldwide. Globally there were nearly 1.2 million incident cases and over half a million deaths from colon cancer in 2020. In Ethiopia colon cancer is the 5th leading cause of death. Lack of timely seeking of medical help and organized screening practice for early identification of diseases combined with lack of access to curative and palliative care has become reasons for the high burden of premature death in the country. Understanding the survival time and determinants of survival is crucial in developing effective strategies to improve patient outcomes and reduce mortality rates in this setting.

Objectives:-To determine five year survival time and associated factors among colon cancer patients at Tikur Anibessa hospital, Addis Ababa, from January 1, 2013 up to December 31, 2018.

Methods: Institutional based retrospective cohort study from 2013-2018 at Tikur Anibessa hospital using medical records and phone call confirmation. Data was collected on the socio-demographic, survival time and determinant factors for colon cancer. Data was entered using Epi-data and analyzed using SPSS version 27. To fit for the presence of covariate differences, a Kaplan Meier curve with a log rank test was employed, and a cox regression was fitted to identify predictors of survival time. Histological conformational date was used as date of diagnosis. The survival time was determined from the date of diagnosis until death occurred. Date of last contact was used for those date of death wasn't ascertained.

Result: The median age of study participants was 49.2± 17.32 years. Median survival time was 2.5 years (95% CI; 2.12, 2.91). The first, three and five year survival was 82.8%, 43.6% and 24.9% respectively. 54.1% of study participants were male and 22.5% of them were diagnosed at stage IV. Receiving treatment using both surgery and chemotherapy [AHR=0.45, 95% CI; 0.31, 0.67], absence of recurrence after surgery [AHR=0.16, 95% CI; 0.09, 0.27], number of lymph nodes removed <12 [AHR=0.70 95%CI; 0.52, 0.94] and having Proctocolectomy surgery [AHR= 2.29, 95% CI; 1.25, 4.19] were predictors of survival time.

Conclusion: Initiation of screening programs for early presentation, using combined treatment modalities and anticipation of recurrence through timely follow-up for the impediment of metastasis plays a key role in increasing the survival time of colon cancer patients.

1. Introduction

1.1 Background

The term "cancer" refers to any condition in which the body's cells develop out of control and spread to other areas of the body (1). As the world's leading cause of mortality resulting in 10 million cancer deaths, and an estimated 19.3 million new cases in 2020; it is becoming a growing burden and evolving into a significant public health problem in many middle and low- income countries, including Ethiopia (2, 3).

Colon cancer is cancer of the large intestine that originates from the colonic epithelial cells that line in the lumen of the intestine, beginning with an aberrant crypt as an end result of multistep neoplasia, which evolves into early to advanced adenoma that extends over several years (4, 5).

Colon cancer is the fourth most frequent and the fifth lethal cancer in the world.(6) The majority of cancer cases are sporadic, with only 20 to 30% of patients having a family history (7). Adenocarcinoma accounts for almost 95% of colon cancer cases; the remaining is caused by carcinoid, malignant melanoma, sarcoma, lymphoma or squamous cell carcinoma (8).

The risk of colon cancer increases with people with diabetics, consuming red and processed meat, and smoking, Alcohol drinking, being obese, physical inactivity, low consumption of fruits, vegetables, calcium, folate and fibers (9,10). Cancer survival is associated with increased age, stage, histological type, tumor recurrence and treatment modality (11–13). Essential parameters for colon cancer prevention and treatment efforts must take into account identification of the phytochemical components that target oxidative stress of plant food sources (14).

With greater diagnostic precision and the ability to determine the tumor's location, colonoscopy is the gold standard for the detection of colon cancer. It is the only screening method that offers both a therapeutic effect and a diagnosis (4). Colonoscopy being time and resource consuming; Non-invasive techniques especially fecal occult blood tests mainly the immunological tests are used primary for its accuracy and specificity in detecting advanced adenomas (15).

Surgical resection is the initial treatment and provides over 90% cure rate at early stage (5). However, recurrence was seen in many as 50% of patients after curative surgery (16). Neo-adjuvant, targeted therapy, and palliative chemotherapy are used for advanced stages (17). Surgical complications like colorectal anastomosis after surgery for colon cancer remain a significant problem, resulting in mortality and morbidity in Ethiopia (18).

Early identification at an earlier stage is highly treatable and can be cured by standard therapies.(19) In Ethiopia for most cases colonoscopy was performed for a diagnostic indication for the signs of Rectal bleeding, altered bowel habits, and abdominal pain but screening colonoscopy is not well developed because of the challenges in the awareness and knowledge of early detection, cost issues and lack of implementation of non-invasive procedures for asymptomatic patients (20–22).

1.2 Statement of the problem

Colon cancer is one of the most prevalent and fatal cancers in the world (10). Globally, there were nearly 1.2 million incident cases and over half a million deaths from colon cancer in 2020 (6). Along with rectal cancer (Colorectal), it is the second leading cause of mortality and third in incident cases, nearly 2 million cases worldwide in both sexes. It causes 9.4% of all cancer deaths and is responsible for 10% of the world's cancer incidence (23).

The global number of new colon cancer cases is predicted to reach 1.92 million in 2040. The increase in incidence is the result of shifting lifestyle and diet towards westernization that is attributed to increased exposure to environmental risk factors (24). Due to this at the initial time of diagnosis 20 - 25% of patients present with distant organ metastasis (25).

Nearly 24,711 new cases are anticipated to occur annually in sub-Saharan Africa, with the crude incidence for both men and women being 4.04 per 100,000 population (26). According to the International Agency for cancer research, incident cases are projected to double by 2030 (27). The survival rate was less than 8-30% in most sub-Saharan countries, all characterized by limited availability and accessibility to curative treatments (28). The five-year overall survival for Uganda was (4.5%), Ghana (16%), Kenya (19.9%), and Benin (21.2%) (29,30). Recurrence after curative surgery is a major factor affecting long term survival and is estimated to be 22.5% at five years (31).

In Ethiopia, colon cancer is one of the five most deadly cancers and the 5th leading cause of death. There were an estimated 3,079 new cases of colon cancer in 2020 (32,33). Colorectal cancer is the first and most prevalent type in the male population, with an estimated 2,632 new cases in 2015 (34). A five-year survival study revealed that the survival rate was 18.1%, with a median survival time of 34.8 months. Among those with colon cancer, those who were diagnosed with rectal cancer had a 76% increased risk of dying (26). Another study done at TASH revealed a survival rate of 33% with a median survival time was 39 months (19), and about two third (68.1%) of the tumor were located on the colon (23).

Despite the increasing societal and economic progress, mortality and incidence rates are still rising sharply in low- and middle-income nations (26) due to sedentary lifestyles, changes in diet intake, and significant costs of diagnostic and treatment services (12). In those countries, including Ethiopia, patients visit the health care facilities late after the disease has progressed, and resulted in poor prognosis (23). The absence of health education and awareness creation, easy access to surgical treatments, chemotherapy, and palliative care, as well as the unavailability of a national screening program for early identification of diseases in decreasing morbidity and mortality, are some of the reasons for the reduced survival of colon cancer(19,20,23).

1.3 Significance of the study

To evaluate and monitor the efficacy of the care and therapy provided to cancer patients, estimating the survival pattern and recurrence time after initial therapy is important. For patients and healthcare professionals, investigating survival rate has practical implications in understanding and comprehending how the prognosis may change over time and in choosing the best treatment options.

In providing significant input for decision-makers, cancer care program managers, and health care providers to implement early detection, targeted intervention, and to make evidence-based decisions about colon cancer as well as to assist the planning systems in enhancing cancer management and control, this study will benefit greatly.

Despite enhancement in both medical and surgical therapy, cure, and recurrent rates the survival time have not improved significantly. Additionally, colon cancer remains significant public health concern and most studies are conducted to assess colorectal cancer survival and mainly the term colorectal should be abandoned due to anatomical and pathological differences (35) this study will focus primarily on determine the survival time and recurrence after surgery of patients with colon cancer and predictors that improve the quality of life and treatment effectiveness.

2. Literature review

2.1 Burden of colon cancer

More than 1.2 million people are diagnosed with colon and rectal cancer every year and more than 600,000 die from the disease (36). The prevalence has been growing dramatically resulting in 1.93 million new cases to be diagnosed and 0.94 million causes of death in 2020 representing 10% of global new case incident and 9.4% of all cancer death (23,24).

Over 5.25 million people are living with colon and rectal cancer. Worldwide it is the third leading cause of death in both sexes, with an estimated 515,637 male deaths and 419,536 female deaths by 2020, with 54.2% occurring in Asia, 26.2% in Europe, and 4.6% in Africa (24). Unfortunately nearly 40% of deaths from rectal cancer were misclassified as colon cancer in the United States (37).

In 2020 there were an estimated 1.15 million new cases of colon cancer and these numbers are predicted to increase to 1.92 million new cases. The majority of the cancer cases occur in adults age 50 and older only 12% was diagnosed in individuals who are younger than age 50 (6,37).

Incident cases vary by country level Hungary, Slovakia, Norway, Netherlands and Denmark have the highest age-standardized incidence rates whereas Guinea, Gambia, Bangladesh, Bhutan, and Burkina Faso have the lowest age-standardized incident rates (24).

Africa has the lowest increasing age-specific incident rate 6.3 per 100,000 followed by Asia and Latin America. Western Africa showed the lowest age-standardized incident cases 4.5 and 3.8 per 100,000 for men and women respectively and the lowest mortality in the world (4).

According to the Global Buren of Cancer study (GLOBOCAN), 2020 report colon cancer was the 5th leading cause of death and one of the four most lethal cancer types in Ethiopia (32). A study showing the burden of mortality using the Addis Ababa Mortality Surveillance Program cancer was responsible for 11% of all deaths studied. From those GI malignancies (Bowel cancer) account for 7% in males and 4.8% in females of total deaths (38). and about two-thirds 68.1% of the patients had tumors located on the colon (23).

Colon with rectal cancer has the highest age-standardized incidence rate accounting for 21% in both genders, (61% in males and 64% in females) and the highest disability-adjusted life years (DALYs) of 54% in 2019 (33). Retrospective cohort study done in northwest Ethiopia showed that the overall incidence of colorectal cancer mortality to be 22.5 per 100 person-years. Delay to confirm diagnosis, delay to first health care visit and having recurrence after treatment was associated with mortality (39). A cross-sectional study done in Tikur Anbessa specialized Hospital (TASH) showed the prevalence of colorectal cancer to be 3.1% from all cancer types that were included in the study (40).

2.2 Factors associated with colon cancer

Genetic and environmental factors take part in the etiology of colon cancer.

Genetic factors

About three-quarters of colon cancer patients have no family history, and the majority of patients have sporadic cancer types. Among colon cancer patients 35-40% of them exhibit a propensity to a hereditable component. The average lifetime risk for most of western population is in the range of 3-5% (37). The risk increases if more than one family member is afflicted. The risk doubles if first-degree family member with colon cancer was diagnosed a 50-70 years of age and triples when diagnosed under 50 years of age. Having a positive family history of colon cancer has role in 15-20% of patients (4).

Socio- demographic characteristics

Despite the higher incidence in men for colon cancer, the lifetime risk is comparable in both genders, but women have a longer life expectancy (37). The global incidence rate in men is 44% higher than that in women. 13.1 colon cancer cases are diagnosed in 100,000 individuals in men and 10.0 cases per 100,000 individuals in women (24). The risk of colon cancer increases with age the incidence increases by about 30% until the age of 50 (37). The incidence is now increasing in younger adult age groups 30-40 years of age due to ignoring of their symptoms and changes in lifestyle (41). A study done at TASH showed patients aged 70 and over were 1.7times more likely to die (AHR= 1.7, 95% CI: 1.02-2.9) than those aged under 40 years old.(26). No

ethnic differences were reported but some studies showed that the incidence is higher among African Americans (blacks) and Asians (24).

Infection

Chronic colitis due to inflammation of bowel disease (IBD) is associated with an increased risk of colon cancer. It accounts for 1% of colon cancer cases. People having IBD have almost double (2.4%) risk of developing colon cancer (37). A recent meta-analysis found that individuals with colitis had a 33% to 50% lower risk, but those with Crohn's disease had no effect (42). A study showed that patients with early recurrence present with bowel obstruction (10%) and change in bowel habit in 20% of patients (16).

A study done in Netherland showed that salmonella-infected patients are more likely to develop colon cancer in the transverse section of the colon. Salmonella infection was found to significantly increase the risk of colon cancer (SIR=1.54: 95% CI: 1.09-2.10) in patients aged 60 and above (43).

Other bacteria such as Helicobacter pylori (H. pylori) which are associated with inflammation of the stomach could also be associated with colon cancer risk (37). Infection by fusobacterium nucleatum has been associated with low survival and increased resistance to chemotherapy treatment in colon cancer patients. This bacterium was detected in 15% of North American people and more than 60% of Chinese people with colon cancer (44).

Lifestyle factors

More than half (55%) of all colorectal cancers are attributable to lifestyle factors in high-income countries (37). A study done in Europe and United States estimates that 16-71% of colon cancer is attributed to lifestyle factors. Modified lifestyle factors like smoking, alcohol intake and increased body weight have been associated with an increased risk of colon cancer (4).

Having a history of alcohol consumption showed to have an association with the mortality of any cancer type. (38) A study done at TASH non-Alcohol consumers survives 1.907 than alcohol consumers (AHR =1.9 95% CI: 1.07-2.2) (45). Moderate consumption of alcohol (2-3 units per day) has been estimated to increase the risk by 20%. Higher consumption increases the risk by up to 50%. Prolonged heavy smoking, and intake of red meat and processed meat are also

associated with an increased risk of colon cancer (4). Smoking was associated with a 1.6 times higher risk of death than non-smokers (AHR = 1.6, 95% CI: 1.1-2.3) (26).

Consumption of a diet low in milk, whole grains, fresh fruits and vegetables, low calcium, fiber, multivitamins and vitamin D, increase the risk and are main contributors of colon cancer. Intake of red meat increases the risk 1.16 fold per 100g increase of daily intake. A daily intake of 10% per daily 10g of fiber, 300mg of calcium, or 200 ml of milk decreases the risk (5, 29).

Excess adiposity in adolescence confers a 28% greater lifetime risk for colon cancer in women. A unit increase in body mass index increases the risk of colon cancer by 2-3%. Obese men and women have about a 50% and 10% higher risk of having colon cancer (37,47).

Physical activity is strongly linked with a reduced risk of colon cancer. A low dose of aspirin and 30 minutes of daily physical activity are also associated with a lower risk of colon cancer (4). The risk of both proximal and distal colon cancers is around 25% lower in the physically active than the least active peoples. Similarly, sedentary people have 25% to 50% of increased colon cancer (37). A study done at TASH showed the survival time of colorectal patients decrease by 52.5% for those who don't do physical activity than who did do physical activity (45).

Comorbidity

Presence of comorbidity was significant predictor of colon cancer mortality (AHR=17.6, 95% CI; 17.1-23.3) patients with comorbid conditions exhibited a reduced median survival (34.0± 6.9 months) than without comorbid disorders (26,30). whereas absence of association was shown in other study done at TASH (19,23).

Patients with type 2 diabetes mellitus are more likely to develop colon cancer. It appears to be stronger in men than in women. Some studies showed that Metformin independently reduces colon cancer incidence but a randomized control trial revealed no association. Diabetes patients are no more likely to die from colon cancer than non-diabetics (37,48).

There are suggestive evidences with HIV/AIDS patients, that there is an increased risk of colonic neoplasia and an earlier age of onset (49).

2.3 Survival time of colon cancer

Several studies have controversial reports regarding the survival of colon cancer depending on the difference in outcome, prognosis, and clinical response to chemotherapy (25). Different studies showed that the survival of colon cancer depends on many factors. Laterality, stage, and type of cancer are listed (50).

Laterality (sidedness)

Colon cancers are typically classified as distal or left-sided when they arise distally from the splenic flexure and as proximal or right when they originate from colon parts proximal to the splenic flexure (7). Right-sided colon cancer had a median overall survival of 87 months (67.6%). However, left-sided colon cancer had a higher colon cancer-specific survival rate (72.5%). (AHR= 0.87; 95% CI: 0.85-0.89) (50).

Stage of cancer

A study done in the United States showed that the median overall survival time for stage III and stage IV was 101 and 17 months with overall survival of 60.2% of the 5 years entire cohort (50). In 2019 the relative survival rate for CRC was 64% at 5 years but declines to 14% for those diagnosed with distant stages (37).

In Germany, the five-year survival rate for patients with stage I cancer ranges from more than 90% to slightly more than 10% for those with stage IV disease (36).

A retrospective cohort study done in china comparing stage III and stage IV colon cancer patients, showed that stage III patients are at a higher risk of death than more advanced stages (51). A study done using African cancer registration network (AFCRN) the overall survival at third year and at five year to be found 50.4% and 43.5% (29).

A study done in Uganda for the survival of colorectal cancer showed the three -year survival to be 33.3%. Patients in stage IV were associated with increased mortality. Treatment approaches with surgery alone or in combination with chemotherapy improves the survival (28).

A study done in Addis Ababa for colorectal cancer showed the overall 5-year survival was 18.1% with a median survival time of 34.8 months. the median survival time who were diagnosed with stage I, II, and IV at baseline survived longer than those diagnosed with stage IV at baseline (26).

Study done at TASH showed that the death rate for those diagnosed in stage IV was 2.7 times higher than for those diagnosed in stages I and II (AHR=2.66.95%CI;1.44-4.91). Mucinous cell carcinoma had a nearly 5-fold higher mortality rate than adenocarcinoma. (AHR = 4.92,95% CI; 1.27-4.19) (23) Patients with poorly differentiated tumor grades had a 1.7-fold increased risk of death compared to those with well-differentiated tumors (AHR= 1.7, 95% CI: 1.17-2.4) (26).

Recurrence after surgery

A study done in United States showed that the median time from recurrence to death was 13.3 months. 14.3% of six years overall survival following recurrence was observed in stage II patients. Age at recurrence is significantly associated with survival time (52).

A study done at France reveled the five year cumulative rate was 12.8% for local recurrence and distance metastasis. Emergency surgery was also associated with increase local recurrence risk (53).

A study done at Tunisia revealed that the recurrence rate after surgery was 44.6% at five years. Distal margin ≤ 2cm, lymph node metastasis, tumor stenosis and partial invasion (HR=3, 95% CI:1.1-1.9) were associated with risk of recurrence (54).

A study done in north western Ethiopia showed that patient recurrence after treatment has been associated with mortality (AHR=1.61; 95% CI, 1.05-2.47) (39). Local recurrence was the reason for tumor board presentation in 45% and the recurrence rate was 1% at TASH (45).

Conceptual frame work

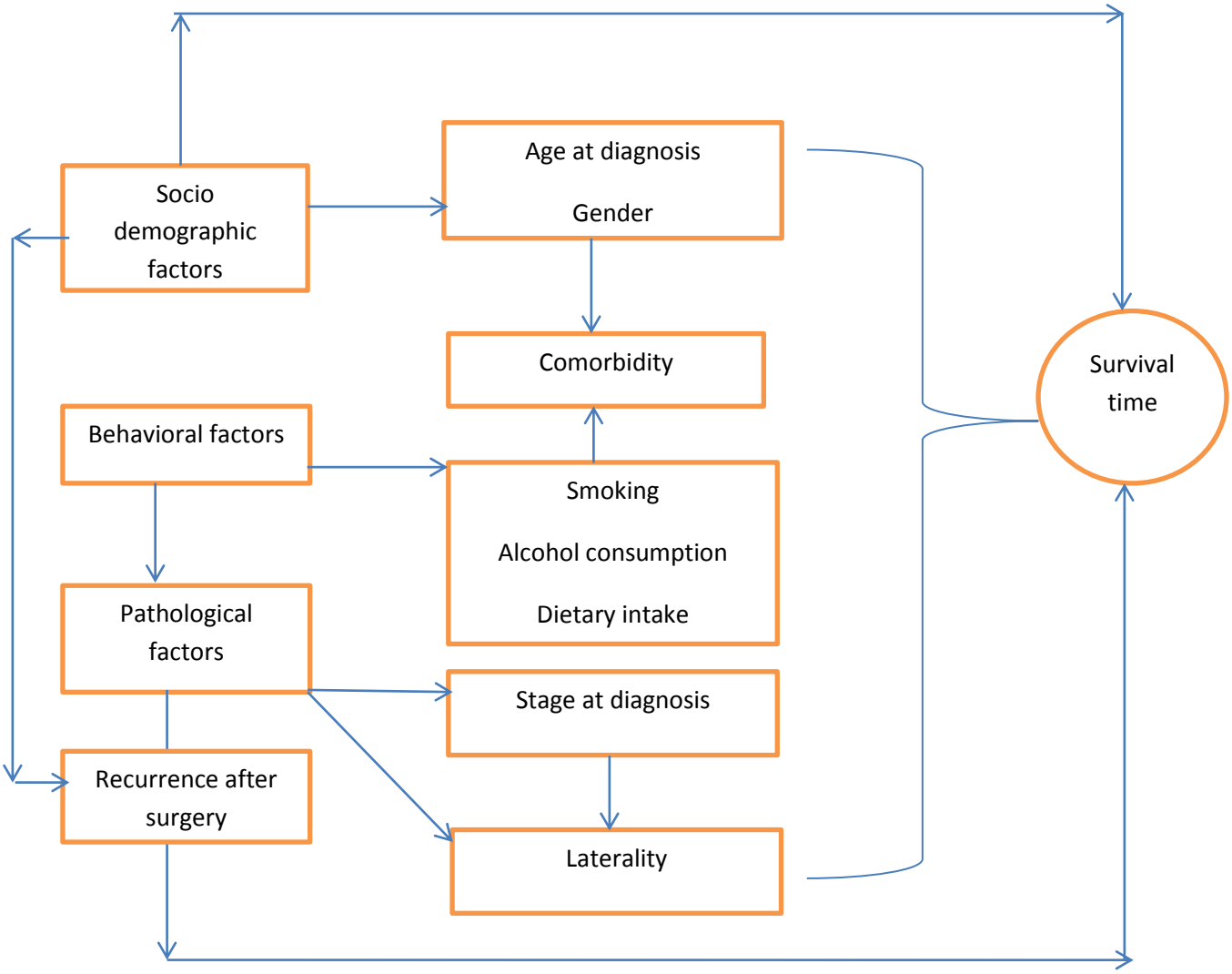


Figure 1 Conceptual frame work for determinants of survival among colon cancer patients at TASH.

3. Objectives

3.1 General objective

- To determine five-year survival time and its associated factors among colon cancer patients at Tikur Anbessa Hospital, Addis Ababa, Ethiopia from January 1, 2013 up to December 31, 2018.

3.2 Specific objectives

- To estimate five year survival of colon cancer patients at Tikur Anbessa Specialized Hospital, Ethiopia.
- To estimate the recurrence time after surgery among colon cancer patients at Tikur Anbessa Specialized Hospital, Ethiopia.
- To identify predictors of survival time among colon cancer patients at Tikur Anbessa Specialized Hospital, Ethiopia.

4. Methodology

4. 1 Study Area and Period

This study was conducted on data from January 1st, 2013 to December 31, 2018 at Tikur Anbessa specialized hospital, which is situated in Addis Ababa, the nation's capital of Ethiopia. Tikur Anbessa is a teaching, tertiary level generalized referral hospital with approximately 800 inpatients beds. It was established in the early 1960's and is the biggest and most renowned public hospital. (55)

TASH is now the main teaching hospital for both clinical and preclinical training of most disciplines. TASH Oncology Department occupies all treatment coverage's related to oncologic problems. In this context, TASH Oncology Department is the center of excellence for cancer treatment in which radiotherapy, surgery, chemotherapy, and comprehensive care services are delivered for cancer patients.(26)

TASH strives to become a center of excellence in the detection, management and care of patients with cancer. The hospital wants to create a comprehensive cancer care program that includes cancer registry, standard treatment and palliative care with the help of Ethiopians governmental institutions, non- governmental organizations and international partners, including International Network on Cancer Treatment (INCTR). (55)

4.2 Study Design

Institutional based, retrospective cohort study was used to assess the survival time among colon cancer patients at Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia.

4.3 Source Population

All colon cancer patients found at Tikur Anbessa hospital.

4.4 Study Population

All histologically confirmed medical records of colon cancer patients at Tikur Anbessa hospital oncology and surgical departments of those were diagnosed from January 1, 2013 up to December 31, 2018, who fulfill eligibility criteria.

4.5 Inclusion and Exclusion Criteria

→ All colon cancer patients who were diagnosed and enrolled in TASH during the time period (2013- 2018) were included.

- Incomplete patient charts regarding to important variables,
- Patients who registered during the time period but their diagnosis is prior to that, and
- Patients with a diagnosis of pre-cancer lesion were excluded.

4.6 Sample Size Determination

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

$$d = (Z_{\alpha/2} + Z_{\beta})^2 \frac{4}{ln\Delta^2}$$

Assuming that Δ= hazard ratio is constant in time. For two sided log-rank test (H0: Δ = 1; HA: Δ ≠ 1).then the required total number of patients can be calculated as $\frac{d}{probaility\ of\ an\ event}$ previously conducted study (19) showed that survival function *s(t)=0.33*. Thus Δ = *-log s(t)*= -log(0.33)=1.108. $\beta = 20\%, \alpha = 5\%$, hazard ratio of 1.108 the required number of events will be $d = (1.96 + 0.84)^2 \frac{4}{ln(1.108)^2} \approx 153$ then

$n = \frac{d}{probaility\ of\ an\ event} = \frac{153}{0.67} = 228$. Adjusting for a loss of 20%, $n = \frac{n}{1-loss} = \frac{228}{1-0.2} = 285$

The required sample size was 285 however; all colon cancer patients diagnosed between January 2013 to December 2018 and those that fulfill the eligibility criteria were included.

4.7 Variables in the Study

4.7.1 Dependent variable

Survival time of colon cancer: - from first confirmed diagnosis to death that was measured in years.

4.7.2 Independent variables

- Sex
- Age
- Family history
- Alcohol consumption
- Residency
- Marital status
- Smoking status
- BMI
- Infection
- Comorbidity
- Site and stage of tumor
- Histology type
- Tumor grade
- Treatment modality
- Laterality
- Recurrence after surgery

4.8 Operational Definitions

Event: the death of colon cancer patients

Censored: patients who survived beyond the end of the follow-up period or patients who were lost to follow-up

Survival: lack of death of colon cancer patients after being diagnosis in the study period.

Date of diagnosis: the date at which histological confirmation was made for colon cancer patients.

Date of Last contact: the last date of colon cancer patients recorded on the chart.

Time to event: the time in the study period from the diagnosis of colon cancer until death.

Infection: presence of colitis, H. pylori, fusobacterium nucleatum and salmonella on colon cancer patients.

Comorbidity: according to international classification of disease -10, disease from Charleson comorbidity index was used during data collection. The co-occurrence of any of the disease with colon cancer at the time of diagnosis was labeled as yes response.

Recurrence: development of any new malignant lesion after initial resection was judged to be curative after colon cancer diagnosis.

4.9 Data Collection Tools and Procedures

A data extraction tool that was adapted from various literatures (39, 47) were used to observe and record the data that was currently present in the medical records which consisted of socio-demographic factors, clinical and pathological related factors, and treatment-related factors. Data was collected from April 15 to May 20, 2023. The charts of all colon cancer patients at Tikur Anbessa hospital, who were diagnosed between January 1, 2013 and December 31, 2018, were retrieved, and baseline and follow-up records and phone call verification supplements were identified from cancer registries using medical record numbers, and study participants were selected accordingly. Histological conformational date was used as date of diagnosis. The survival time was determined from the date of diagnosis until death occurred. Date of last contact was used for those date of death wasn't ascertained. Before data collection, three BSC nurses working at the cancer center and a supervisor received training on the record review for two days. Every task were overseen by the principal investigator, and in the absence of principal investigator, the supervisor handled the work. The primary investigator and supervisor compiled the filed review checklist that was gathered and was checked for completeness on daily basis.

4.10 Data Processing and Analysis

Data was coded, manually checked, entered by double entry and cleaned by Epi data software and exported to SPSS version 27 for analysis. Basic descriptive analysis was done. Survival table was used to estimate probability of survival after a colon cancer diagnosis at various time intervals. Kaplan Meier curve with log rank test was used to fit for the presence of difference among the covariates. To identify predictors of survival time, Cox regression was fitted.

The subset of covariates were selected after Cox-PH was fitted first by fitting a multivariable model containing all variables significantly in the bivariate analysis at (P value < 0.25) as well as any other variable not selected but judged to be of clinical importance. Backward selection was used to examine the effect of explanatory variables at 5% of significance and each of the non-significant variables using forward selection the model was fitted at 5% of significance to determine the final variables. Necessary assumptions were checked by Schoenfeld residual test.

4.11 Ethical Considerations

The research ethics committee of the school of public health at Addis Ababa University provided the ethical approval and letter of permission. The medical director of Tikur Anbessa Hospital and the cancer treatment center were asked for consent permission. Prior to the phone conversation, patients' verbal consent were sought. In order to ensure the confidentiality of the data throughout the study, names were not used for identification, and the data was only utilized for the planned study.

4.12 Dissemination Plan

The final finding of this study be disseminated to interested parties including Addis Ababa university school of public health department of preventive medicine, for Tikur Anbessa specialized hospital oncology center and as well as for the community.

5. Results

5.1 Socio-demographic characteristics

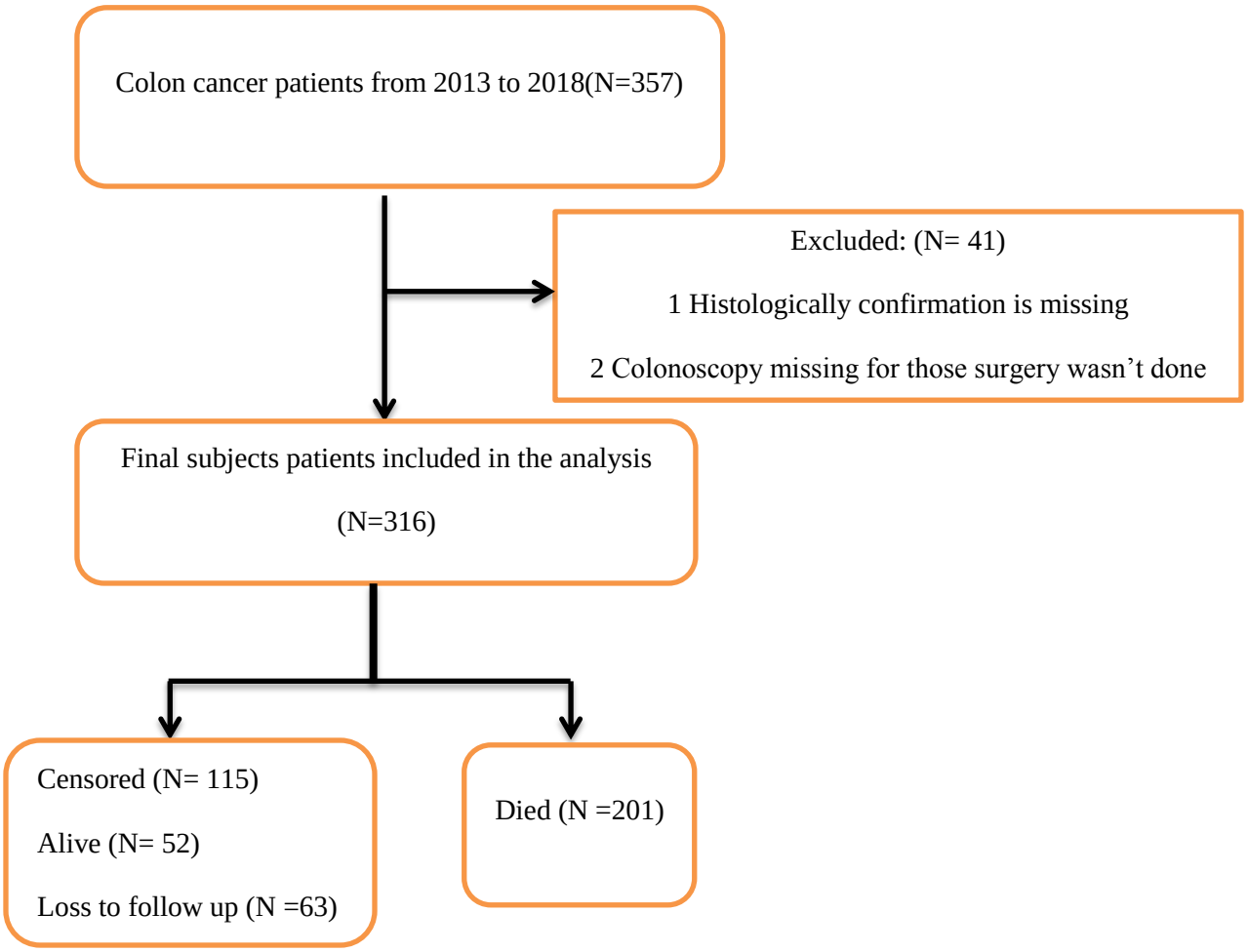


Figure 2 flowchart of patient selection.

Out of the participants 171(54.1%) of them were males, 78(24.7%) of them are >60 years of age, 34(10.8%) of them had family history, 235(74.4%) were married, 172(54.4%) were from Addis Ababa and 211(66.8%) were orthodox religion followers.

Table 1Socio-demographic characterestics of colon cancer patients at TASH, 2013-2018.

Variable	Category	Frequency	Percentage
Age	<30	27	8.5
	30-39	69	21.8
	40-49	67	21.2
	50-59	75	23.7
	.>60	78	24.7
Sex	Male	171	54.1
	Female	145	45.9
Family history	Yes	34	10.8
	No	282	89.2
Marital status	Single	37	11.7
	Married	235	74.4
	Widowed	34	10.8
	Separated	10	3.2
Residency	In Addis Ababa	172	54.4
	Outside Addis Ababa	144	45.6
Religion	Muslim	65	20.6
	Orthodox	211	66.8
	Protestant	39	12.3
	Other	1	0.3

5.2 Behavioral and life style factors

About 22.5% and 5.4% of patients had a history of Alcohol consumption and smoking status respectively. 260(82.3%) of them had normal BMI, 77(24.4%) of the participants had comorbidity from them 27(35.1%) of them had Hypertension, 19(24.7%) of them had DM and HTN, 14(18.2%) of them had DM, 6(7.8%) had RVI, 11(14.3%) of them had anemia, cardiac and asthma. 50(76.9%) had history of H.pylori infection, 10(15.4%)of them had history of IBD.

Table 2 Behavioral and life style factors of colon cancer patients at TASH 2013-2018

Variable	Category	Frequency	Percentage
Alcohol consumption	Yes	71	22.5
	No	245	77.5
Smoking status	Yes	17	5.4
	No	299	94.6
BMI	Underweight	39	12.3
	Normal	260	82.3
	Overweight	17	5.4
Comorbidity	Yes	77	24.4
	No	239	75.6

5.3 Histological and clinical factors

Majority of the participants were diagnosed with stage II 144(45.6%), stage III 100(31.6%) and stage IV 71(22.5%) disease. Adenocarcinoma account for 241(76.3%) of the histopathology type and 180(57.0%) were well-differentiated tumor. 180(57%) of the tumor was located at the left side, 253(80.1%) of them had received both surgery and chemotherapy. Hemi-colectomy was done for 211(66.8%) of the participants and 202(66%) had margin negative.

Table 3 Histological and clinical factors of colon cancer patients at TASH, 2013- 2018

Variable	Category	Frequency	Percentage
Stage of disease	Stage I	1	0.3
	Stage II	144	45.6
	Stage III	100	31.6
	Stage IV	71	22.5
Histology type	Adenocarcinoma	241	76.3
	Mucinous carcinoma	60	19.0
	Single ring cell carcinoma	15	4.7
Tumor grade	Well-differentiated	180	57.0
	Moderately- differentiated	115	36.4
	Poorly- differentiated	21	6.6

Laterality	Right sided	136	43.0
	Left sided	180	57.0
Treatment modality	Surgical alone	53	16.8
	Chemotherapy alone	10	3.2
	Surgery and chemotherapy	253	80.1
Type of surgery done (N=306)	Sigmoid colectomy	80	25.3
	Hemi-colectomy	211	66.8
	Proctocolectomy	15	4.7
Margin (N=306)	Positive	104	34.0
	Negative	202	66.0
Lymph node removal (N =306)	≥ 12 dissected	99	31.3
	< 12 dissected	207	65.5

5.4 Reccurence after surgery

Out of the participants 306(96.8%) underwent surgery for colon cancer from those participants 224(73.2%) had colon cancer recurence. 184(60.1%) died after the cancer had reccured. Majority of the patients had distal recurrence 116(51.8%) of which 105 died, on the otherhand 108(48.2%) of them had local recurrence from which 79(35.3%) died. Majority (48.61%) of patients had Liver metastasis followed by lung metastasis (25.42%).

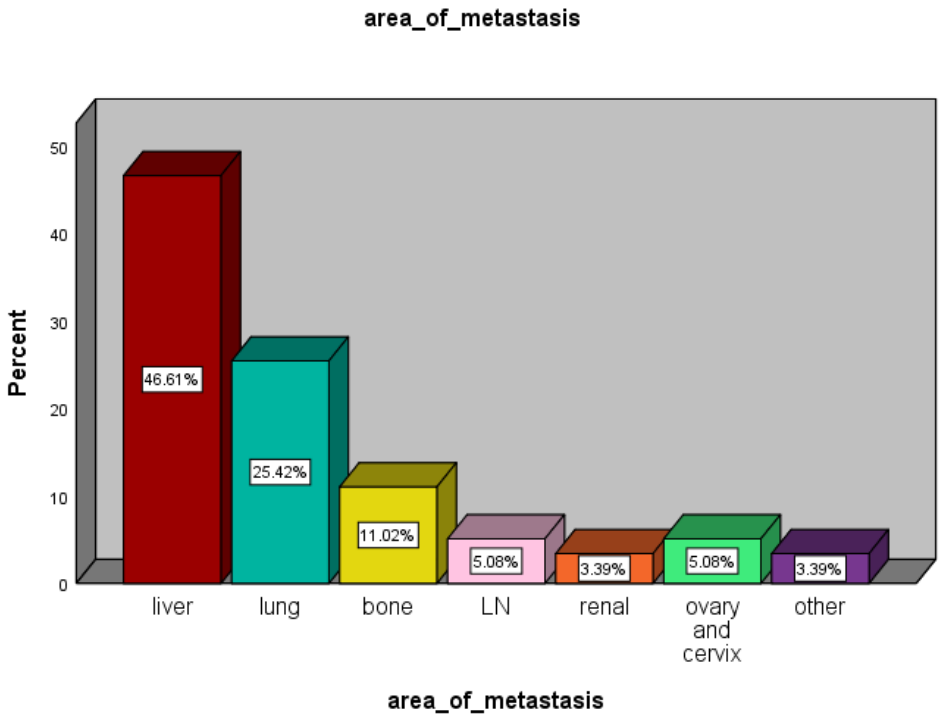


Figure 3 Area of metastesis of colon cancer patient at TASH, 2013-2018

5.4 Survival from colon cancer diagnosis to death

The median survival time was 2.5 years (95% CI; 2.12, 2.91). The five- year overall survival rate was 24.9% and the three-year overall survival was 43.6%.

The Kaplan Meir survival curve also showed that the probability of survival of patients among colon cancer patients decreases as the follow-up time increases. Majority of patients died before reaching three years of follow-up period as shown in the figure below.

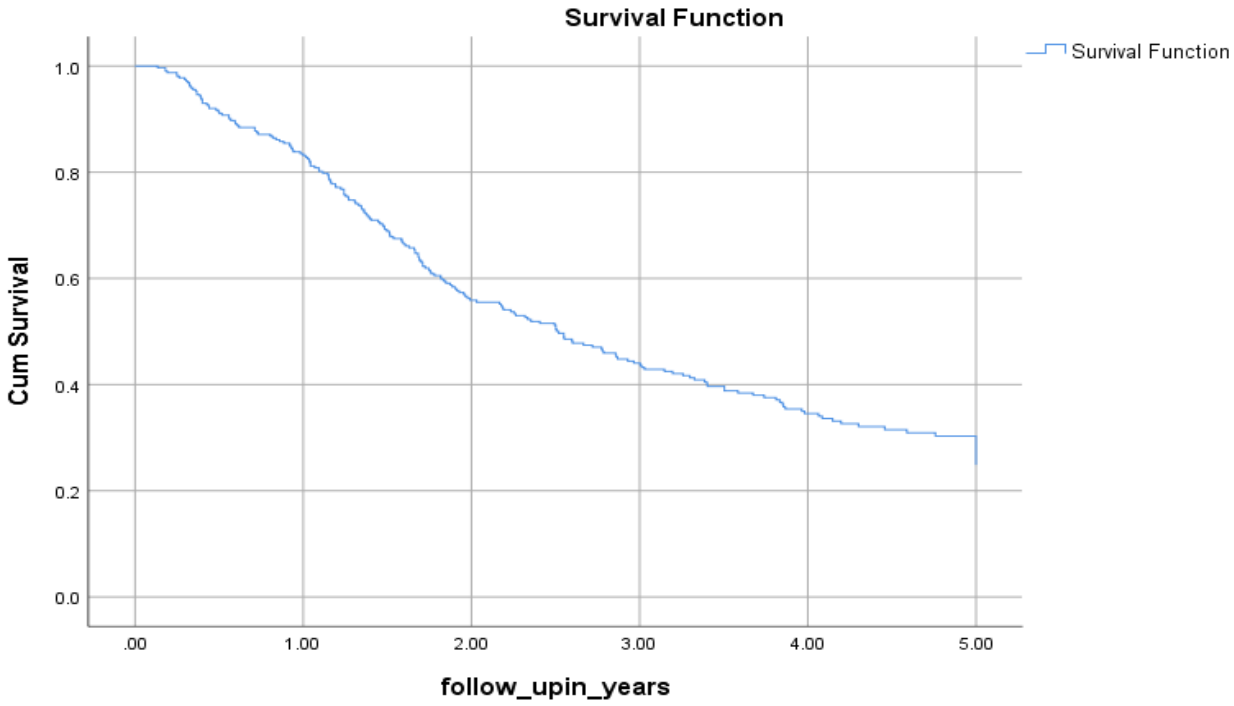
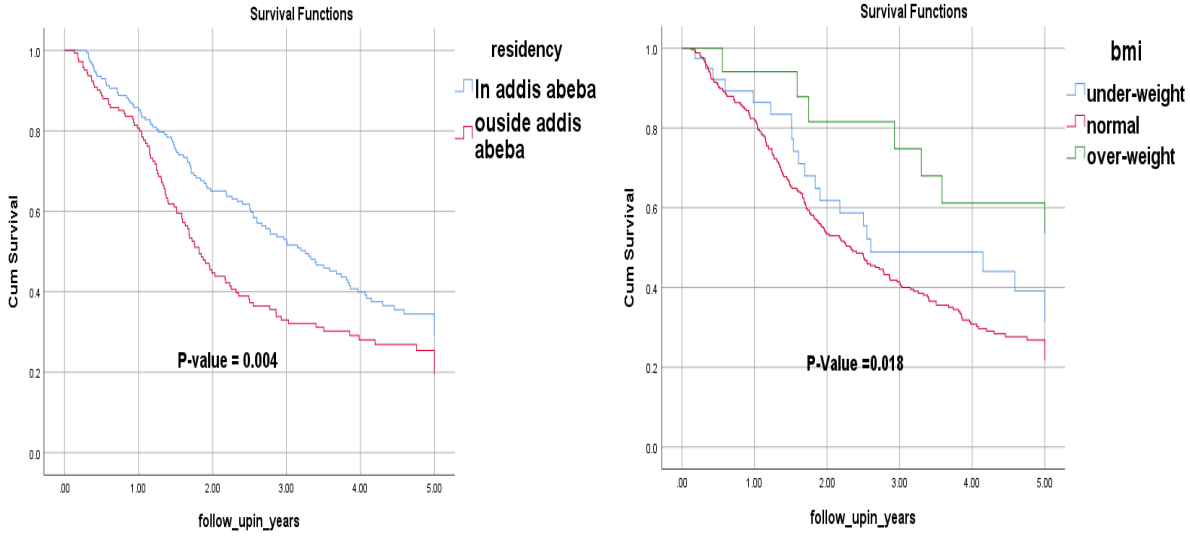


Figure 4 Kaplan Meir survival curve for survival time for colon cancer patients at TASH, 2013-2018

5.5 Survival functions among categorical variables.

In order to see the presence of difference among covariates log-rank test is used for comparing among groups. The following covariates presented on the graph below showed presence of significant difference in surviving among them. Other categories of covariates age, sex, family history, marital status, religion, alcohol consumption, smoking status, physical exercise and laterality did not show significant difference in survival experience between them.



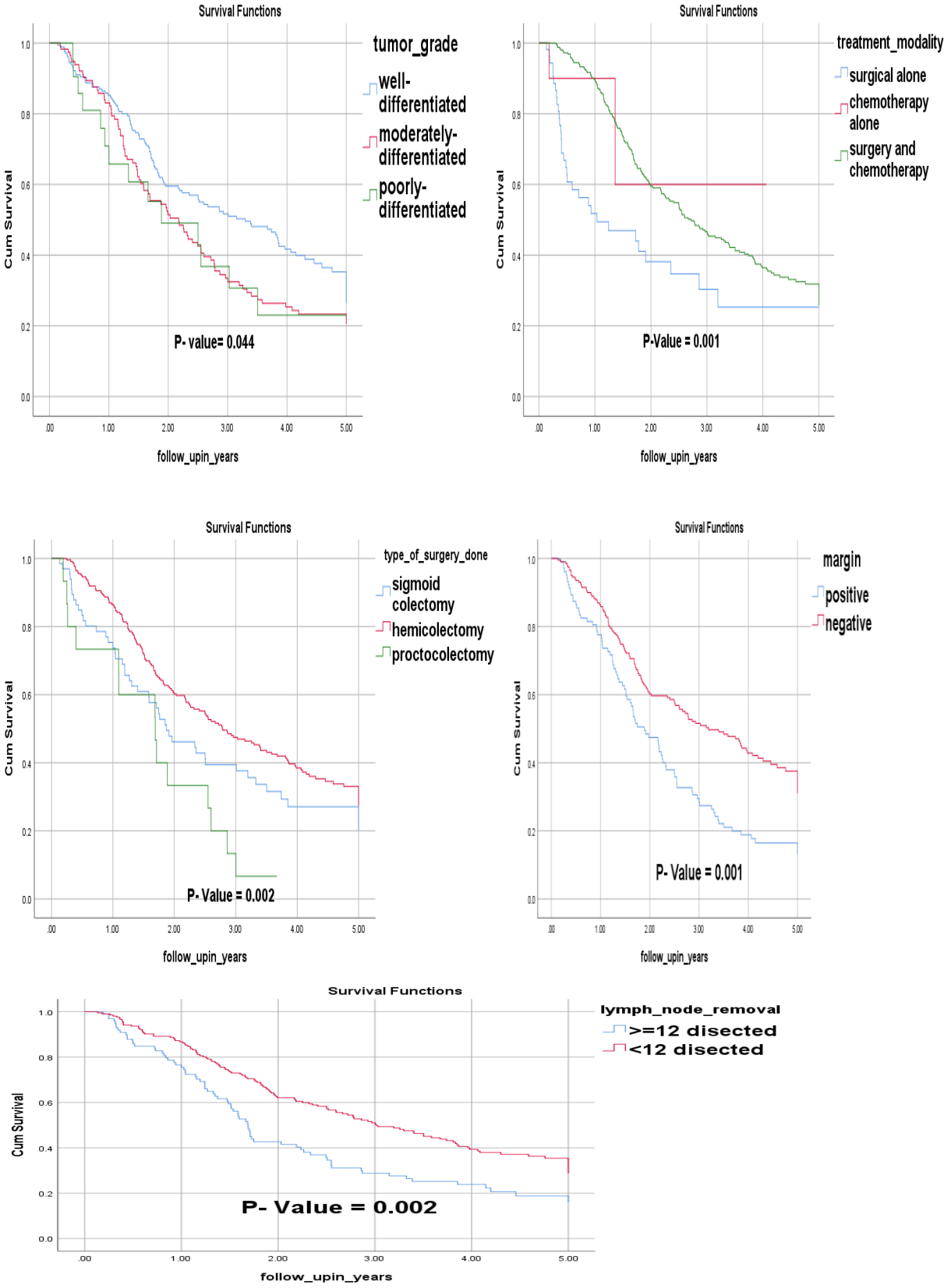


Figure 5. Log-rank test for the presence of difference in survival time among covariates

Survival found to be better in those who lived in Addis Ababa (36.0%)[p-value=0.004], those who were over-weight (47.1%)[p-value=0.018], those patients who were diagnosed at stage II (43.1%)[p-value=0.021], compare to stage III, those diagnosed at stage III (32%)[p-value=0.009], compared to stage IV (16.9%)[p-value=0.0001], those with well-differentiated tumor grade (40.6%)[p-value=0.002], those who were treated by both surgery and chemotherapy (28.2%)[p-value=0.0001], those having negative margin (39.6%)[p-value=0.0002], and those whose lymph node removed < 12 (43.9%)[p-value=0.001], with statistically significant difference.

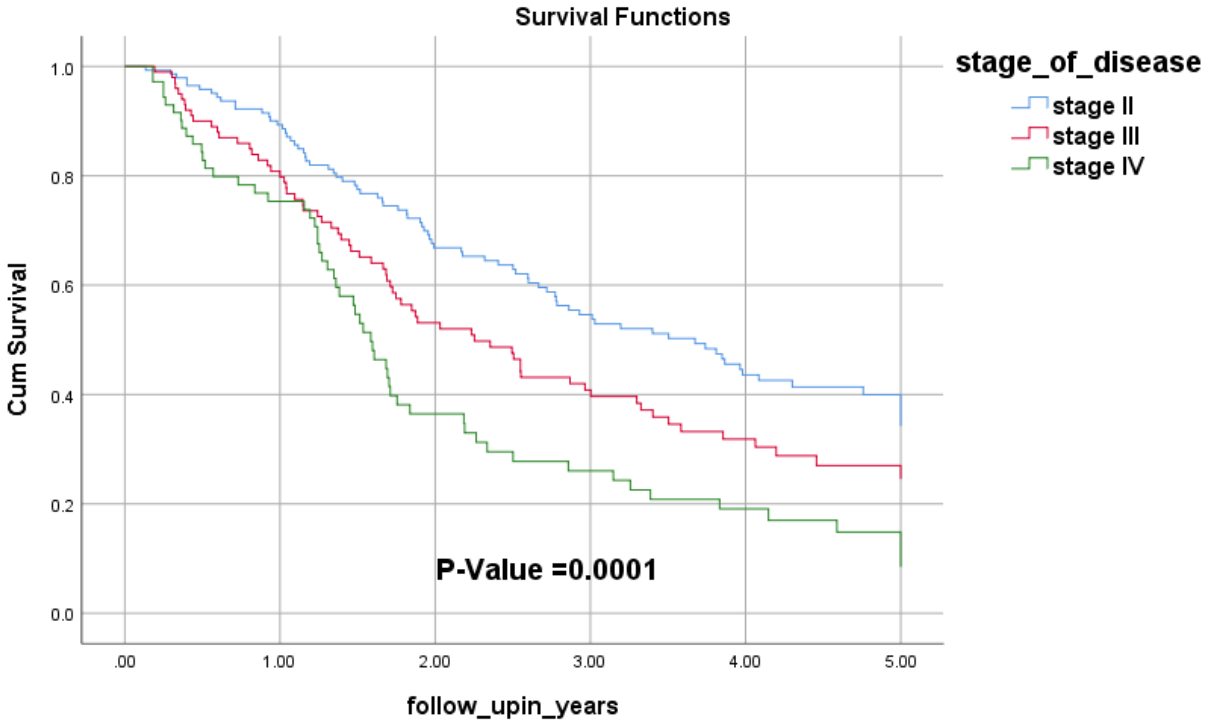


Figure 6 Kaplan Meir survival curve for survival time in different stage of disease of colon cancer patients at TASH, 2013-2018

5.6 Survival and Recurrence after surgery

The survival function against survival time for colon cancer patients undergoing surgery as initial treatment modality and the recurrence after surgery showed a statistically significant difference. The median survival for those with recurrence was 2 years [95%CI; 1.68, 2.31], and for those with local recurrence was 3 years [95%CI; 2.37, 3.62] and for distal recurrence was 2 years [95%CI; 1.71, 2.29].

The overall survival for recurrence after surgery was 14.3%, for patients without recurrence the survival was 77%, patients with local recurrence had an overall survival of 22.2% and patients with distal recurrence the survival was 6.7% at the end of the follow-up period.

Table 4 Difference in survival time of recurrence after surgery at TASH, 2013-2018

Covariates	Difference in survival experience among covariates	P-value (pair wise comparison)	Chi-square
Recurrence after surgery	Yes vs. no	0.00000001	61.350
Type of recurrence	Local vs. distal	0.000001	13.888
Area of metastasis	Renal vs. liver	0.05	3.56

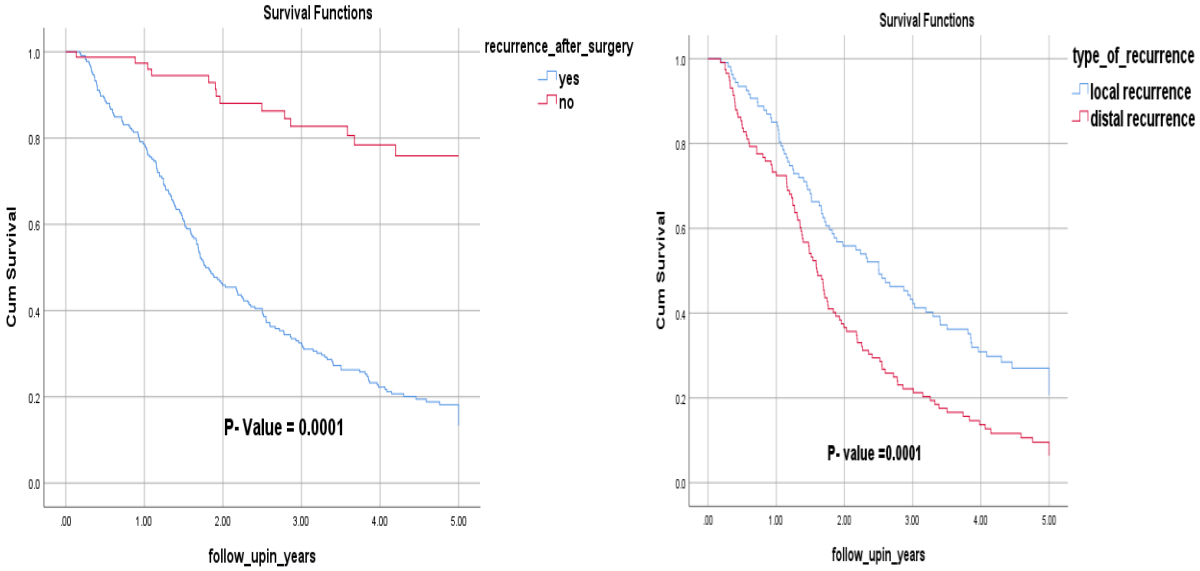


Figure 7 kaplan Meir survival curve for survival time of recurrence after surgry and type of recurrence among colon cancer patients at TASH, 2013-2018

5.7 Predictors of survival time among colon cancer patients

Cox regression model was used to examine each variable with the outcome variable in the bi-variable analysis. From the bivariate cox regression fitted residency, BMI, stage of disease, tumor grade, treatment modality, type of surgery done, margin, recurrence after surgery, and lymph node removal were found to be significant at $p < 0.25$ significance level. The proportionality of hazard assumption was fulfilled when checked using the Schoenfeld residuals [global test; p-value= 0.9275, χ^2=1.37] showing insignificant relationship between residuals and survival time

Table 5 predictors of survival among colon cancer patients at TASH, 2013-2018

Variables	CHR(95% CI)	AHR(95% CI)	P- value
Residency			
Addis Ababa	1	1	
Outside Addis Ababa	1.51(1.14, 1.98)	1.32(0.99, 1.75)	0.053
BMI			
Underweight	1	1	
Normal	1.39(0.88, 2.22)	1.35(0.83, 2.19)	0.226
Overweight	0.54(0.23, 1.29)	0.62(0.26, 1.48)	0.288
Stage of disease			
Stage II	1	1	
Stage III	1.48(1.07, 2.01)	1.01(0.66, 1.52)	0.973
Stage IV	2.29(1.62, 3.23)	1.25(0.79, 1.97)	0.452
Tumor grade			
Well-differentiated	1	1	
Moderately- differentiated	1.40(1.05, 1.87)	1.01(0.74, 1.36)	0.693
Poorly- differentiated	1.51(0.86, 2.63)	0.96(0.54, 1.72)	0.780
Treatment modality			
Surgery alone	1	1	
Chemotherapy alone	0.43(0.09, 1.72)	0.39(0.18, 1.89)	0.225
Surgery and chemotherapy	0.55(0.33, 0.71)	0.44(0.31, 0.65)	**0.0004**
Type of surgery done N=306			
Sigmoid colectomy	1	1	
hemi colectomy	0.72(0.52, 1.01)	1.89(0.63, 1.26)	0.534
Proctocolectomy	1.76(0.96, 3.22)	2.17(1.18, 4.02)	**0.013**
Margin (N=306)			
Positive	1	1	
Negative	0.55(0.41, 0.73)	0.81(0.58, 1.12)	0.178

Recurrence after surgery N= 306)			
Yes	1	1	
No	0.15(0.09, 0.26)	0.16(0.09, 0.27)	**0.00001**
Lymph node removal N=306)			
≥ 12	1	1	
< 12	0.59(0.44, 0.78)	0.62(0.46, 0.83)	**0.002**

From the table above, variables with P–value < 0.25 in the bi-variable analysis were included to the final model. Treatment modality, type of surgery done, recurrence after surgery and lymph node removal showed significant relation and predictors of survival among colon cancer patients.

The result of the multivariable analysis showed colon cancer patients who were treated by both surgery and chemotherapy had 45% better survival than patients who were treated by surgery alone after controlling for other variables[AHR=0.45, 95% CI; 0.31, 0.67].

Having Proctocolectomy surgery has a 2.29 times more likely to die than patients who undergo sigmoid colectomy [AHR= 2.29, 95% CI; 1.25, 4.19]. Patients who hadn't experience colon cancer recurrence after surgery had 16% increased survival than patients who had cancer recurrence [AHR=0.16, 95% CI; 0.09, 0.27].

Among colon cancer patients whose lymph nodes removed less than 12 had 70% better survival than patients whose lymph nodes removed ≥ 12 after controlling for other variables[AHR=0.70 95% CI; 0.52, 0.94].

6. Discussion

The main aim of this study was to determine the five-year survival and associated factors among colon cancer patients in TASH enrolled from January 1, 2013 to December 31, 2018. The covariates of treatment modality, type of surgery done, recurrence after surgery, and lymph node removal were the final predictors of survival time in the final model.

The five-year survival among colon cancer patients was 24.9%. This result is in-line with a study done in Addis Ababa 21.7% (45) on CRC patients. However the finding was lower than studies done in USA 60.2% (50), Jordan 58.2% (56), Iran 54% (57), Malaysia 43% (58) and Kenya 45.4% (30) on CRC patients. The three-year survival in this study was 43.6% which was higher than a study done in Uganda 33.3% (28). This might be due to late identification for the disease, delayed individual health-seeking behavior, and lack of advanced medical services and care for cancer patients in developing countries.

Kaplan- Meier survival curve showed the probability of survival decreases as the follow-up time increases. This was consistent with other studies done in Uganda (28), Addis Ababa (19) and Taiwan (59) showing as the follow-up time increases, the survival becomes very low.

The overall survival of colon cancer patients for stage II, stage III and stage IV was 37%, 26.8% and 9% respectively. This result is in line with study done in Uganda 35.7%, 31.2% and 4.3% (28), and much lower than study done in Germany (36), Taiwan (13), Jordan (56) and China (51) this might be due to diagnosis at later stages in this study and lack of awareness in receiving medical care.

Majority of the patients were diagnosed with late-stage disease (54.1%) and almost two-thirds of patients died at stage III and IV. This result was consistent with a study done in Tunisia (60) and Addis Ababa on CRC patients (45). It may be due to the absence of early screening using either colonoscopy or non-invasive methods for early identification of the disease and early initiation of treatment modalities with shorter waiting times.

Colon cancer patients who were treated by both surgery and chemotherapy had 45% better survival than patients who were treated by surgery alone; this result was consistent with a study done in Belgium (17) and Uganda (28); Showing that treatment with surgery alone or together with chemotherapy is associated with better survival.
Having Proctocolectomy surgery has a 2.29 [AHR= 2.29, 95% CI; 1.25, 4.19] times more likely to die than patients undergoing sigmoid colectomy. This result is inconsistent with a study done in Tunisia (60) showing undergoing sigmoid colectomy has increased risk of dying.

Out of colon cancer patients treated for surgery as an initial modality, 73.9% showed recurrence after surgery; this finding was much higher than studies done in the USA(52), Iran (11), and Morocco(61); this might be due to the difference in diagnosis, at an earlier stage of disease and time to initiation of additional therapies.

Colon cancer patients with no recurrence survived better 77%, than those whose disease recurred either distally or locally, showing consistency with a study done in northwestern Ethiopia (39), which revealed that patients having recurrence are about 1.61 times more likely to die than those without recurrence.

Patients whose lymph nodes removed less than 12 had 70% [AHR=0.70 95%CI; 0.52, 0.94] better survival than patients whose lymph nodes removed ≥ 12; this finding is inconsistent with study done in Morocco(61).

This study showed having a negative surgical margin has a significant difference with a p-value < 0.001. This was consistent with a study done in Tunisia; having a negative margin is associated with an increased risk of surviving from colon cancer (54). Moderately differentiated tumor grade also showed a significant difference with a p-value<0.05, though was not significant in the multivariable analysis. This finding was inconsistent with a study done in China (51) that a poorly differentiated tumor grade was associated with decreased survival.

7. Strength and limitation of the study

The major strength of this study was inclusion of all medical records of patients during the study period, as well as five year follow-up period, renders the findings credible.

The limitations of this study include death ascertainment via phone interview rather than mortality data, which may under or over identify death, and the commencement of diagnosis via histopathology report, which may result in a temporal lag of survival status. The other is moderately high (18.9%) lost to follow-up, which is less than the 20% considered in when determining sample size. Patients with colon cancer may die from causes other than cancer, which this study did not take into consideration.

8. Conclusion and Recommendation

The five-year survival rate was 24.9% after 60 months of follow-up. There were significant variations in groups of factors such as residency, BMI, stage of disease, tumor grade, treatment modalities, surgical margin, recurrence after surgery, type of surgery and lymph node dissection.

In the final model the variables treatment modality, type of surgery done, recurrence after surgery and lymph node removal were predictor for survival time among colon cancer patients.

With regards to the predictors, colon cancer patients who were treated by surgery and chemotherapy, who do not have a recurrence and lymph node resection less than 12 had longer survival rates, whereas having Proctocolectomy surgery had shorter survival times.

Initiation of screening programs for early presentation, using combined treatment modalities and anticipation of recurrence through timely follow-up for impediment of metastasis plays a key role in increasing the survival time of colon cancer patients.

Recommendation

The following recommendations are made based on the study's findings.

FMOH

- To initiate colon cancer screening programs for early detection and progression to advanced stages of the disease.
- Establishing oncology centers and strengthening diagnostic and therapeutic features of health-care facilities.

TASH

- The necessity to improve comprehensive patient characteristics in medical registration.
- Making advancement in treatment initiation and use of targeted therapy.
- Setting routine follow-up checking in-order to minimize recurrence after initial treatment.

Researchers

- Conducting further research to address the limitations of this study.

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Annex

I. Dummy tables

1. Socio demographic

Table 6Dummy table on socio-demographic characterestics of participants

s.no	Variables	Category	Remark
1.1	Age	1. <30 2. 30-39 3. 40-49 4. 50-59 5. >60	
1.2	Sex	1. Male 2. Female	
1.3	Family history	1. Yes 2. no	
1.4	Marital status	1. Single 2. Married 3. Widowed 4. Separated	
1.5	Residency	1. In Addis Ababa 2. Outside Addis Ababa	
1.6	Religion	1. Muslim 2. Orthodox 3. Protestant 4. Other ……..	

2. Behavioral and life style factors

Table 7 Dummy table on Behavioral and lifestyle factors of colon cancer among participants

	Variable	Category	Remark
2.1	Alcohol consumption	1. Yes 2. No	
2.2	Smoking status	1. Smoking 2. Non –smoking	
2.3	BMI	1. Under weight 2. Normal 3. Over weight	
2.4	Comorbidity	1. Yes 2. No	
2.5	Infection	1. Yes 2. No	If yes specify

3. Histological factors

Table 8 Dummy table on Histological factors of colon cancer among participants

	Variable	Category	Remark
3.0	Family history	1. Yes 2. No	
3.1	TNM Stage of disease	1. Stage I 2. Stage II 3. Stage III 4. Stage IV	
3.2	Histology type	1. Adenocarcinoma 2. Mucinous carcinoma 3. signet ring-cell carcinoma	
3.3	Tumor grade	1. Well-differentiated 2. Moderately differentiated	

		3. Poorly differentiated	
3.4	Tumor position	1. Right sided 2. Left sided	
3.5	Treatment modality	1. Surgical treatment alone 2. Chemotherapy alone 3. Surgery + chemotherapy	
3.6	Recurrence after surgery	1. Yes 2. No	
3.7	Type of surgery done	1. Total colectomy 2. sigmoid colectomy 3. Hemi colectomy 4. Proctocolectomy	
3.8	Type of recurrence	1. Local recurrence 2. Distal recurrence	
3.9	Date of last contact	_____/_____/_____	
4.0	Status of the patient during last contact	1. Alive 2. Dead	
4.1	Current status of the patient	1. Alive 2. Dead	Skip to 3.9 if 2
4.2	If alive, functional status of the patient	1. Working 2. Ambulatory 3. Bed ridden	
4.3	If dead, date of death If lost to follow up, date of lost to follow up	_____/_____/_____ _____/_____/_____	

II. Annex Information sheet

Title of the research project: Determinants of survival and recurrence after surgery among colon cancer patients at Tikur Anibessa and Saint Paul hospitals, A.A, Ethiopia.

Name of principal investigator: Sara Teklewold

Name of the organization: Addis Ababa University, College of health science, school of public health.

Introduction: this information sheet and consent form was prepared for Tikur Anibessa and Saint Paul hospitals cancer treatment center. The aim of the form is to make the respected concerned office clear about the purpose of the research work, data collection procedures and getting permission to undertake the research.

Purpose of the research project: the main aim of this research is to determine five year survival time and associated factors among colon cancer patients.

Procedure: To arrive at the aforementioned findings, a total document of colon cancer patients enrolled between January 1, 2013 and December 31, 2018 will be chosen and a review of the required information from the records will be performed using a checklist. A phone call will be made to patients to gather information on some variables.

Risk and/or Discomfort: By participating in this research project, there is absolutely no risk to the person whose documents are reviewed and phone calls are made, despite the fact that doing so is critical to the research project, which is critical for overall planning and improvement of the program.

Benefits: The research has no direct benefit for the person whose document/record is included in this study. However, the research's indirect benefit to the participant and others in the program is clear. This is because if program planners prepare a predicted plan, there is a benefit for patients in the program of receiving appropriate care and treatment services.

Above all, research work has a significant direct benefit for health care planners and managers, particularly those involved in cancer prevention and treatment planning and management.

Confidentiality: To maintain the confidentiality of the patients' records, the records will be extracted by two trained cancer treatment center staff members using randomly selected card numbers. The data will then be reviewed, and a phone interview will be conducted.

The information gathered from this research project will be kept strictly confidential, and the information reviewed about the patients by this study will be saved in a file without a name, i.e. investigators will assign number codes to the records during the review. The information gathered will be kept secure and will not be accessible to anyone other than the principal investigator.

Person to contact: The institutional review board of Addis Ababa University's college of medicine and health sciences will review and approve this research project. Anyone interested in knowing more about the research and its activities should contact the committee at the address listed below.

1. Dr. Muluken Gizaw (Ph.D.): Addis Ababa University, College of Medicine and Health Sciences, School of Public Health. (Telephone: 0966809345)

2. Sara Teklewold: Addis Ababa, Arada Sub-city (Telephone: 0931220170).

Permission: The aforementioned body is kindly requested to grant and forward its permission to the appropriate body within its organization so that the researchers can obtain cooperation from the data clerks and other responsible bodies in place.

III. Annex Consent form (English version)

My name is …….. I am collaborating with Sara Teklewold, who is conducting research as part of her MPH requirements at Addis Ababa University. This study is intended to determine the survival time among colon cancer patients at Tikur Anibessa and Saint Paul specialized hospitals.

The study aims to fill the information gap and provide evidence for program planners, implementers, and decision makers at various levels by providing access to baseline data. It will also aid in the development of a system to improve the survival of colon cancer patients.

The information will be gathered by reviewing secondary data in the cancer treatment center and conducting phone interviews with patients. We will request your assistance in this study. All information will be numbered and coded, and no names will be used during the research process.

Your responses to any of the questions will not be shared with anyone else, and no study reports will ever identify you. The interview is entirely optional. Your participation, non-participation, or refusal to answer questions will have no bearing on the services that you or any member of your family may receive from the health care provider.

Are you willing to participate in the study?

1. Yes 2. No

IV. Annex ፈቃደኛነት መጠየቂያ ቅፅ (consent form, Amharic version)

ስሜ……ይባላል፡፡

በአሁኑ ሰአት በአዲስ አበባ ዩኒቨርሲቲ ለሁለተኛ ዲግሪአቸው የመመሪቂያ ፅሁፋቸውን ከሚያዘጋጁት ከወ/ሪት ሳራ ተክለወልድ ጋር በመሆን የአንጀት ካንሰር ህሙማንን በሚመከት በጥቁር አንበሳ እና በቅዱስ ጳውሎስ ሆስፒታሎች መረጃ በመሰብሰብ ላይ እገኛለሁ፡፡

ጥናቱ ለፕሮግራም አስፈፃሚዎች እንዲሁም ለውሳኔ ሰጪዎች መረጃ በመስጠት የህሙማኑን የጤና ሁኔታ ለማሻሻል ጉልህ አስተዋፆ ያደርጋል፡፡

መረጃው የሚሰበሰበው በካንሰር ህክምና ማእከል ከሚገኘው የህሙማን ምህደርና ለህሙማን ስልክ ደውሎ በማነጋገር ነው፡ ፡የሚሰጡት መረጃ ሚስጥራዊነት እጅግ የተጠበቀ ሲሆን ስምዎትንም ሆነ የእርሶን ማንነት የሚገልፅ በዚህ ጥናት ሂደት ውስጥ የማንጠቀም መሆኑንና መረጃውንም ለሌላ ወገን አሳልፈን እንደማንሰጥ ላረጋግጥልዎት እወዳለሁ፡፡

ቃለ ምልልሱ በፈቃደኝነት ላይ የተመሰረተ ሲሆን በዚህ ጥናት ውስጥ የመሳተፍ ወይም ያለመሳተፍ እንዲሁም በማንኛውም የማስቆም መብትዎ የተጠበቀ ነው፡፡ ይሁም በመሆኑ በእርሶም ሆነ በቤተሰቦዎ ላይ ከሆስፒታሉ በሚያጉት አገልግሎት ላይ ምንም አይነት ተፅእኖ እንደሌለው በድጋሚ ልገልፅልዎት እወዳለሁ፡፡

ለጥናቱ መረጃ ለመስጠት ፍቃደኛ ነዎት?

1. አዎን 2. አይደለሁም

V. Annex : Assurance of investigator

I, the undersigned senior MPH candidate, agree to accept responsibility for the scientific, ethical, and technical conduct of the research project as well as the provision of required progress reports to my advisors and seek the necessary advice approval from my Advisors in the course of the research in accordance with the terms and conditions of Addis Ababa University's research and publications office.

Name of the Investigator: Sara Teklewold

Signature…….

.Date……../……./…….

Approval of the Advisor

Name of primary Advisor: Dr. Muluken Gizaw (Ph.D.)

Signature…….

Date……../……../…….