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Research article

Histological characteristics, survival pattern and prognostic determinants among colorectal cancer patients in Ethiopia: A retrospective cohort study

Mohammed Ahmed Teka [a,1], Aman Yesuf [b], Foziya Mohammed Hussien [c], Hamid Yimam Hassen [d,*,1]

[a] Ethiopian Field Epidemiology Training Program, Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
[b] Department of Public Health, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
[c] Department of Public Health Nutrition, School of Public Health, College of Medicine and Health Science, Wollo University, Ethiopia
[d] Department of Public Health, Faculty of Medicine and Health Sciences, Mizan Tepi University, Mizan Teferi, Ethiopia

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ABSTRACT

Background: The incidence of colorectal cancer (CRC) and associated mortality are rising in low- and middle-income countries. In Ethiopia, colorectal cancer is among the leading causes of cancer morbidity and mortality in both sexes. Although some studies provided estimations on the national burden and regional distribution, the histological characteristics, survival pattern and determinants among colorectal cancer patients are not well-documented.

Aim: This study aimed to describe the histological characteristics, to determine the patterns of survival, and identify factors that determine mortality rate among CRC patients in Ethiopia.

Methods: A retrospective cohort study was conducted among CRC patients registered at cancer treatment center of Tikur Anbessa Specialized Hospital, from January 2012 to December 2016. Data were extracted from a total of 161 patient medical records using a pretested abstraction form and supplemented by phone calls with the patients/caregivers. To determine colorectal cancer specific survival overtime, we performed a Kaplan-Meier survival analysis and significance of variation in survival across covariates and treatment categories was tested using log-rank test. A multivariable Cox proportional-hazards model was performed to identify determinants of survival after diagnosis with colorectal cancer.

Results: Overall, the median survival time was 21 months [95%CI: 16–35], with two-, three- and five-year CRC-specific survival rates of 46.8%, 39.5% and 28.7% respectively. In the multivariable Cox regression model, the rate of death due to CRC is significantly higher for patients with elevated baseline carcinoembryonic antigen (CEA) level (Adjusted Hazard Ratio (AHR) = 2.31, 95%CI: 1.27–4.19), stage IV at diagnosis (AHR = 2.66, 95%CI: 1.44–4.91), and mucinous or signet-ring cell carcinoma histology type (AHR = 4.92, 95%CI: 1.75–13.80). Moreover, patients who underwent surgery showed a better survival than those who did not (AHR = 0.35, 95%CI: 0.14–0.88).

Conclusion: In Ethiopia, patients diagnosed with CRC showed a low rate of cancer-specific survival. Histology type, stage of cancer and CEA level at diagnosis, and the type of treatment a patient received significantly determine mortality rate. Hence, cancer screening programs could help to detect the disease at an earlier stage and to initiate available treatments timely so as to extend the lifespan of CRC patients.

1. Introduction

Globally, with an estimated 24.5 million cases and 9.6 million deaths in 2017, cancer continued to be the second leading cause of morbidity and mortality [1]. Colorectal cancer (CRC) is ranked third in incidence and second leading cause of cancer deaths in both sexes worldwide, with nearly 2 million new cases and more than a million new deaths in 2020 [2], accounting for 10% and 9.4% of all cancer cases and deaths respectively.

* Corresponding author.
E-mail address: abdulhamidy71@gmail.com (H.Y. Hassen).
[1] These authors have contributed equally to this work.

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Previously, cancer and other non-communicable diseases (NCDs) were considered as a disease of high-income countries, however, now evidence shows that they are also becoming a major public health issue in low- and middle-income countries (LMICs). Studies indicated the change in lifestyle, urbanization, cultural transition (physical inactivity and unhealthy dietary habit), and an increase in life expectancy in LMICs could be the possible reasons for increasing burden of cancer [3,4,5]. Improvement in individual income and economic growth in LMICs has shifted the dietary pattern towards an increased intake of fat, sugar, and animal-source packed foods [6]. From 2007 to 2017, the largest increase (52%) in cancer incidence was observed in countries with the middle Socioeconomic Development Index (SDI) [1]. In sub-Saharan Africa, the cancer burden is expected to increase by 85% in 2030 [7]. Similarly, in Ethiopia, the burden of NCDs including cancer is increasing. With 3,121 estimated new cases and 5.9% mortality rate in 2020, CRC was the third most incident and the fourth cause of mortality in both sexes [8].

Existing challenges, including poor screening services, inadequate research, and limited population-based cancer registry make the burden to be underestimated in LMICs and less attention is given in policies [9, 10,11,12]. The rise in prevalence of cancer in LMICs puts pressure on already overwhelmed healthcare and economic infrastructure, and poses additional challenges on health service delivery [13]. The mortality due to cancer is significantly higher in LMICs, accounting for nearly 70% of all cancer deaths [14]. Particularly, people younger than 65 years of age are most commonly affected [15,16], leading to a greater economic impact as a result of premature mortality and lost years of productivity.

In LMICs, including Ethiopia, patients visit healthcare facilities late and are expected to have poor prognosis. Estimating the survival pattern is necessary in order to assess and monitor the effectiveness of treatment and care given to patients with cancer. Investigating the survival has practical implications for patients and healthcare providers to understand how the prognosis could change over time and to decide on better treatment options. Moreover, it enables public health professionals and policy makers to understand the quality and effectiveness of care and treatments introduced in improving survival and quality of life. However, little is known on the survival of patients with CRC in Ethiopia. Recently, Atinafu *et al* investigated the predictors of mortality from CRC among patients treated in Tikur Anbessa Specialized Hospital (TASH) [17]. Nevertheless, the study has some methodological limitations in the event ascertainment and missing data management. Therefore, taking the limitations into consideration, we assessed the overall two-, three- and five-year survival pattern and identified factors that determine mortality rate among CRC patients in Ethiopia.

2. Methods and materials

2.1. Study setting and period

We used data from the Addis Ababa Population-Based Cancer Registry (AAPBCR), which was established in 2011 under TASH radiotherapy center. TASH is a tertiary level hospital equipped with cancer diagnostic and treatment facilities and is one of the cancer treatment centers in Ethiopia. The registry uses hospitals, higher diagnostic clinics, and pathology services as the main source of cases. Patients were followed up starting from Jan 1, 2012 until the end of the study (Dec 31, 2016).

2.2. Study design and participants

We retrospectively followed a cohort of CRC patients registered in the cancer registry of TASH, who were newly diagnosed or referred from January 1, 2012 to December 31, 2016. Records with neither histopathology report nor cancer stage at diagnosis were excluded from the analysis. The charts of all patients were retrieved using the medical record number obtained from the cancer registry. Out of 174 CRC patient charts retrieved, 13 (7.5%) were excluded due to no report of histopathology nor cancer stage. Finally, the patient characteristics and all the required information were extracted from 161 patient medical records and included in the analyses.

2.3. Data collection procedures

Upon literature review on potential determinants, we developed an abstraction form considering the availability of patient characteristics on medical records and feasibility to collect through phone interviews. The medical records of all CRC patients were identified and retrieved using the medical registration number of the central card room. Then, data collectors reviewed baseline and follow up patient characteristics including sign and symptoms, laboratory and imaging results, and pathology report from the patient chart. All data that were available in the patient chart were entered into a data abstraction form manually. To ascertain the main outcome, death, we looked for the death certificate identified from the TASH cancer registries using the medical record number. In case of absence of the death certificate, a phone interview was done to all patients and/or their attendants. During the phone interview, we collected additional information that was not available from the medical record, including current event status, date of death if died, presence of comorbidities such as hypertension or diabetes, and lifestyle factors including smoking and alcohol consumption. We defined an event as the death of the patient due to CRC. Patients were censored to the last follow up date if they have incomplete information on the date of death, lost to follow up before developing the event, died due to other known causes unrelated to CRC, or have no registered phone number and whose current status is unknown. While those who did not die until the end of follow-up were censored to Dec 31, 2016. The data were collected by trained oncologic nurses who were working at the cancer treatment center. To improve the data quality, a two days training was given to the data collectors on how to retrieve patient charts, the objective, methodology, how to fill the data abstraction form and perform phone interviews.

2.4. Data processing and analysis

Upon checking for completeness, data were coded and entered into EpiInfo version 7.1 and exported to a free software R programming version 3.6.1 for further processing and analysis. Categorical variables were summarized using frequencies with percentages and rates, whereas for continuous variables we carried out mean with standard deviation (SD) or median with interquartile range (IQR). The incidence rate of death throughout the observation period was calculated as the number of deaths due to CRC identified during the period of observation divided by the sum total of the time each person was observed. Due to the variation in follow up time across participants, we used person-time incidence rate, which is the recommended measure [18]. To test for the presence of a significant difference in the overall CRC-specific survival across covariate categories, we employed a Kaplan-Meier curve along with the log-rank test. We estimated the median follow up time using a reverse Kaplan-Meier estimator [19]. To evaluate the crude association of variables with time to death, we performed a bivariate Cox proportional hazards regression. Finally, upon checking for the assumptions, we conducted a multivariable Cox regression model. There was collinearity between the variable clinical stage and TNM stage, then we excluded clinical stage from the final model. Determinants with p-values less than 0.05 in the multivariable Cox proportional hazards model were considered as significantly associated. Finally, we presented the results using crude and adjusted Hazard Ratios (HR) with 95% confidence intervals (95%CIs). The death and survival rates are death due to CRC and cancer specific survival respectively, unless otherwise specified.

There were missing values on CEA (0.6%), clinical stage (4.3%), smoking (2.5%), alcohol consumption (1.2%), and family history of cancer (5.6%). Under missing data at random (MAR) assumption, we performed Multivariate Imputation by Chained Equations (MICE) using

the 'mice' package in R [20]. We imputed 50 datasets using all available variables and the parameters were estimated in each imputed dataset separately, and combined using Rubin's rules [21]. Missing results were imputed for the determinant variables used in the multivariable Cox regression model. We did not impute for the outcome variable, death, as we analyzed only participants for whom the death was ascertained. We performed a sensitivity analysis to assess whether the assumption of MAR is valid, and the results were reasonably comparable, except for a slightly wider confidence interval of parameters in the complete case analysis (Annex I).

2.5. Participant consent and ethical approval

The institutional review board of Saint Paul's Hospital Millennium Medical College approved this study. Verbal consent was also obtained from patients or caretakers before starting the phone interview. Patient's data was extracted anonymously and at each step of data collection and processing confidentiality was assured. The study is in compliance with the principles of the declaration of Helsinki.

3. Results

3.1. Sociodemographic and behavioral characteristics of patients

Table 1 displays sociodemographic and behavioral characteristics of patients. The mean age of patients was 45.9 years (SD: 14.5), 102 (63.4%) were females, and 44 (27.3%) had no formal education. Eighty-two (50.9%) were from Addis Ababa city administration and 127 (78.9%) were married. Thirteen (8.1%) and 9 (5.6%) had a history of alcohol intake and tobacco use respectively. Four (2.6%) of them reported family history of cancer from their first degree relatives and 12 (27.9%) had history of associated comorbidities.

3.2. Clinical, laboratory, and pathology results of colorectal cancer patients

Out of 161 cases registered, 151 (93.8%) were adenocarcinoma NOS (not otherwise specified), and 10 (6.2%) were either mucinous (three) or signet-ring cell type (seven) of adenocarcinoma. Out of 151 adenocarcinoma NOS, 90 (59.6%) and 28 (18.5%) were moderately and poorly differentiated, respectively. Whereas, out of 10 mucinous or signet-ring cell carcinoma, seven were poorly differentiated (all were signet-ring cell carcinoma) and three were well differentiated (all were mucinous carcinoma). Above two-third (68.1%) and 31 (19.8%) had a tumor located in the colon and rectum, respectively. According to TNM staging, 77 (47.8%) and 22 (13.7%), respectively were at stage IV and III during their first diagnosis. Seventy-eight (50.7%) of them had metastatic cancer and 82 (50.9%) had elevated CEA level during diagnosis (Table 2).

3.3. Treatment options given to patients

Most (84.5%) were treated with surgery, 135 (83.9%) received chemotherapy, and 13 (8.1%) were treated by radiotherapy. Twenty-three patients (14.3%) treated by surgery only, 22 (13.7%) received systemic chemotherapy, 113 (70.2%) received adjuvant chemotherapy after surgery, whereas 13 (8.1%) received adjuvant chemotherapy and radiotherapy in combination after surgery (Table 3).

3.4. Survival pattern of patients

Seventy-five (46.6%) patients died due to CRC during the 2937 person-months of follow-up over a five years period. The median follow up time was 25 months with IQR of 14–44 months. The overall event rate was 25.5 per 1000 person-months [95%CI: 14.2 to 33.1]. The overall CRC-specific survival was low, with a two-, three- and five-year survival rate of 46.8% [95%CI: 38.6–56.8], 39.5% [31.0–50.5] and 28.7% [17.5–36.1] respectively. The median survival time was 21 months [95% CI: 16–35]. (Figure 1).

3.5. Survival rates among different groups of colorectal cancer patients

Figures 2, 3, 4 and 5 shows the difference of CRC-specific survival based on covariate categories. The survival rate varied across covariate categories, including baseline CEA level, TNM stage and the treatment patients received. The survival varied according to the TNM stage at diagnosis, with stage I and II showed a better survival (log-rank test, $p < 0.01$). Similarly, survival rate varied based on the clinical stage of cancer, in which metastasized cancer had a poor overall survival ($p < 0.01$). Patients with elevated CEA at diagnosis also showed a lower overall survival than their counterparts ($p < 0.01$). Furthermore, patients who underwent surgery showed relatively a better overall survival ($p =$

Table 1. Sociodemographic and behavioral characteristics of colorectal cancer patients in cancer registry of TASH, Ethiopia, 2012–2016 (n = 161).

Variables	Frequency	Percent
Age group		
<50	99	61.5
50–59	27	16.8
60–69	26	16.1
≥70	9	5.6
Sex		
Male	102	s
Female	59	36.6
Educational status		
No formal education	44	27.3
Primary level	40	24.8
Secondary	57	35.4
Higher education	20	12.4
Marital status		
Single	31	19.2
Married	127	78.8
Widowed	2	12.4
Divorced	1	0.6
Residence region		
Tigray	7	4.3
Afar	3	0.9
Amhara	24	14.9
Oromia	31	19.3
Somali	2	1.2
SNNPR	11	6.8
Gambella	1	0.3
Harari	2	1.2
Dire-dawa	2	1.2
Addis Ababa	82	50.9
Tobacco use (n = 157)		
Yes	8	5.1
No	149	94.9
Alcohol (n = 159)		
Yes	13	8.2
No	146	91.8
Family history of cancer (n = 152)		
Yes	4	2.6
No	152	97.4
Comorbidity (n = 43)		
Yes	12	27.9
No	31	72.1

TASH: Tikur Anbessa Specialized Hospital; SNNPR: Southern Nations, Nationalities and Peoples Region.

0.025). No significant variation was observed on overall survival according to sex, age group, presence of comorbidity and tumor location.

3.6. Prognostic determinants of survival among colorectal cancer patients

Table 4 displays the prognostic determinants of CRC-specific survival among CRC patients in Ethiopia. The multivariable Cox proportional hazards model indicates that histology type, TNM stage, baseline CEA level and surgery treatment option significantly determine the CRC-specific mortality. The death rate was 2.7 times higher for those diagnosed at stage IV compared to stage I and II (AHR = 2.66, 95%CI: 1.44–4.91). Whereas, the rate of death was nearly 5 times higher for mucinous or signet-ring cell carcinoma than adenocarcinoma NOS (AHR = 4.92, 95%CI: 1.75–13.8). Patients with elevated CEA level during diagnosis showed 2.3 times higher rate of death than their counterparts (AHR = 2.31, 95%CI: 1.27–4.19). On the other hand, patients who underwent surgery showed a 65% lower rate of death than those who did not regardless of the stage at diagnosis (AHR = 0.35, 95%CI: 0.14–0.88).

4. Discussion

Aiming to avail evidence on survival of CRC patients and determinants, we found that, the overall two-, three- and five-year survival after diagnosis of CRC was relatively low in Ethiopia. We also found that almost half of the patients had stage IV and had metastasis during diagnosis, indicating patients visit healthcare facilities at a very late stage of the disease, leading to a poor prognosis. Elevated CEA level, advanced stage of cancer at diagnosis, and those with mucinous or signet-ring cell carcinoma type showed worse prognosis. Despite low overall survival, patients who underwent surgery had a better survival than those who did not.

Table 2. Distribution of histologic types and grades of colorectal cancer patients in cancer registry of TASH, Ethiopia, 2012–2016 (n = 161).

Clinical characteristics	Frequency	Percent
Histologic type		
Adenocarcinoma NOS	151	93.8
Mucinous or Signet-ring cell carcinoma	10	6.2
Histological grade		
Adenocarcinoma (n = 151)		
Well differentiated	33	21.9
Moderately differentiated	90	59.6
Poorly differentiated	28	18.5
Mucinous and Signet-ring cell carcinoma (n = 10)		
Well differentiated (all mucinous type)	3	30.0
Poorly differentiated (all signet-ring cell)	7	70.0
Tumor location (n = 160)		
Colon	109	68.1
Recto-sigmoid junction	17	10.6
Rectum	31	19.4
Anorectal	3	1.9
TNM Stage at diagnosis		
Stage I	5	3.1
Stage II	57	35.4
Stage III	22	13.7
Stage IV	77	47.8
Clinical stage at diagnosis (n = 154)		
Localized	31	20.1
Locally advanced	45	29.2
Metastasis	78	50.7
Distant metastasis (Yes)	78	48.4
Regional lymph node involvement *(Yes)*	37	23.0
Vascular invasion (Yes)	5	3.1
Residual tumor identified (Yes)	2	1.2
Baseline CEA (n = 160)		
Not elevated (<5 ng/ml)	78	48.8
Elevated (≥5 ng/ml)	82	51.2

CEA - carcinoembryonic antigen; TASH: Tikur Anbessa Specialized Hospital.

The present study showed that majorities of CRC patients were younger than 50 years. A study by Mohammed and colleagues also indicated a high incidence of early-onset colon cancer in Ethiopia with no family history or inflammatory bowel diseases, in which 13% of them were younger than 30 years [22]. Recently, an increasing trend of early-onset CRC has also been reported in several countries [23,24,25]. Hence, it is crucial to elucidate the possible cause of early-onset CRC in Ethiopia so as to develop and implement targeted effective preventive interventions, early detection and treatment strategies.

In our study, the two- and three-year survival for all stages combined was below 50% and the five-year survival was 28.7%. A study by Atinafu *et al* reported 21.7% of five-year survival among patients treated in TASH [17]. However, the study has methodological limitations in the event ascertainment and missing data management that could lead to discrepancy in survival estimate. Although only a small proportion of patients have hospital death records in Ethiopia, the method of death ascertainment of patients who were discharged from hospital was not mentioned clearly in the study. Furthermore, albeit missing data is inevitable in studies using patient charts, the article lacks methodological descriptions on supplementary data collection techniques and missing data management procedures. On the other hand, the discrepancy could also be due to the difference in participants, in which we assessed patients in the cancer registry whereas the study by Atinafu and his colleagues enrolled patients who were being treated in the clinical setting. Overall rate of survival in our study is also worse than the rate reported from Asian LMICs [26,27,28,29], but better than that of Uganda [30] and Ghana [31], which reported 8.3% and 16.0% 5-year survival respectively. The discrepancy in survival might be mainly due to the variation in the availability of screening facilities and initiation of early treatment. The higher cancer stage at diagnosis along with lack of specialized treatment options make the cancer survival in LMICs, including Ethiopia to be worse. In our study, patients seek healthcare at later stages of the disease, nearly two-thirds of patients were diagnosed either at stage III or IV.

The lower survival could also be attributed to the lower socioeconomic development index of the country that determines the availability of diagnostics facilities and advanced treatment options [32,33,34]. In Ethiopia, TASH was the only cancer treatment center in the country until the establishment of additional cancer centers in 2016. Patients who are residents of Addis Ababa or neighboring regions had relatively better access than those who live in remote areas. Due to the high cost related to treatment, transportation and accommodation, only a small segment of the country's population afford the service. Consequently, with such socioeconomic discrepancy within the country, the survival could be even worse than what we found. Hence, the federal and state health ministries should give more emphasis to establish additional cancer treatment centers to improve access to remote areas.

In our study, patients with elevated CEA during diagnosis showed a higher rate of death due to CRC in comparison with their counterparts. Consistent findings were reported from similar other studies [35,36,37], indicating the relevance of CEA as a prognostic marker of CRC patients. Jessup et al suggested that the higher tumorigenic potential of CEA-producing tumors might be the possible reason for poor prognosis associated with high baseline CEA level [38].

Patients diagnosed at stage IV showed a higher rate of death than those diagnosed at stage I or II. This finding is supported by studies from Ethiopia, Taiwan and Ghana, which showed advanced stage at diagnosis is associated with poor survival [17,27,31]. Similarly, a study done in Iran also indicated cancer grade significantly associated with mortality from CRC [39]. Regardless of the variation in overall survival across countries, cancer stage at diagnosis is an independent indicator of

Table 3. Treatment options given to colorectal cancer patients at cancer registry of TASH, Ethiopia, 2012–2016 (n = 161).

Treatment received	Frequency	Percent
Surgery (all type)	136	84.5
Chemotherapy	135	83.9
Adjuvant	113	70.2
Systemic	22	13.7
Surgery only	23	14.3
Surgery and adjuvant chemotherapy	113	70.2
Surgery, adjuvant chemotherapy and radiotherapy	13	8.1

TASH: Tikur Anbessa Specialized Hospital.

survival from CRC. This implies the importance of screening and detection of cancer at an earlier stage for a better survival and quality of life.

On the other hand, our study found that the rate of death was nearly 5 times higher for mucinous or signet-ring cell carcinoma than adenocarcinoma NOS. A study by Nitsche and his colleagues also found that mucinous and signet-ring cell CRCs are different in biology and associated with poorer prognosis than adenocarcinoma [40]. A 10-year follow up study also found that although adenocarcinoma has higher incidence, signet-ring cell carcinoma subtype showed a worse prognosis [41]. Our study also found only 6.2% were mucinous or signet-ring cell carcinoma type, however, associated with a very poor prognosis. Therefore, pathologists need to give more emphasis in identification of such types of cancer for a better treatment option.

Patients who underwent surgery showed a 65% lower probability of death than those who did not, supporting the hypothesis that surgery is an effective treatment option for CRC patients. Coherently, a study in Kenya indicated that curative surgery improves survival by 70% [42]. Similarly, a multi-country study in Europe also showed surgery improved the survival of patients with CRC irrespective of the stage at diagnosis [43]. Hence, curative surgical therapy improves survival and it could be a feasible option for resource limited settings including Ethiopia.

This study has the following strengths. First, we used a multivariable Cox regression analysis, which enabled us to estimate survival among patients with an unequal follow-up period and also took account of censored data. Second, we included all patients who fulfilled the eligibility criteria during the study period, which avoids sampling error. At last, due to the nature of medical records, missing data was inevitable. Hence, we then handled it employing a robust statistical imputation method for missing data, which showed to be more precise in the sensitivity analysis. However, interpretation of the findings from this study need to be in the context of the following limitations. First, due to lack of vital event registration system in Ethiopia, the ascertainment of vital status/death and the cause for the majority of the participants was using phone interviews with the patient or caregiver. As a result, there could be minor misclassification in the cause of death, might lead to overestimation of deaths due to CRC, which in turn may cause outcome ascertainment bias. However, as the mis-classification is independent of the covariates under study, the impact on the hazard ratios is presumed to be minimal. Secondly, the patients included in this study are only a small proportion of CRC patients in Ethiopia. Due to lack of cancer treatment facilities in the country, a number of patients from remote areas of the country might not afford the treatment cost, transportation and accommodation to stay in Addis Ababa. Half of the patients included in this study were residents of Addis Ababa, that means those from remote areas have less access to the cancer treatment center, indicating a huge socioeconomic disparity. As a result the survival pattern might be worse than what is observed in the present study. Future prospective studies with a larger sample and in different contexts could identify other additional determinants of patient survival. Lastly, some of the patient charts do not have sufficient information of family history, lifestyle risks, comorbidities, and detailed clinical and histological descriptions. Hence, health professionals working at oncology units should give more emphasis in documenting all relevant patient information to improve utility of data for research and decision making.

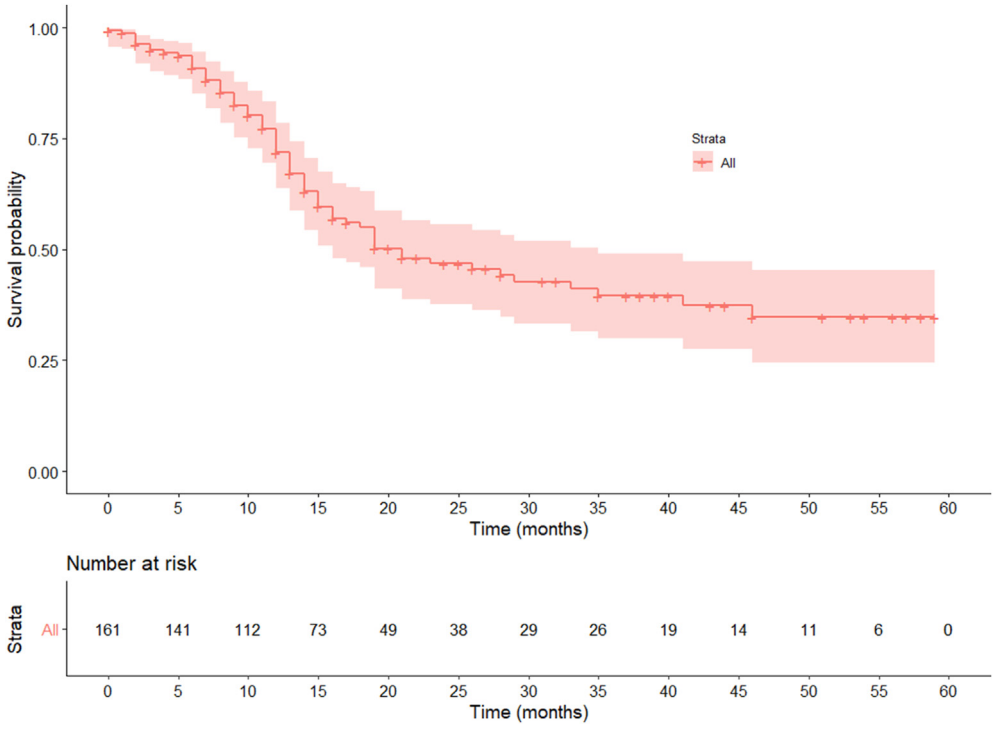

Figure 1. Kaplan-Meier survival curve of the overall survival for colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016. The curve shows the median survival is 21 months [95%CI: 16–35].

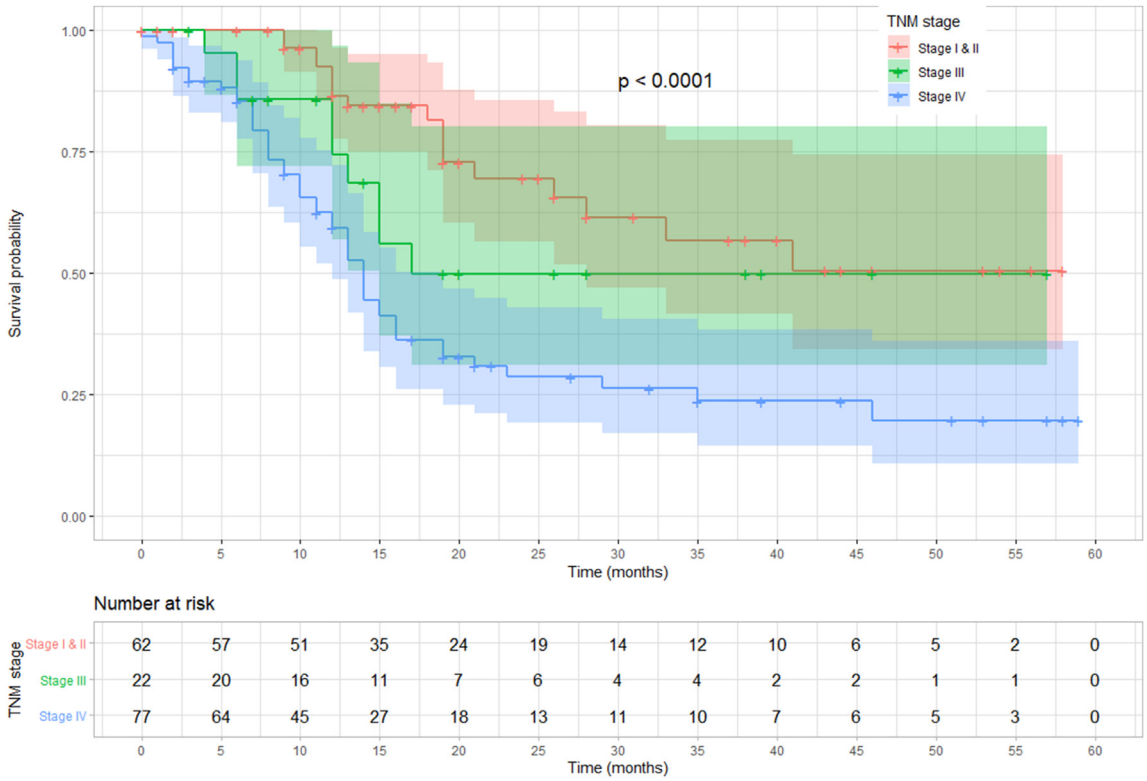

Figure 2. Kaplan-Meier survival curve of the overall survival by TNM stage of cancer at diagnosis among colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016. The log-rank test showed that the difference in mortality rate according to TNM stage is statistically significant ($p < 0.001$).

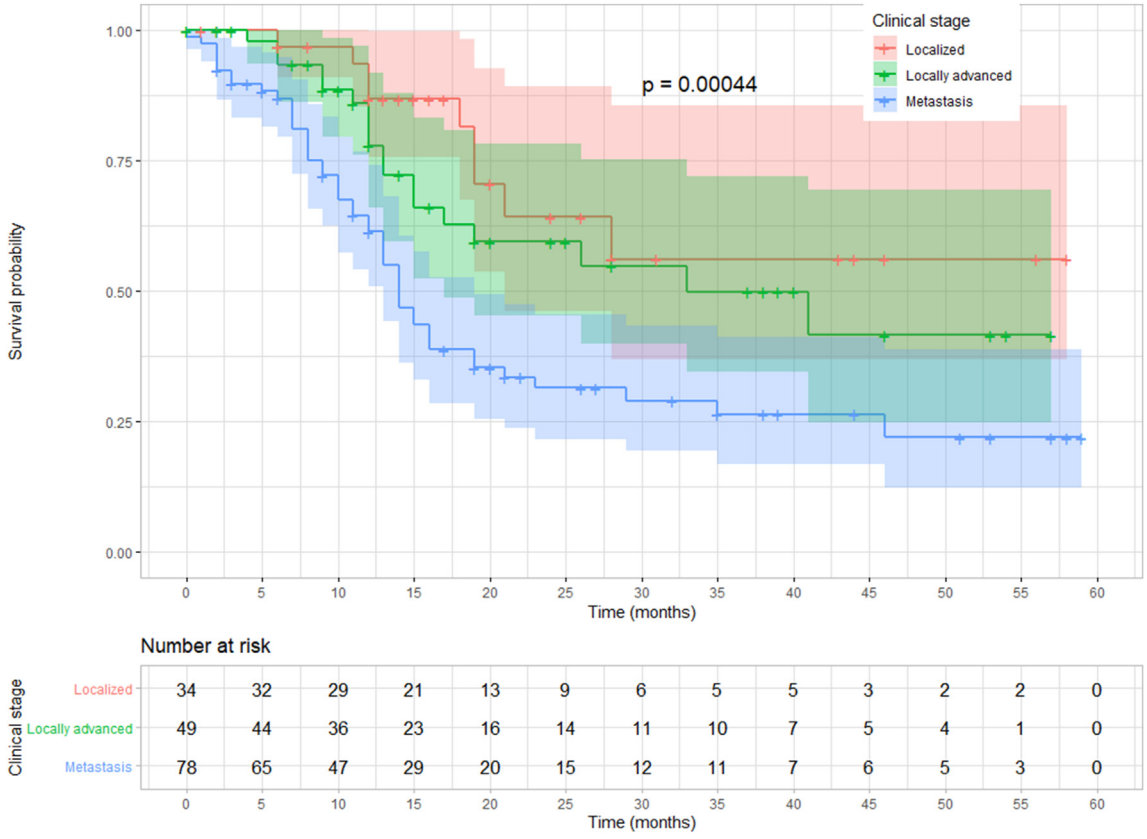

Figure 3. Kaplan-Meier survival curve of the overall survival by clinical stage of cancer at diagnosis among colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016. The log-rank test showed the difference in mortality according to clinical stage at diagnosis is statistically significant ($p < 0.001$).

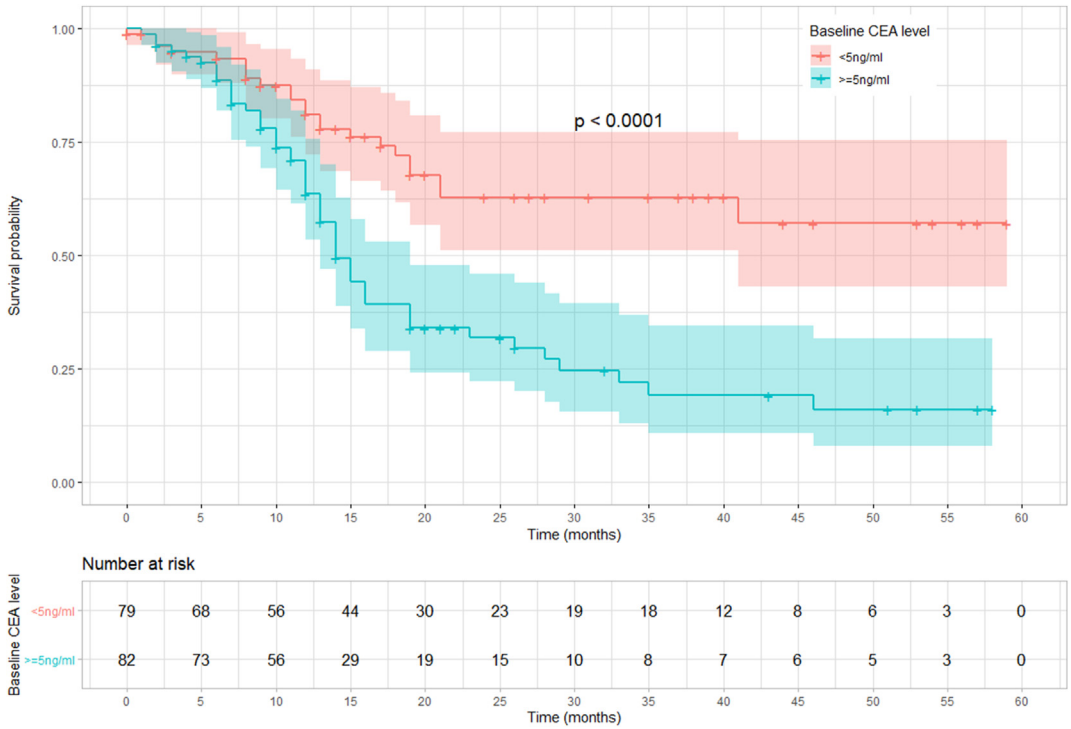

Figure 4. Kaplan-Meier survival of the difference in overall survival by baseline CEA level among colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016. The log-rank test indicated a significant difference in survival according to baseline CEA level ($p < 0.001$). *CEA: carcinoembryonic antigen.*

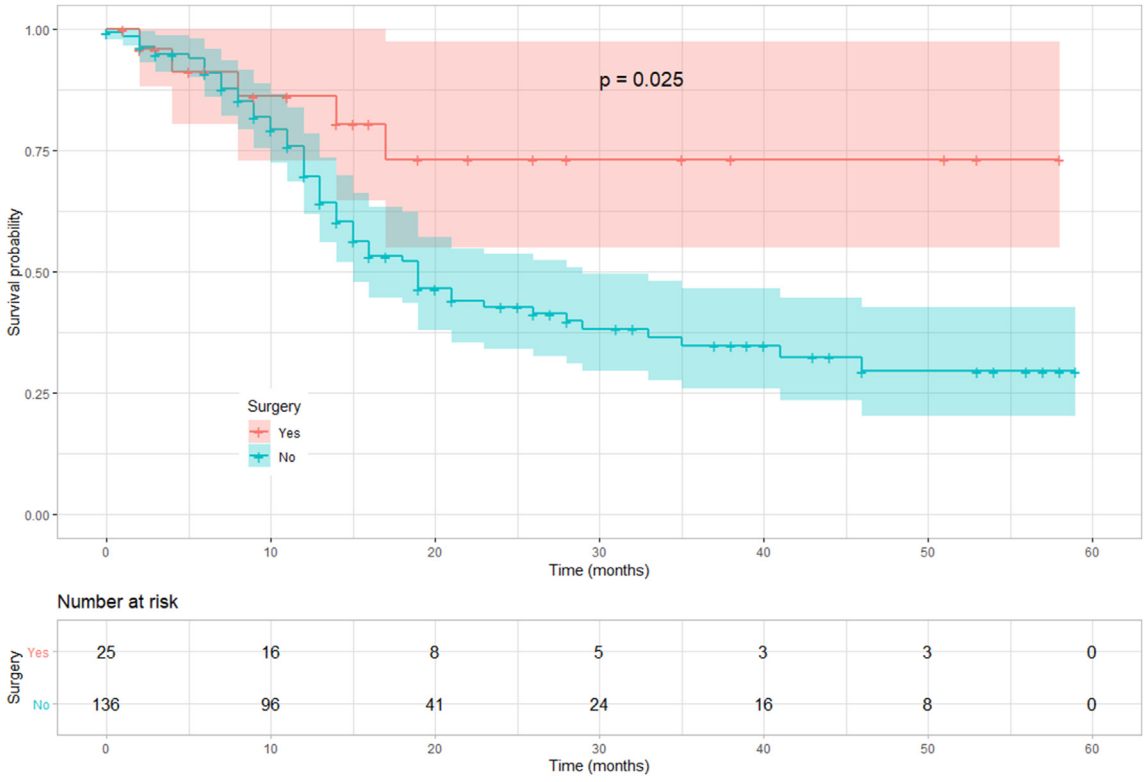

Figure 5. Kaplan-Meier survival curve of the overall survival based on surgery among colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, 2012 to 2016. The log-rank test indicated those who underwent surgery showed a better overall survival than those who did not ($p = 0.025$).

Table 4. Cox proportional hazards model indicating the prognostic determinants of survival among colorectal cancer patients at cancer registry of TASH, Ethiopia, 2012–2016.

Determinants	CHR (95%CI)	AHR (95%CI)
Age (cont.)	0.99 (0.98–1.01)	0.99 (0.98–1.01)
Sex (Female)	0.75 (0.46–1.21)	0.76 (0.46–1.27)
Cancer TNM stage		
I and II	1	1
III	1.70 (0.76–3.81)	2.03 (0.97–4.66)
IV	3.31 (1.02–2.15)**	2.66 (1.44–4.91)**
Histologic type		
Adenocarcinoma NOS	1	1
Mucinous/Signet-ring cell carcinoma	5.27 (2.05–13.5)***	4.92 (1.75–13.80)**
Chemotherapy (Yes)	0.71 (0.39–1.30)**	0.55 (0.29–1.06)
Baseline CEA		
<5 ng/ml	1	1
≥5 ng/ml	2.77 (1.69–4.53)	2.31 (1.27–4.19)**
Surgery (Yes)	0.37 (0.15–0.92)*	0.35 (0.14–0.88)*
Radiotherapy (Yes)	0.72 (0.33–1.56)	0.98 (0.42–2.22)

*P < 0.05; **P < 0.01.
CHR: Crude Hazard Ratio; AHR: Adjusted Hazard Ratio; CEA: carcinoembryonic antigen; TASH: Tikur Anbessa Specialized Hospital.
Multivariate multiple imputations were performed (n = 161).

5. Conclusions

We found that the overall cancer specific survival of CRC patients in Ethiopia is low in comparison with high-income countries. The rate of survival after diagnosis significantly varied across categories of stage of cancer and the treatment options they received. The death rate is significantly higher for patients with elevated CEA level and higher cancer stage at diagnosis, indicating the key role of early detection and timely initiation of treatment to improve survival and quality of life of patients with CRC. Therefore, we recommend the national cancer control program to improve screening services, diagnostic facilities and timely initiation of treatment. Furthermore, public health practitioners working on cancer prevention should put more effort to improve public awareness about early symptoms and signs of CRC to facilitate early visit to healthcare facilities. Further large scale studies in various contexts employing prospective research designs is recommended.

Declarations

Author contribution statement

Mohammed Ahmed Teka: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Aman Yusuf, and Foziya Mohammed Hussien: Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Hamid Yimam Hassen: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

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