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Survival Status and Predictors of Mortality Among Colorectal Cancer Patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Retrospective Follow-up Study

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Colorectal cancer is one of the commonest cancer types that has a great public health impact both in developed and developing countries. However, in Ethiopia, the survival status of colorectal cancer patients was not well understood. Therefore, the aim of this study was to determine the survival status and predictors of mortality among colorectal cancer patients in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia in 2019. The institution-based retrospective follow-up study was conducted with 621 subjects who were selected from patients registered between January 1, 2013 and December 30, 2017 with follow-up until December 30th, 2018. Data were collected from patient record review charts. A Kaplan–Meier analysis with a log-rank test, and bivariate and multivariable analysis using the Cox proportional hazard model were used. Of the 621 colorectal cancer patients who were included in the analysis, 202 (32.5%) died. The overall mortality rate was 20.3% per year (95% CI: 17.7-23.3). The overall survival was 18.1% with median survival time of 34.8 months (95% CI: 30.4-36.8). Comorbidity (adjusted hazard ratio [AHR] = 1.8, 95% CI: 1.3-2.5); stage (II [AHR = 3.8, 95% CI: 1.3-11.1], III [AHR = 8.0, 95% CI: 2.8-23.3], IV [AHR = 17.6, 95% CI: 6.1-50.7]); smoking (AHR = 1.6, 95% CI: 1.1-2.3); alcohol consumption (AHR = 1.5, 95% CI: 1.07-2.2); age ≥ 70 (AHR = 1.7, 95% CI: 1.02-2.9); and marital status (married [AHR = 2.4, 95% CI: 1.5-3.8], widowed [AHR = 2.4, 95% CI: 1.2-4.6], divorced [AHR = 2.0, 95% CI: 1.1-3.7]) were significant predictors of colorectal cancer mortality. It is crucial to implement early detection and screening, giving priority to rural dweller, comorbid patients and advanced stage diagnosed patients.

Key Words Colorectal cancer, Survival, Mortality, Ethiopia

INTRODUCTION

Colorectal cancer is the third most commonly occurring malignancy and the second most common cause of cancer-related death next to lung cancer in men and breast cancer in women globally [1]. The global burden of colorectal cancer increased from 1.36 million to 1.80 million between 2012 and 2018, of which about 881,000 mortality cases were documented [1,2]. Colorectal cancer incidence varies from 6.5 per 100,000 in the Middle East and Africa to 83.7 per 100,000 in high-income Asia-Pacific regions [3].

The crude incidence of colorectal cancer in Sub-Saharan Africa for both men and women was found to be 4.04 per 100,000 population, and about 24,711 new cases were estimated annually [4]. In Ethiopia, It is the first most common cancer among the male population [5]. In 2014, the 2011-2014 Addis Ababa cancer registry reported that the incidence rate of colorectal cancer was 19% among male population [6]. Decreasing trends were seen in high-income countries while the incidence and mortality rates are still rising rapidly in many low-income and middle-income countries, which are linked to ongoing societal and economic development [7,8]. In addition, this is due to the inaccessibility of diagnostic modalities, problems in the implementation of prevention and control of the disease and absence of regular screening for the diseases, as well as obesity and smoking [3,9].

The 5-year survival rate of colorectal cancer varied from greater than 90% in patients with stage I disease to

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slightly higher than 10% in patients with stage IV disease in Germany [10]. The same study in American Pacific Islanders indicated that 5-year survival rates after a colorectal cancer diagnosis were 69% and 60% among both blacks and American Indians, respectively but lower survival rates were seen in Malay (48.5%), Chinese (39.68%), and Asian Indians (47.49%) [8,11]. However, a 5-year retrospective hospital-based study in Ghana indicated that none of the colorectal cancer patients diagnosed at stage IV survived [12].

In Ethiopia, the Federal Ministry of Health gives emphasis to non-communicable diseases, such as cancer to reduce the incidence and mortality. However, colorectal cancer patients' survival status and associated factors have not been well studied. Moreover, interventions to enhance survival and reduce mortality in colorectal cancer lack the necessary empirical evidence. As a result, there could be evidence-based decison-making gap about colorectal cancer, such as prioritizing interventions, estimating the survival rate of patients, and supporting the planning systems of the cancer control and prevention program. Hence, the aim of this study was to assess the survival status and predictors of mortality among colorectal cancer patients in Tikur Anbessa Oncology Department, Addis Ababa, Ethiopia.

MATERIALS AND METHODS

Study design, study setting and study period

The Institutional Review Board (IRB) of Addis Ababa University, School of Nursing and Midwifery approved the study. The permission letter was obtained from hospital administration (IRB protocol no.: 017/19/SNM; Institute: AAU, CHS, School of Nursing and Midwifery).

A 6-year institution-based retrospective follow-up study was conducted with eligible colorectal cancer patients registered from 1st of January, 2013 to the 30th of December, 2017. The study was conducted in Tikur Anbessa Specialized Hospital (TASH) Oncology Department which is located in Addis Ababa, the capital of Ethiopia. It is the largest and well-known public hospital which was built in the early 1960s. TASH Oncology Department occupies all treatment coverages 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. The actual data collection was carried out from February 15 to April 21, 2019, by reviewing medical records of colorectal cancer patients enrolled in TASH Oncology Department. The study subjects were monitored from the January 1, 2013 to the December 30 2018. Source population consisted of all medical records of colorectal cancer patients in TASH Oncology Department. Study population includes all medical records of colorectal cancer patients in TASH diagnosed from January 1, 2013 to December 30, 2017 who fulfilled eligibility criteria. All medical records of confirmed colorectal cancer patients at TASH during the defined period (2013-2017) were incuded, whereas incomplete and missing patients' charts during data collection period, and referred patients with confirmed diagnosis to TASH for advanced management were excluded.

Sample size determination, sampling procedure and study variables

At the beginning, all medical records of a confirmed diagnosis of colorectal cancer patients registered from January 1, 2013 to December 30, 2017 were identified. From 887 identified medical records of colorectal cancer patients, 191 charts were incomplete, 72 charts were missing at the time of data collection and 3 were referred for advanced treatment (radiation) were excluded from the study. Finally, all study participants who fulfilled the inclusion and exclusion criteria from January 1, 2013 to December 30, 2017 were selected. The primary outcome variable was time to death. Other variables of interest extracted from record review included: age, sex, family history, marital status, residence, insurances status, smoking status, alcohol consumption, body mass index (BMI), comorbidity, grade at diagnosis, stage at diagnosis, a primary site, and histologic type and treatment.

Operational definitions

Censored: Patients whose status was unknown, patients who did not develop the outcome of interest (death) at the end of the follow-up period, and patients who were lost during follow-up.

Event: Death of patients due to colorectal cancer.

Beginning date and closing date to follow-up: The beginning date was the first date of confirmed diagnosis of colorectal cancer (January 1, 2013 to December 30, 2017). The closing date was the date at the last status of the patient on the follow-up (December 30, 2018).

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

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

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

Comorbidity: According to International Classification of Disease-10, Disease from Charles comorbidity index was used during data collection. The co-occurrence of any of these diseases with colorectal cancer at the time of diagnosis labeled as "yes" response [13].

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

BMI according to disease prevention and control: underweight, BMI less than 18.5 kg/m^2; healthy weight, BMI 18.5-24.9 kg/m^2; overweight, BMI 25-29.9 kg/m^2; obese, BMI 30 kg/m^2 or higher [14].

Stage at diagnosis: according to American Joint Committee

of Cancer: stage 0: Carcinoma in situ, no lymph node, and no metastasis, stage I: Tumor invades muscularis propria, submucosa, no lymph node, and no metastasis, stage II: Tumor invades muscularis propria, penetrates to the surface of the visceral peritoneum, adherent to other organs or structure, no lymph node and no metastasis, stage III: Tumor metastasis in seven or more regional lymph nodes, stage IV: Tumor metastasis into different organs [15].

Data collection tools and procedures

The information available in the eligible patients' medical records was observed and then recorded using data extraction tool prepared by adapting from different studies [8,12,16-19], which consisted of patient-related factors, clinicopathological factors, and treatment factors. Then, all charts of colorectal cancer patients, diagnosed between January 1, 2013 to December 30, 2017 at TASH were retrieved and then reviewed. Death certificate supplemented was identified from TASH cancer registries by their medical record number. Then, the records of all the study participants were selected according to the eligibility criteria. Five BSc nurses, two supervisors, and one MSc student were involved in the data collection.

Data quality assurances

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

Table 1. Characteristics of colorectal cancer patients in TASH Oncology Department, Addis Ababa, Ethiopia

Variable	Category	Status at last contact		Total
		Death	Censored	
Sex	Male	130 (36.1)	230 (63.9)	360 (57.9)
	Female	72 (27.6)	189 (72.4)	261 (42.1)
Age of patient (yr)	< 40	79 (31.8)	170 (68.2)	249 (40.1)
	40-49	27 (27.6)	71 (72.4)	98 (15.8)
	50-59	34 (24.3)	106 (75.7)	140 (22.5)
	60-69	36 (40.5)	53 (59.5)	89 (14.3)
	≥ 70	26 (57.8)	19 (42.2)	45 (7.3)
Family history	Yes	19 (44.2)	24 (55.8)	43 (6.9)
	No	183 (31.7)	395 (68.3)	578 (93.1)
Region	Amhara	19 (25.7)	55 (74.3)	74 (11.9)
	Oromia	51 (29.5)	122 (70.5)	173 (27.9)
	Tigray	7 (23.3)	23 (76.7)	30 (4.8)
	SNNP	20 (34.5)	38 (65.5)	58 (9.3)
	Addis Ababa	98 (36.7)	169 (63.3)	267 (43.0)
	Others	7 (36.8)	12 (63.2)	19 (3.1)
Residence of patients	Urban	140 (34.7)	263 (65.3)	403 (64.9)
	Rural	62 (28.4)	156 (71.6)	218 (35.1)
Marital status	Single	32 (30.8)	72 (69.2)	104 (16.7)
	Married	118 (29.4)	284 (70.6)	402 (64.8)
	Widowed	22 (37.3)	37 (62.7)	59 (9.5)
	Divorced	30 (53.6)	26 (46.4)	56 (9.0)
Insurance status	Free paid	86 (27.9)	222 (72.1)	308 (49.6)
	Paid	116 (37.1)	197 (62.9)	313 (50.4)
Smoking status	Smoker	77 (52.4)	70 (47.6)	147 (23.7)
	Not smoker	125 (26.4)	349 (73.6)	474 (76.3)
Alcohol consumption	Yes	107 (42.1)	147 (57.9)	254 (40.9)
	No	95 (25.9)	272 (74.1)	367 (59.1)
Body mass index (kg/m^2)	≤ 18.5	53 (32.3)	111 (67.7)	164 (26.4)
	18.5-24.9	145 (32.7)	298 (67.3)	443 (71.3)
	25-29.9	4 (28.6)	10 (71.4)	14 (2.3)
	≥ 30.0	0	0	0
Comorbidity	Yes	98 (58.3)	70 (41.7)	168 (27.1)
	No	104 (22.9)	349 (77.1)	453 (72.9)

The total number of 621 subjects were selected from patients registered between January 1, 2013 and December 30, 2017 with follow-up until December 30, 2018. Values are presented as number (%). TASH, Tikur Anbessa Specialized Hospital.

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

Data processing and analysis

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

Before running the Cox proportional hazard regression model, multi-collinearity was checked. The necessary assumptions for the model were checked using goodness-of-fit test by Schoenfeld residual and variables having $P > 0.05$ were considered as fulfilling the assumption. Residuals tested by goodness-of-fit fulfilled the model assumptions. Bivariable Cox regression was fitted and those independent variables which fitted on the bivariable regression less than or equal to the 0.25 level of significance were included in the multivariable analysis [20,21]. Multiple Cox regression was done at the 0.05 level of significance to determine the net effect of each explanatory variable on time to death

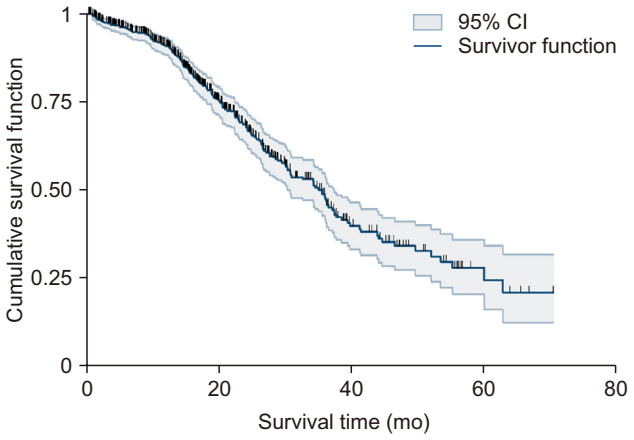

Figure 1. Overall Kaplan–Meier estimation of survival functions of colorectal cancer patients diagnosed in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. The subjects were monitered between January 1, 2013 and December 30, 2018.

Table 2. Clinicopathological and treatment related characteristics of colorectal cancer patients in TASH Oncology Department, Addis Ababa, Ethiopia

Variable	Category	Status at last contact		Total
		Death	Censored	
Primary site of tumor	Colon	122 (34.9)	228 (65.1)	350 (56.4)
	Rectum	80 (29.5)	191 (70.5)	271 (43.6)
Stage of the diseases[a]	Stage I	4 (8.0)	46 (92.0)	50 (8.1)
	Stage II	33 (20.2)	130 (79.8)	163 (26.2)
	Stage III	66 (27.1)	178 (72.9)	244 (39.3)
	Stage IV	99 (60.4)	65 (39.6)	164 (26.4)
Grade	Differentiated	70 (23.6)	226 (76.4)	296 (47.7)
	Moderately differentiated	51 (29.7)	121 (70.3)	172 (27.7)
	Undifferentiated	81 (52.9)	72 (47.1)	153 (24.6)
Histology type	Adenocarcinoma	148 (30.3)	340 (69.7)	488 (78.6)
	mucinous carcinoma	36 (38.7)	57 (61.3)	93 (15.0)
	Signet ring-cell carcinoma	18 (45.0)	22 (55.0)	40 (6.4)
Treatment modality	Radiotherapy alone	11 (31.4)	24 (68.6)	35 (5.6)
	Surgical treatment alone	10 (24.4)	31 (75.6)	41 (6.6)
	Chemotherapy alone	41 (34.2)	79 (65.8)	120 (19.3)
	Surgery plus chemotherapy	53 (28.5)	133 (71.5)	186 (30.0)
	Radiation as neo-adjuvant to surgery	19 (31.1)	42 (68.9)	61 (9.8)
	Radiation + surgery chemotherapy	67 (38.3)	108 (61.7)	175 (28.2)
	Didn't receive treatment	1 (33.3)	2 (66.7)	3 (0.5)

The total number of 621 subjects were selected from patients registered between January 1, 2013 and December 30, 2017 with follow-up until December 30, 2018. Values are presented as number (%). TASH, Tikur Anbessa Specialized Hospital. [a]According to American Joint Committee of Cancer.

of colorectal cancer. The *P*-value less than 0.05 in the multivariable analysis was considered statistically significant. The results of these models were expressed as hazard ratios with 95% CI and *P*-values are used to measure the strength of association and to identify statistically significant factors.

RESULTS

Patient-related characteristics of the study participants

Out of the 621 study participants, 419 were censored and 202 died. About 360 of study participants (57.9%) were males and 64.9% came from urban areas. A little more than two-fifths of them were from Addis Ababa (43%). The mean age of the study participants was 46.9 ± 13.9 years; of these, two hundred forty-nine (40.1%) were less than 40 years old. BMI of more than two-thirds of the participants (71.3%) was in the 18.5-24.9 kg/m^2 range. Slightly more than one-quarter (27.1%) of participants had comorbid conditions, of which 58.3% died (Table 1).

Clinicopathological and treatment-related cha-racteristics

More than half (56.4%) of the primary site of tumor was found to be colon. Of those patients, 34.9% died. A large percentage of the patients (65.7%) were diagnosed at late stages. Three-fifth of the patients (60.4%) who had been diagnosed at stage IV died. Nearly half of the tumor grade (47.7%) was differentiated; about 488 (78.6%) were adenocarcinoma type (Table 2).

Overall survival rate of colorectal cancer patients

As Kaplan–Meier analysis showed that the overall survival rate was 18.1% at 72 months follow-up (Fig. 1).

The estimated cumulative survival rates of colorectal cancer patients at 12, 24, 36, 48, and 60 months were 90.7%, 67.4%, 47.0%, 31.8%, and 21.7%, respectively. The overall median survival time of colorectal cancer patients was found to be 34.8 months (95% CI: 30.4-36.8). The probability of survival was highest at the first day of diagnosis of colorectal cancer, but it relatively fell later as follow-up time increased.

Table 3. Survival time, cumulative survival probability and log-rank test for the study population according to patient related characteristics during six-year of follow-up (Kaplan–Meier method) of colorectal cancer patients in TASH Oncology Department

Variable	Category	Median survival (mo) (95% CI)	1-year survival	2-year survival	3-year survival	4-year survival	5-year survival	Overall survival	Log-rank test (*P*-value)
Sex	Male	30.4 (26.1-34.8)	91.7	62.8	38.5	26.9	20.6	13.7	0.023
	Female	38.3 (36.5-52.8)	89.3	72.7	60.2	39.2	25.2	25.2	
Age (yr)	< 40	38.0 (30.5-54.3)	91.5	71.5	54.1	44.7	27.4	22.0	< 0.001
	40-49	36.1 (26.7-39.1)	95.1	74.5	44.5	20.9	0	0	
	50-59	41.8 (33.1-47.2)	93.2	73.5	60.3	28.7	28.7	0	
	60-69	24.4 (19.0-28.5)	85.1	48.9	22.8	22.8	0	0	
	≥ 70	22.3 (15.5-30.7)	81.0	34.2	11.4	0	0	0	
Family history	Yes	30.7 (23.8-52.8)	92.2	66.8	39.7	31.7	23.8	0	0.86
	No	35.5 (30.4-37.6)	90.5	67.5	48.0	30.6	22.5	18.7	
Residence	Urban	34.7 (26.9-36.8)	90.0	63.1	45.0	28.1	19.3	19.3	0.073
	Rural	36.7 (31.2-37.1)	92.1	75.8	51.4	34.6	25.9	17.3	
Marital status	Single	42.0 (36.5-54.3)	95.6	81.9	67.2	45.2	9.0	0	0.0002
	Married	36.1 (28.9-40.3)	91.2	68.1	45.0	33.0	26.4	26.1	
	Widowed	29.3 (17.0-37.6)	80.3	53.6	28.7	19.2	0	0	
	Divorced	24.4 (18.5-31.2)	86.7	47.7	10.5	0	0	0	
Insurance	Free paid	36.5 (29.8-44.6)	92.2	71.7	50.5	33.2	14.2	0	0.187
	Paid	31.3 (27.0-36.8)	89.2	63.5	43.9	30.0	18.9	18.9	
Smoking status	Yes	23.3 (20.4-25.9)	86.7	47.6	19.9	13.4	0	0	< 0.001
	No	38.3 (36.1-45.3)	92.0	74.2	57.4	38.5	23.1	27.7	
Alcohol consumption	Yes	25.6 (22.6-30.7)	89.5	54.1	32.1	17.7	6.3	0	< 0.001
	No	40.3 (36.1-52.8)	91.5	76.1	57.3	41.8	28.1	28.1	
Body mass index (kg/m^2)	< 18.5	31.3 (25.2-45.3)	92.9	64.3	47.4	14.8	0		0.99
	18.5-24.9	34.8 (29.3-37.1)	90.7	68.5	46.5	30.9	19.2	19.2	
	25.0-29.9	36.6 (17.8-…)	84.4	72.4	30.9	0	0	0	
	≥ 30.0								
Comorbidity	Yes	23.2 (18.3-25.9)	87.0	45.3	21.7	8.2	2.7	0	< 0.001
	No	44.6 (36.8-52.8)	92.2	77.3	60.9	43.7	30.8	30.8	

The total number of 621 subjects were selected from patients registered between January 1, 2013 and December 30, 2017 with follow-up until December 30, 2018. Values are presented as percent only. TASH, Tikur Anbessa Specialized Hospital.

Survival estimate among predictor variables

The study found that the median survival time of colorectal cancer having comorbid condition was lower than non-comorbid conditions (23.2 months 95% CI: 18.3-25.9) as shown by statistical significance with $P < 0.001$. Those colorectal cancer patients whose marital status was 'divorced' had the lowest median survival (24.4 months 95% CI: 18.5-31.2) with statistical difference of $P < 0.001$. The median survival time of colorectal cancer patients who were clinically diagnosed as stage I, II, and IV at baseline survived longer than those who were clinically diagnosed stage IV at base line (22.7 months 95% CI: 19.1-25.9). This difference was significant at $P < 0.001$. The overall four years' survival rates of clinically stage I, II, III, and IV were 83.2%, 45.4%, 22.4%, and 8.6%, respectively; however, the 5- and 6-year overall survival rates of stage III and IV were found to be zero (Table 3, 4).

Predictors of colorectal cancer mortality

In bivariable Cox proportional hazard regression, sex, age (60-69 and = 70 years), residence, marital status, insurance status, smoking, alcohol consumption, comorbidity, stage, grade, histology and treatment given were fitted in bivariable analysis at ($P < 0.25$). Those variables with $P < 0.25$ in the bivariable analysis were included in multivariable analysis. In multivariable Cox proportional hazards model; age, marital status, smoking, alcohol consumption, comorbidity, stage and grade were significant predictors of colorectal cancer mortality ($P < 0.005$).

As the multivariable analysis showed that patients aged 70 and over were 1.7 times at higher risk to die (adjusted hazard ratio [AHR] = 1.7, 95% CI: 1.02-2.9) than those aged below 40 years old as a reference. Colorectal cancer patients who married 2.4 times (AHR = 2.4, 95% CI: 1.5-3.8), widowed 2.4 times (AHR = 2.4, 95% CI: 1.2-4.6), and divorced 2 times (AHR = 2.0, 95% CI: 1.1-3.7) were at higher risk of mortality than single marital status. Colorectal cancer patients having a comorbid condition were 1.8 times at higher hazard to die than patients with non-comorbid conditions (AHR = 1.8, 95% CI: 1.3-2.5). Those colorectal cancer patients who smoke cigarettes and drink alcohol were 1.6 and 1.5 times at higher risk of death than non-smokers (AHR = 1.6, 95% CI: 1.1-2.3) and alcohol users (AHR = 1.5, 95% CI: 1.07-2.2), respectively. Patients who were diagnosed at clinical stage IV were 17.6 times at higher hazard to die than those who were diagnosed as clinical stage I (AHR = 17.6, 95% CI: 6.1-50.7). Among colorectal cancer patients diagnosed as undifferentiated tumor grade were 1.7 times at higher risk of mortality than those who were differentiated type of tumor (AHR = 1.7, 95% CI: 1.17-2.4) (Table 5).

Table 4. Survival time, cumulative survival probability and log-rank test for the study population according to clinical and treatment characteristics of patients during six-year of follow-up (Kaplan–Meier method) of colorectal cancer patients in TASH

Variable	Category	Median survival (mo) (95% CI)	1-year survival	2-year survival	3-year survival	4-year survival	5-year survival	Overall survival	Log-rank test (*P*-value)
Primary site	Colon	35.5 (28.5-37.6)	88.7	67.7	48.8	30.8	17.5	21.5	0.68
	Rectum	33.1 (28.0-44.6)	93.2	66.8	44.2	33.7	23.1	-	
Stage of cancer at diagnosis[a]	Stage I	-[b]	98.0	94.6	89.6	83.2	83.0	83.0	< 0.001
	Stage II	37.6 (35.0-…)	97.2	82.3	60.8	45.4	22.7	22.7	
	Stage III	34.8 (27.2-38.0)	91.2	67.2	44.5	22.4	-	-	
	Stage IV	22.7 (19.1-25.9)	81.6	46.6	20.9	8.6	-	-	
Grades of cancer	Differentiated	45.3 (38.3-61.0)	93.5	79.6	64.3	46.5	30.7	23.3	< 0.001
	Moderately differentiated	33.1 (27.0-36.6)	92.4	66.8	36.5	22.8	-	-	
	Undifferentiated	23.1 (19.4-27.0)	83.5	47.1	24.2	11.7	8.7	8.7	
Histologic	Adenocarcinoma	36.7 (31.2-41.8)	91.5	68.0	51.8	37.1	26.2	21.8	0.020
	mucinous carcinoma	29.3 (24.4-36.8)	86.4	65.7	38.2	9.3	-	-	
	Signet-ring-cell carcinoma	30.7 (23.3-36.1)	85.3	64.5	21.5	7.2	-	-	
Treatment	Radiotherapy alone	37.9 (34.8-…)	84.4	71.7	47.5	46.5	46.5	46.5	< 0.001
	Surgical treatment alone	-	89.0	71.9	50.3	50.3	50.3	50.3	
	Chemotherapy alone	27.2 (23.2-26.1)	87.3	60.7	30.3	24.3	-	-	
	Surgery plus chemotherapy	37.6 (34.7-45.3)	91.6	70.4	55.0	36.4	18.2	-	
	Radiation as neo-adjuvant to surgery	36.8 (18.3-…)	96.4	60.0	46.8	37.4	-	-	
	Radiation + surgery + chemotherapy	30.4 (25.9-36.6)	90.8	67.3	40.3	17.4	8.7	-	
	Didn't receive treatment	-	-	-	-	-	-	-	

The total number of 621 subjects were selected from patients registered between January 1, 2013 and December 30, 2017 with follow-up until December 30, 2018. Values are presented as percent only. TASH, Tikur Anbessa Specialized Hospital. [a]According to American Joint Committee of Cancer. [b]It means more than half of patients survived. Median survival time could not be calculated.

Table 5. Results of the bivariable and multivariable cox regression analysis of colorectal cancer patients in TASH, Addis Ababa, Ethiopia

Variable	Category	Bivariable CHR (95% CI)	Multivariable AHR (95% CI)
Sex	Female	1	1
	Male	1.4 (1.047-1.86)*	0.89 (0.64-1.24)
Age of patient (yr)	< 40	1	1
	40-49	1.1 (0.71-1.73)	0.97 (0.60-1.55)
	50-59	0.93 (0.62-1.39)	0.86 (0.50-1.34)
	60-69	2.2 (1.46-3.28)***	1.5 (0.98-2.40)
	≥ 70	2.9 (1.89-4.66)***	1.7 (1.02-2.90)*
Residence	Rural	1	1
	Urban	1.3 (0.97-1.77)	1.3 (0.93-1.80)
Marital status	Single	1	1
	Married	1.4 (0.96-2.105)	2.4 (1.50-3.80)***
	Widowed	2.3 (1.31-3.9)**	2.4 (1.20-4.60)**
	Divorced	2.7 (1.62-4.4)***	2.0 (1.1-3.7)*
Smoking status	No	1	1
	Yes	2.4 (1.80-3.19)***	1.6 (1.10-2.30)*
Alcohol consumption	No	1	1
	Yes	2.1 (1.59- 2.76)***	1.5 (1.07-2.20)*
Comorbidity	No	1	1
	Yes	2.7 (2.10-5.66)***	1.8 (1.30-2.50)***
Stage at diagnosis[a]	Stage I	1	1
	Stage II	4.8 (1.7-13.9)**	3.8 (1.3-11.1)*
	Stage III	8.9 (3.2-24.7)***	8.0 (2.8-23.3)***
	Stage IV	18.1 (6.6-50.1)***	17.6 (6.1-50.7)***
Grades of cancer	Differentiated	1	1
	Moderately differentiated	1.6 (1.14-2.4)**	1.4 (0.94-2.03)
	Undifferentiated	2.8 (2.04-3.89)***	1.7 (1.17-2.4)**
Histology type	Adenocarcinoma	1	1
	Mucinous carcinoma	1.4 (0.97-2.02)	1.2 (0.80-1.75)
	Signet-ring-cell carcinoma	1.8 (1.1-2.9)*	1.3 (0.71-2.19)
Treatment modality	Radiation alone	1	1
	Surgical treatment alone	0.89 (0.37-2.07)	0.85 (0.35-2.1)
	Chemotherapy alone	1.8 (0.92-3.5)	0.82 (0.40-1.7)
	Surgery plus chemotherapy	1.2 (0.61-2.2)	0.67 (0.34-1.3)
	Radiation as neo-adjuvant to surgery	1.2 (0.58-2.6)	0.82 (0.37-1.8)
	Radiation + surgery + chemotherapy	1.5 (0.80-2.89)	0.69 (0.34-1.4)
	Didn't receive treatment	0.83 (0.10-6.47)	0.6 (0.07-5.4)

The total number of 621 subjects were selected from patients registered between January 1, 2013 and December 30, 2017 with follow-up until December 30, 2018. TASH, Tikur Anbessa Specialized Hospital; CHR, crude hazard ratio; AHR, adjusted hazard ratio. [a]According to American Joint Committee of Cancer. *Significant (P < 0.05), **significant (P < 0.01), ***significant (P < 0.001).

DISCUSSION

This retrospective follow-up study aimed to assess the survival status and predictors of mortality among confirmed diagnosis of colorectal cancer at the TASH Oncology Department. This study showed that the overall 1-, 3-, and 5-year survival rates of colorectal cancer patients were found to be 90.7%, 47.0%, and 21.7% respectively. This finding is in line with the result of a study which has been conducted in South Iran [16]. However, these values are lower than those from studies conducted in Taiwan [22], Kurdistan [19], North Iran [23], Malaysia [8], and New Zealand [24], Jordan [25], Saudi Arabiya [26] at 5 years. In addition, the values are higher compared to those from the study conducted in Ghana [12]. This discrepancy may be due to lack of early screening program, a higher proportion of advanced stage cancer at time of diagnosis, lack of specialized care, and delay in receiving care.

With regards to age, the survival time of patients diagnosed with colorectal cancer in this study is lower than other study done in Netherlands [27]. The survival difference between young and older colorectal patients arises from different attributes of survival such as: difference in treatment modalities, the unfavorable effects of medication and intoxication, comorbidity in older patients, and low progression of disease in younger patients [28]. This could be due to lack of health awareness in receiving medical care, adherence to treatment during outpatient treatment and frequent follow-up constraint.

In this study, married colorectal cancer patients had

a better survival rate (26.1%) than single, divorced and widowed ones as assessed by using a log rank test at P = 0.0002 which is similar to the study conducted in Taiwan [29]. In addition, marital status was found to be a statistically significant predictor of colorectal cancer mortality, taking single marital status as a reference corresponding to the study conducted in Florida [30]. However, in the current study, the reason why marital status was a statistically sigificant predictor could be owing to relatively a large number of older participants who probably had spouse. On the other hand, divorced, and widowed status may lack advocator to seek early cancer detection, treatment, and regular follow-up, social support, health related behavior, etc.

The overall 3-year and 4-year survival rates of confirmed diagnosis of stage I, II, III, IV were 89.6%, 60.8%, 44.5%, 20.9% and 83.2%, 45.4%, 22.4%, 8.6%, respectively. These values were lower than those of a study conducted in Malaysia [18]. The overall 4-year survival of stage I in this study was in line with 5-year overall survival study in Jamaica at stage I, and 5-year overall survival in Taiwan at stage II, whereas the overall 4-year survival is lower than that observed in studies conducted in Taiwan at stage I, II, III, IV [22] and in Jamaica [31]. Furthermore, the overall 5- and 6-year survival rates found in this study for both stage III and stage IV were similar to the 5-year overall survival of stage IV which was conducted in Ghana [12]. This discrepancy perhaps is due to late presentation of cancer stage, early screening and detection, early initiation of different treatment modalities and inadequate health information regarding the nature of the disease. In addition, it might also be due to poor adherences to treatment and discontinuing the medical outpatient follow-up.

The overall 3- and 5-year survival rates for confirmed diagnosis of colorectal cancer having comorbid condition were 21.7% and 2.7%, which are lower than than those from previous studies conducted in Malaysia [32] and Spain [33]. This difference could be due to early implementation, advanced treatment modality and adherence to treatment. Furthermore, colorectal cancer patients having comorbid conditions had a significantly higher hazard to die than non-comorbid patients as seen in the study conducted in Japan [34] because comorbidity is associated with alterations in morphology, histology, differentiation, and proliferation of tumor status. For example, hyperinsulinemia associated with diabetes mellitus can be implicated in cancer [35]. Colorectal cancer patients with comorbid conditions are less capable to receive standard treatments due to treatment related increased side effects and toxicity; increased disabilities and geriatric syndromes. Furthermore, a comorbid condition causes the early sign and symptoms of the colorectal cancer [36].

Being clinically diagnosed as stage IV, stage III, and stage II at base line has 17.6 times (P < 0.001), 8.0 times (P < 0.001) and 3.8 times (P < 0.05) at higher risk of death than stage I. This finding is similar to that of other studies in terms of increased hazard to die, but the rate of risk to die differs from that of a previous study conducted in Iran [37]. Similarly, the study in Iran revealed that the stage was a significant factor for colorectal cancer mortality as patients diagnosed at an early stage had lower risk of death than those at a late stage at base line [38].

In the current study,a siginificantly increased risk was found in cigarette smokers (AHR = 1.6, 95% CI: 1.1-2.3 at P < 0.05). This finding is similar to that of another study conducted in Germany [17]. Alcohol consumption was also found to be associated with increased (AHR = 1.5, 95% CI: 1.07-2.2 at P < 0.05) as seen in the study done in Germany [39]. This is possibly related to a carcinogenic effect of alcohol and smoking. Indeed, being diagnosed as colorectal cancer creates negative illness perception which leads to behavioral change and poor outcome for survival [40]. Smoking has an effect on carcinogenesis because it stimulates the tumor growth, increases survival of tumor, and facilitates proliferation of tumor and decreases the effectiveness of chemotherapy. Moreover, patients with micro satellite instability had higher risk of mortality if they smoke cigarettes [41].

In conclusion, the overall survival probability of confirmed diagnosis of colorectal cancer was 18.1% at 72 months of follow-up. The findings revealed that lower survival probability of confirmed colorectal cancer patients in TASH as compared with those of high- and middle-income countries. Age over 70 years, marital status, comorbidity, smoking, and alcohol consumption as well as stage and grade of tumor were found to be significant predictors of mortality patients with confirmed diagnosis of colorectal cancer.

This study recommends early colorectal cancer screening and detection programme with special attention to patients from the country side and with comorbid conditions. Further studies could be conducted by including laboratory findings, societal and health system related factors, and molecular biomarkers.

Strength of this study includes: a fairly longer follow-up study time, which makes the finding reliable. Data were collected by oncology nurses who had an important role in maintaining the quality of the data. Limitations includes: Selection bias possibly introduced during secondary data collection because patients with incomplete records were excluded. Cause specific survival was not determined as data on specific cause of death were not available. Some important predictors which might have significant prediction for colorectal cancer mortality (biological biomarkers, treatment adherence, physical exercise, cycle of chemo, aim of treatment, educational status and multidiscip-linary care) could not be found on the medical cards and were not assessed.

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CONFLICTS OF INTEREST

No potential conflicts of interest were disclosed.

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