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Research Article

Identify Primary Risk Variables Influencing the Recurrence of Cervical Cancer in Patients, Using Non-Parametric Methods at Tikur Anbessa Specialized Hospital

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Abstract

Background: This study aimed to identify the primary risk variables influencing the recurrence of cervical cancer in patients, at Tikur Anbessa Specialized Hospital. Cervical cancer deaths in Ethiopia reached 4,595, or 0.76% of total deaths. The age-adjusted death rate is 18.51 per 100,000 of the population in Ethiopia. *Method*: Among patients with cervical cancer, an institution-based retrospective follow-up research was conducted from January 2015 to March 2017 at TASH and is under follow-up. Out of a population of cervical cancer patients who were taking treatment in the hospital during that period, data on 420 patients is included in this study. Non-parametric methods, such as log-rank tests and the Kaplan-Meier method, were used to compare the rate of recurrence among the different explanatory variable categories. *Results*: After the medical cards of women were reviewed among those patients with cervical cancer, 170 (40.5%) were recurrent, and the remaining 250 (59.5%) were censored. Out of the total patients, 6.2% were at stage I, 32.6% were at stage II, 51.7% were at stage III, and 9.5% were at stage IV. The recurrence proportions of stage I, stage II, stage III, and stage IV patients were 5.88%, 27.05%, 52.35%, and 14.705%, respectively. *Conclusion*: Finally, the findings of this study implied that age, smoking cigarettes, stage of disease, initial treatment patients took, types of treatment patients took, and place were major factors related to the recurrence time of cervical cancer patients.

Keywords

Survival Analysis, Proportional Hazard, Cervical Cancer, Recurrence Time

1. Introduction

1.1. Background of the Problem

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer and can spread to other areas of the body. It is estimated that over 500,000 women globally receive a new diagnosis of cervix uteri cancer each year [1]. Cervical cancer is the world's most deadly but easily preventable cancer in women, responsible for more than 270,000 deaths annually, of which 85% occur in developing countries [2]. It was the fourth most commonly diagnosed cancer in women in 2012, with an estimated 527,600 new cases worldwide. With a rising population and aging, the number of cervical cancer cases is expected to increase 1.5 fold by 2030 [3].

On the other hand, cervical cancer is the second-greatest cause of cancer-related deaths worldwide, behind breast

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cancer, and it is the leading cause of death for women in reproductive age in several countries that are developing [4]. The lack of successful screening programs is the reason for this regional discrepancy, since biological and epidemiologic research have not revealed appreciable variations in tumor biology in nations with high prevalence of cervical cancer.

Cervical cancer is the second most frequently diagnosed cancer (80,400) and the leading cause of cancer death (50,300) in African women. Rates vary substantially across regions, with the incidence and death rates in East Africa and West Africa as high as the rates in North Africa [5]. Cancer patients in Sub-Saharan Africa tend to present with advanced disease [6]. Despite this, in 2010, radiotherapy was available in only 23 of 52 African countries, mostly in the northern and southern states of the continent. Brach therapy was available in only 20 countries [7] Only a small amount of epidemiological data on cervical cancer is currently available [8].

In Ethiopia, the death toll from cervical cancer was 4,595, or 0.76% of all deaths. Ethiopia's age-adjusted mortality rate is 18.51 per 100,000 people [9]. Ethiopia has an age-adjusted incidence rate of 35.9 cases of cervical cancer per 100,000 women. Even still, relatively few women make use of screening services. Despite the lack of a national cancer registry, findings from retrospective assessments of biopsy data indicate that among Ethiopian women, cervical cancer is the most common malignancy, followed by breast cancer.

Ethiopia is the second-most populated country in sub-Saharan Africa, with more than 42 million females [10]. Ethiopia is one of the least urbanized countries in the world, with only 16% of the population living in urban areas [10]. There are an estimated 7,000 new cases of cervical cancer in Ethiopia per year; nearly 5,000 people are estimated to die of the disease per year [11]. Public oncological treatment in Ethiopia, including radiotherapy, is limited to the Radiotherapy Center at Tikur Anbessa University Hospital, which is staffed by four radiation oncologists. Treatment options for patients with cervical cancer include radical hysterectomy (Wertheim operation) in the early stages at the Department of Gynecology at Tikur Anbessa Hospital. External-beam radiation can be given combined with chemotherapy at the radiotherapy department. Brachytherapy is not available in Ethiopia. When attending the hospital, patients first have to register at the radiotherapy department for an appointment with the radiation oncologist. At this appointment, evaluation and planning of radiotherapy are performed by the radiation oncologist. Thereafter, patients receive an appointment to start radiotherapy. Because of huge patient loads, a considerable amount of time may pass between these appointments. Patients with acute bleeding receive priority for appointments for emergency radiation. Little is known about the outcome of cervical cancer patients who receive therapy in such settings with limited resources. Recent publications point toward the need for more epidemiological data on non-communicable diseases, including cancer [5, 12].

According to data from the Tikur Anbessa Specialized Hospital Oncology Unit, more than 500 adult and pediatric cases with hematologic malignancies are seen in the hematology clinics every year. Many patients with cancer are also seen at the surgical, gastrointestinal, and gynecology clinics. The most common adult cancers are cervical, breast, sarcomas, head and neck, and colorectal cancers, while leukemia, lymphoma, retinoblastoma, and osteosarcoma constitute the bulk of pediatric cancers. The hospital aspires to become a center of excellence in the diagnosis, treatment, and care of patients with cancer. With the support of Ethiopia's governmental institutions, non-government organizations, and international partners, it is hoping to develop a comprehensive cancer care program, including a cancer registry, early detection, prevention, standard treatment, and palliative care [13]. As stated by the study from September 2008 to September 2012 of 2,300 CC patients, 1,059 patients with standardized treatment were included. At the end of the study, 249 patients had died [14].

Recurrent cancer is when cancer cells are detected following the initial treatment with surgery (operation), radiotherapy, or chemotherapy. Treatment options for recurrent cancer vary depending on the previous treatment, the location of the recurrence, and the overall condition of the patient.

1.2. Statement of the Problem

In addition to serving as the most frequently cause of cancer-related morbidity and mortality, cervical cancer is the most common cause of death for women. Based to current estimates, cervical cancer claims the lives of 265,672 women globally each year, with 527,624 women receiving a diagnosis. Cervical cancer is not well known to be prevalent, and many patients frequently arrive at medical facilities much later than expected [15]. Through screening programs, many developing nations have decreased the incidence of cancer and, consequently, the cost of treatment. Regretfully, unlike many other low-resource nations, Ethiopia lacks a routine screening program. As a result, patients often come at an advanced stage, contributing to the alarmingly high fatality rates associated with cervical cancer. [16].

The survival time for the recurrence of cervical cancer patients who are already treated may depend on different factors, such as demographics, health conditions, and the initial treatments given to the patients. This case study is intended to identify the primary risk variables influencing the recurrence of cervical cancer in patients. This study was trying to fill the gaps in understanding the status of cervical cancer patients by identify the primary risk variables influencing the recurrence of cervical cancer in patients in Ethiopia.

Generally, this study would attempt to answer the following basic research questions:

1) Which factors have a significant effect on the recurrence of cervical cancer for patients after their treatment?
2) Is there a difference in the recurrence of cervical cancer for patients after their treatment among place states in Ethiopia?

3) Within a factor, which levels have a statistically significant effect on the recurrence of cervical cancer?

1.3. Objectives of the Study

1.3.1. General Objective

The overall aim of this research is identify the primary risk variables influencing the recurrence of cervical cancer in patients in Tikur Anbessa specialized hospital.

1.3.2. Specific Objectives

The study has the following specific objectives:

1) To identify and compare the recurrence of cervical cancer disease among different levels of risk factors.
2) To describe the influence of predictors on the recurrence of cervical cancer for patients after their treatment.

1.4. Significance of the Study

The outcome of this study will provide information about the risk factors or the most influential covariates that have a significant impact on the recurrence of cervical cancer for patients after their treatment. The results of this study will help in reducing the recurrence of cervical cancer by raising awareness in society about the factors that increase the probability of recurrence of the disease. It will also be used as a source of information for the government of Ethiopia, the Ministry of Health that enables policymakers to enhance the awareness of society about factors that increase the probability of recurrence due to cervical cancer, which is protectable and curable if it is screened and treated in its earlier stages with appropriate treatment.

2. Data and Methodology

2.1. Study Area

Tikur Anbessa Specialized Hospital is the largest general public hospital located in Addis Ababa. The Federal Ministry of Health estimates that there could be more than 160,000 cancer cases in Ethiopia each year, but available data is limited. As the nation's sole cancer referral center, the hospital is treating only about one percent of these patients. The hospital gives service to the population of Addis Ababa city and its surroundings, but patients come to the hospital from all over Ethiopia.

2.2. Study Populations

This retrospective cohort study aims to determine the recurrence of cervical cancer based on the hospital registry at TASH Oncology Center. The population of this study was all cervical cancer patients who had been registered at Tikur Anbessa Referral Hospital from January 2015 G.C. up to March 2017 G.C. and were under follow-up. Patients registered on the computer, which includes their card number, patient name, sex, and region. The card number of patients used to find patients follow-up card room the cards are prepared by clinicians to early Identify and document clinical and laboratory variables. Thus, the data were collected from patient follow up records based on the variable in the study.

2.3. Data Collection Procedure

The training enumerator and the principal investigator collected the data from patient records. So in this study, we incorporated secondary data. From the patients' card, the age, the stage of the disease when they were referred to the hospital, the date the treatment in the hospital, the initial treatment the patients took (surgery, chemotherapy, and radiotherapy), place, and other medical information were collected. Data collection was carried out in the time interval of May 11, 2017 G.C. to May 21, 2017 G.C.

2.4. Exclusion and Inclusion Criteria

Inclusion Criteria

All patients' registrations with full information, including the registration log book or the patients' identification card, were considered to be eligible for the study. And also, the patients should take cancer treatment at least once in the hospital.

Exclusion criteria

Patients with insufficient information about one of the vital variables, either in the registration book or on the card, were not eligible. Also, the patients 'lost from the study without starting any cervical cancer treatment was not included.

2.5. Study Variables

2.5.1. Dependent Variable

In this study, the outcome of interest (recurrent) is the duration of time until recurrent occurs. The status variable is coded as 0 for censored and 1 for recurrent.

2.5.2. Independent Variables

The predictor variables in survival data analysis are called covariates. These covariates can be categorical or continuous. The predictor variables (factors) that are assumed to influence the recurrence of cervical cancer patients are listed under Table 1.

Table 1. *Explanatory variables issued to use in the study.*

Variables	Description	Values
Age	Age of the patients	≤ 50 or >50
Marriage	Age at Marriage	$\leq 20, 21-30, \geq 31$
Chemotherapy	Cycles of Chemotherapy	No chemotherapy, 1st cycle and 2nd cycle
Treatment	Treatment taken	Surgery, chemotherapy, radiotherapy, chemo-radiation, surgery and chemotherapy, surgery and radiotherapy
Radiotherapy	Aim of radiotherapy	No RT, Palliative and radical
Sexual	Sexual partner	One, two, few (2-3), multiple (>3) and unknown
HIV	Status	No or Yes
Abortion		No or Yes
Family	Family planning	No or Yes
Family2	Family history	No or Yes
smoking	Smoking status	No or Yes
Children	Number of children	No child, 1-3, 4-7 and 8 and above
Stage	Stage of cervical cancer	Stage I, II, III, and IV respectively.
Initial treatment		Surgery, chemotherapy, radiotherapy and combination.
Birth	Age at first birth	$\leq 20, 21-30, 31 and\ above, not give\ birth$
Tumor	Tumor size (cm)	$\leq 4, \geq 4, not\ give\ birth$
Tumor2	Tumor grade	Well, moderate and poor
Place	Place of origin	Urban/rural

Urban (Addis Abeba, Mekelle, Adama, Diredawa, Bahirdar, Hawasa, Harar)

Due to the limitations of the secondary data, the variables the researcher used here were age of patients, stage of disease, smoking status, initial treatment the patients took, tumor size, aim of radiotherapy, number of cycles patients took, types of treatment patients took, HIV status, and place.

2.6. Methods of Data Analysis for Recurrence of Cervical Cancer Censored

In summarizing survival data, the two common functions of applied are the survivor function and the hazard function and Standard Cox PH model were applied.

3. Results and Discussion

3.1. Explanatory Data Analysis and Non-Parametric Analysis

The study intended to find the determinant risk of the time to recurrence of cervical cancer in patients at TASH for those patients who took their treatment from January 2015 GC up to March 2017 GC and were under follow-up. The time interval between screening and recurrence was of interest in this research paper. The minimum observed event time was 2 months, and the maximum was 26 months. In this study, only those who took the cervical cancer treatment at least once in the hospital were included. For this study, from a total population size of 952, samples of 420 cervical cancer patients fulfilling the inclusion criteria were considered. After the medical cards of women were reviewed among those patients with cervical cancer, 170 (40.5%) were recurrent, and the remaining 250 (59.5%) were censored.

As shown in Table 4 in the appendices of total cervical cancer patients, 13.82% smoked cigarettes and 86.2% did not smoke cigarettes. The recurrence proportions of smokers and non-smokers of cigarettes were 29.41% and 70.58%, respectively. Similarly, when considering the age groups of the patients, 47.6% and 52.3% were in the age groups of less than or equal to 50 and greater than 50, respectively. The recurrence proportions of the age groups of the patients (22.35% and 77.64% were in the age groups of less than or equal to 50 and greater than 50, respectively.

Out of the total patients, 6.2% were at stage I, 32.6% were

at stage II, 51.7% were at stage III, and 9.5% were at stage IV. The recurrence proportions of stage I, stage II, stage III, and stage IV patients were 5.88%, 27.05%, 52.35%, and 14.705%, respectively. Among the cervical cancer patients included in the study, 16.9% took the initial treatment of surgery, 35% took the initial treatment of chemotherapy, 38.3% took the initial treatment of radiotherapy, and 9.8% took the initial treatment of chemotherapy radiation. The recurrence proportion of patients who took the initial treatment of surgery, the initial treatment of chemotherapy, the initial treatment of radiotherapy, or the combination of two or three was 21.76%, 31.76%, 40.5%, and 5.88%, respectively. Out of the total patients, 69.8% had no HIV status, and 30.2% had HIV status. The recurrence proportions of patients who had no HIV and had HIV were 66.47% and 41.17%, respectively.

Considering the number of cycles' patients who took chemotherapy for cervical cancer, 55.7%, 30.2%, and 14.1% were in no chemo, first cycle, and second cycle, respectively. The recurrence proportion of the number of cycles' patients who took chemotherapy with no chemotherapy, second cycles, and third cycles was 52.94%, 31.76%, and 15.29%, respectively. Out of the total patients, 75.5% and 24.5% were less than or equal to 4 and greater than 4 tumor sizes, respectively. The recurrence proportions of less than or equal to 4 and greater than 4 tumor sizes were 74.117% and 25.88%, respectively. Out of the total patients with the aim of radiotherapy, 33.3%, 57.4%, and 64.2% were for no radiotherapy, palliative, and radical, respectively. The recurrence proportions for radiotherapy, palliatives, and radicals were 2.35%, 65.88%, and 31.77%, respectively. Besides Out of the total patients, 3.1%, 4.5%, 69.5%, 20.7%, 0.7%, and 1.2% took the treatment of surgery, chemotherapy, radiotherapy, radiotherapy surgery-chemotherapy, and surgery-radiotherapy, respectively. The recurrence proportions of those who took surgery, chemotherapy, radiotherapy, surgery-chemotherapy, and surgery-radiotherapy were 6.4%, 4.7%, 68.8%, 18.235%, 1.17%, and 0.58%, respectively. Out of the total patients, 46.4% and 53.6% lived in urban and rural areas, respectively. The recurrence proportion of those who lived in urban and rural areas is 40% and 60%, respectively.

3.1.1. The Kaplan-Meier Estimate of Time-to-Recurrence of Cervical Cancer Patients

The mean survival time for the patients who have taken chemotherapy is 19.887 with standard error of 0.679; for the palliative aim of radiotherapy, the mean is 18.892 with a standard error of 0.504. For the cervical cancer patients taking radical radiotherapy, the mean and standard error are 19.380 and 0.703 respectively. Considering the chemotherapy radiation therapy, the mean and standard error are 19.945 and 0.894 respectively and the patients who that took surgery have a mean and standard error of 11.929 and 2.010, respectively.

The estimated mean survival time and 95% confidence interval for recurrence of cervical cancer patients with different covariate characteristics are summarized in Table 5 in the appendix. The mean survival time of cigarette smoker women was [95%, 11.189–14.649], which was less than that of non-smokers [95% CI: 19.387–21.047].

In table 4 in the appendix, the log-rank (Mantel-Cox) test shows that the survival curves are not different across the number of cycles, aim of radiotherapy, and tumor size. But the survival curves for the variables of initial treatment, age, smoking status, and stage of the disease, types of treatment, HIV status, and place are all different across their levels.

3.1.2. Compare Survival Time-to-Recurrence for Different Covariates Groups

The survival time plot by age and stage of disease is given in Figure 1. This plot showed that the risk of recurrence was different for age groups that were less than or equal to 50 and greater than 50. The log rank test in Table 4 in the appendix also revealed that age and stage of disease had a statistically significant association with the survival time of women (p = 0.00) and (p = 0.000) at at 25% level of significance. This plot showed that the risk of recurrence was different for patients by category of stage of disease, respectively.

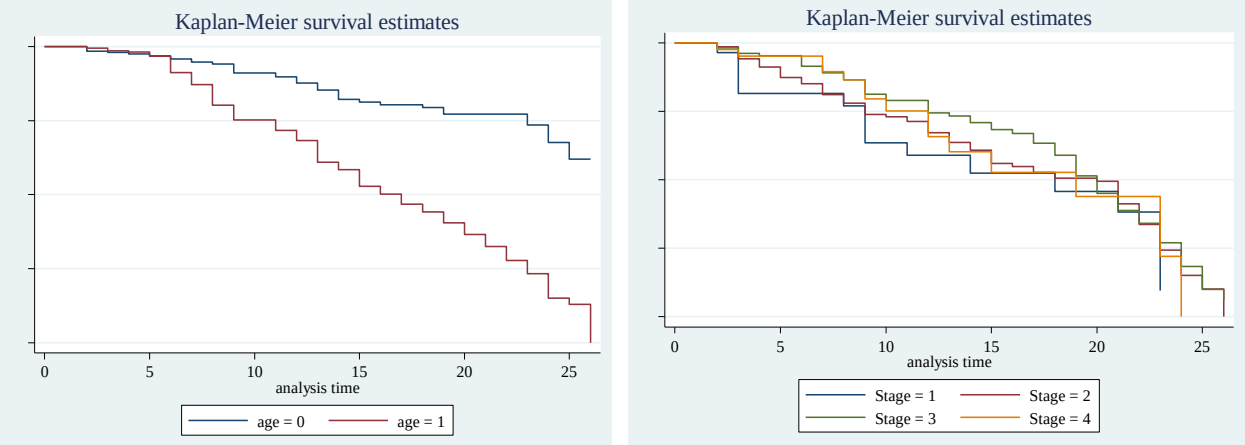

Figure 1. *K-M survival time plot by age of cervical cancer patients.*

The survival time plot by HIV status is given in Figure 2. This plot showed that the risk of recurrence was different for patients who were living with HIV/AIDS and free from HIV. The log rank test in Table 4 in the appendix also revealed that HIV status had a statistically significant association with the survival time of women (p = 0.041) at the 25% level of significance. According to the survival time plot by chemotherapy cycles (Figure 2), the risk of recurrence of cervical cancer that had different cycles of chemotherapy was the same. The log rank test in Table 4 in the appendix also revealed that chemotherapy cycles had no significant association with the survival time of patients (p = 0.912) at the 25% level of significance.

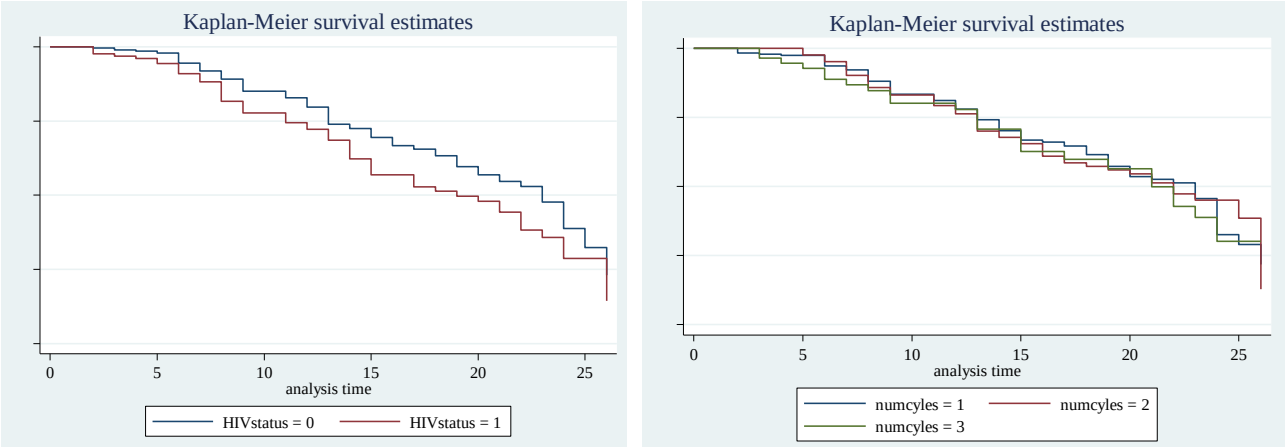

Figure 2. *K-M survival time plot by HIV status and number of cycles of CC patients.*

The survival time plot by smoking status is given in Figure 3. This plot showed that the risk of recurrence was different for patients who were smoking cigarettes and those who were not. The log rank test in Table 4 in the appendix also revealed that smoking status had a statistically significant association with the recurrence of cervical cancer patients (p = 0.000) at the 25% level of significance. According to the survival time plot of the aim of radiotherapy (Figure 3), the risk of recurrence of cervical cancer that had a different aim of radiotherapy was the same. The log rank test in Table 4 in the appendix also revealed that the aim of the radiotherapy had no statistically significant association with the recurrence of cervical cancer in patients (p = 0.636) at the 25% level of significance.

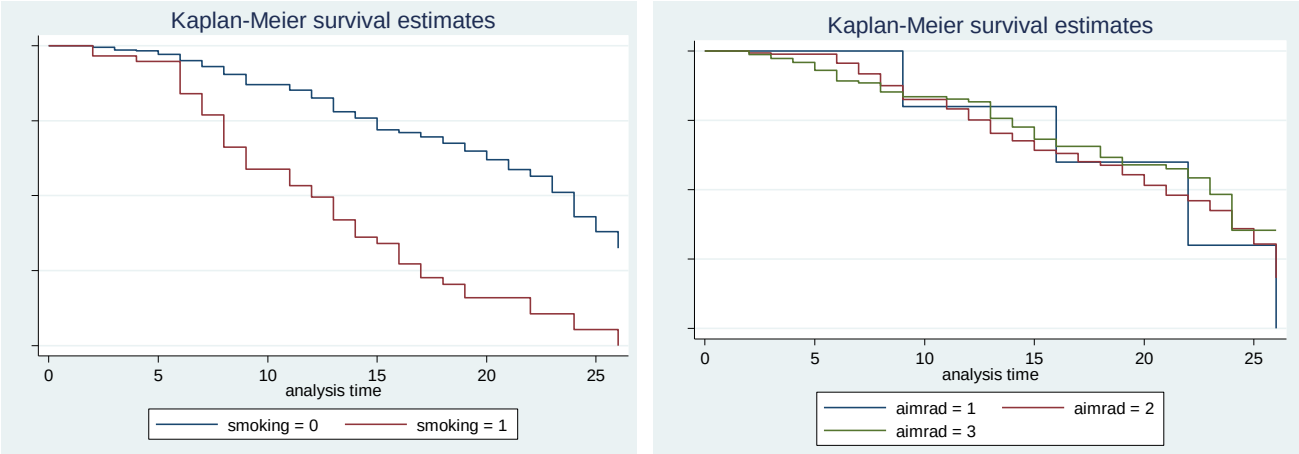

Figure 3. *K-M survival time plot by smoking status and aim of the radiotherapy of CC patients.*

The survival time plot by initial treatment is given in Figure 4. This plot revealed that the risk of recurrence was different for patients who received the initial treatment. The log rank test in Table 5 in the appendix also revealed that initial treatment had a statistically significant association with the recurrence of cervical patients (p = 0.002) at the 25% level of

significance. According to the survival time plot in Figure 4, the risk of recurrence of cervical cancer in different places varied. The log rank test in Table 4 in the appendix also revealed that place had a significant association with the recurrence of cervical cancer in patients (p = 0.003) at the 25% level of significance.

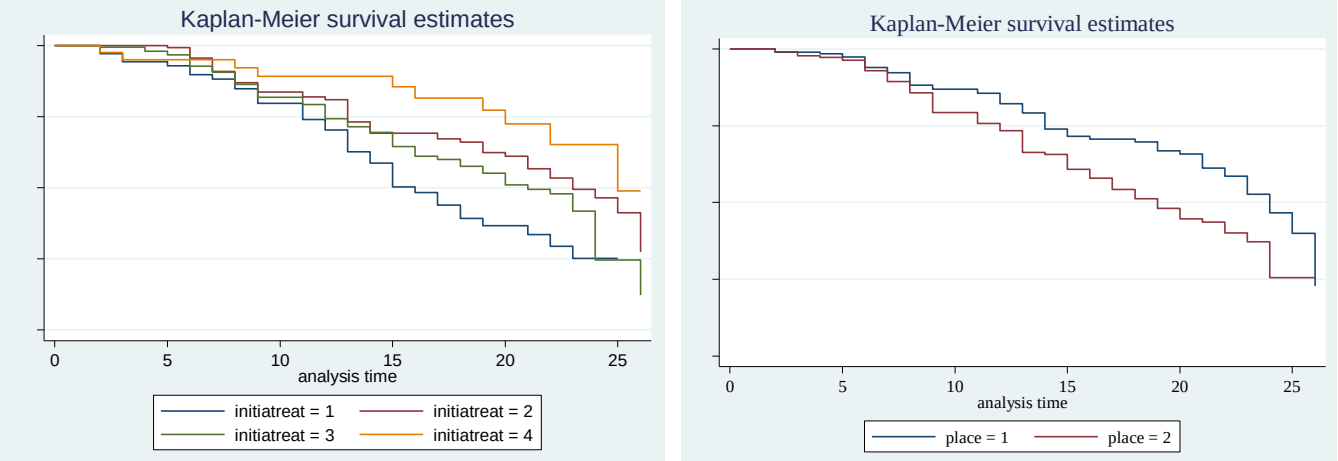

Figure 4. *K-M survival time plot by initial treatment and place of CC patients.*

According to the survival time plot for tumor size (Figure 5), the risk of recurrence of cervical cancer with different tumor sizes was the same. The log rank test in Table 4 in the appendix also revealed that tumor size had no significant association with the recurrence of cervical cancer in patients (p = 0.255) at the 25% level of significance. However, in the survival time plot type of treatment Figure 5, the risk of recurrence of cervical cancer that had different types of treatment varied. The log rank test in Table 4 in the appendix also revealed that treatment had a significant association with the recurrence of cervical cancer in patients (p = 0.001) at the 25% level of significance.

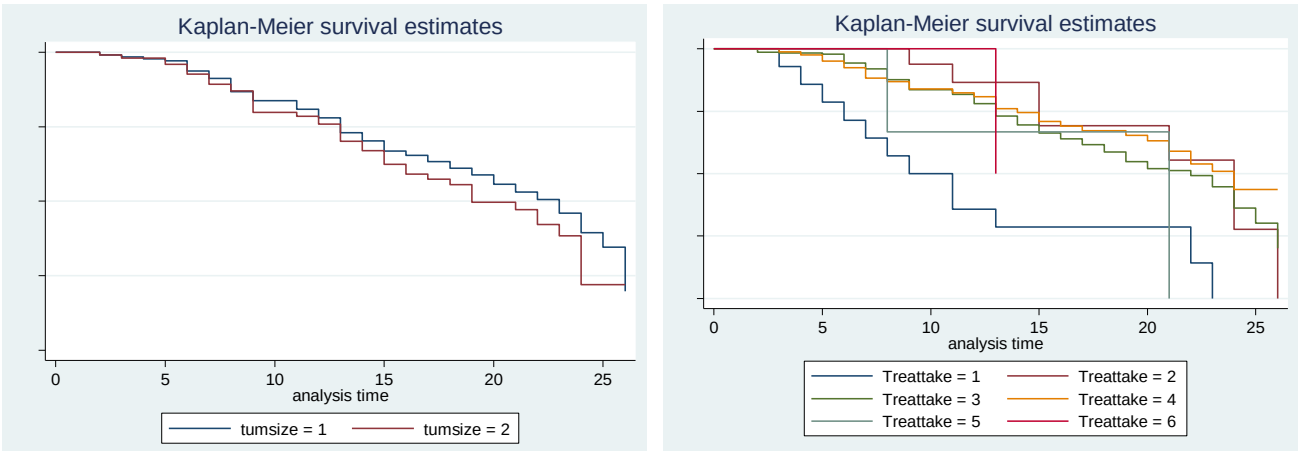

Figure 5. *K-M survival time plot by tumor size and type of treatment taken of CC patients.*

3.2. Standard Cox PH Model

3.2.1. Univariate Analysis

As shown from Table 2, survival of the patients is significantly related to age, smoking status, stage of disease, initial treatment, and type of treatment, HIV status, and place at a 25% level of significance. We are going to study the effect of some covariates using Cox regression on the recurrence of cervical cancer. As we mentioned before, there are quite a lot of covariates. We start out by focusing on a bit of them. The ages are grouped into two different levels.

3.2.2. Multivariate Analysis

In a single-covariate approach, it ignores the possibility that a collection of variables, each of which is weakly associated with the outcome, can become an important predictor of the

outcome when taken together. For this reason, we used a large P-value of 0.25 for the selection of variables that may be significantly predicted in the multi-covariate analysis from single covariate findings.

Table 2. *Univariate and multivariate Cox PH model for the relative hazard of survival time for recurrence of cervical cancer patients at TASH based on the variables under study and hazard ratio results (January, 2015 G.C. up to March, 2017 G.C.).*

Covariate	**Univariate Analysis**				**Multivariate Analysis**			
	B	**Unadjusted HR**	**p-value**	**95% CI**	**B**	**Adjusted HR**	**p-value**	**95% CI**
Age	1.3971	4.0434	4.69e-14*	(2.812, 5.814)	1.1728	3.2309	1.3e-09*	(2.21, 4.72)
Smoking	1.2979	3.6616	2.35e-14 *	(2.623, 5.111)	0.6783	1.9705	0.0004*	(1.35, 2.86)
Stage of disease								
StageI	Ref.							
StageII	-.6191	0.5384	0.00404 *	(0.353,.8211)	-0.0794	0.9235	0.831	(0.44, 1.91)
StageIII	-.3198	0.7263	0.11730	(0.4867, 1.08)	-0.0794	0.9236	0.8201	(0.46, 1.83)
StageIV	-1.124	0.3250	0.00167 *	(0.1612 0.65)	0.84615	2.3306	0.0263*	(1.10, 4.92)
Initial treat								
Surgery	Ref							
Chemotherapy	-0.619	0.5384	0.00404 *	(0.3530, 0.82)	-0.6192	0.5383	0.0079*	(0.34, 0.85)
Radiotherapy	-0.319	0.7263	0.11730	(0.4867, 1.08)	-0.4164	0.6594	0.0508	(0.43, 1.00)
Comnbination	-1.124	0.3250	0.00167 *	(0.1612, 0.65)	-0.8191	0.4408	0.0260*	(0.21, 0.90)
Types of treat								
Surgery	Ref.							
Chemotherapy	-1.374	0.2529	0.00393 *	(0.0993, 0.64)	-0.8947	0.4087	0.0780	(0.15, 1.10)
Radiotherapy	-1.200	0.3011	8.04e-05 *	(0.1658, 0.54)	-0.7021	0.4955	0.0415*	(0.25, 0.97)
Chemoradition	-1.431	0.2389	2.94e-05 *	(0.1220, 0.46)	-0.9217	0.3978	0.0148*	(0.18, 0.83)
Surgery and chemoradiation	-0.739	0.4773	0.33328	(0.1067,2.13)	-0.0102	0.9898	0.9895	(0.21, 4.56)
Surgery and radiotherapy	-1.008	0.3646	0.33312	(0.0472, 2.81)	-0.6870	0.503	0.5181	(0.06, 4.04)
HIV status								
Have HIV	Ref							
No HIV	0.3288	1.3893	0.0434 *	(1.01, 1.911)	0.1730	1.1888	0.3273	(0.84, 1.68)
Place								
Urban	Ref.							
Rural	0.4653	1.5925	0.00318 *	(1.169, 2.169)	0.3427	1.4088	0.042*	(1.01, 1.96)
likelihood ratio test								129.6
AIC								1676.602

The baseline numbers of cycles of chemotherapy that patients took, the aim of radiotherapy, and tumor size were not significant in the unadjusted analysis (not shown in the table).

AIC Akaike Information Criterion; β: coefficient for co-

variate; HR: hazard ratio; p-value: probability value; 95%CI: 95% confidence interval for HR.

In the final model, the survival time of women with cervical cancer was significantly affected by age, smoking status, stage of disease, initial treatment, types of treatment, and place.

3.2.3. Statistical Tests for Proportional Hazard Model Assumptions Checking

The goodness-of fit testing approach is appealing because it provides a test statistic and p-value for assessing the PH assumption for a given predictor of interest. Rho is a relationship between time and residuals. The test of correlation (rho) is insignificant, which indicates the proportional hazards assumption is fulfilled. The P-values given in Table 3 provide goodness-of-fit tests for each variable in the fitted model adjusted for the other variables in the model, which are quite high for variables of smoking status, stage of disease, initial treatment patients took, types of treatment patients took, HIV status, and place, suggesting that all the listed variables satisfy the PH assumption. But variable age does not satisfy the PH assumption. However, it is also possible to see its global test, and if it is greater than 0.05, the assumption has been satisfied by the covariates in the model. In this study, the global test is greater than 0.05, satisfying the assumptions satisfied by the covariate in the model.

Table 3. *Test of Proportional Hazard Assumptions.*

	rho	chisq	p
Age	0.1543	4.8143	0.0282
Smoking	-0.0440	0.3866	0.5341
as.factor(stage)2	0.0278	0.1821	0.6696
as.factor(stage)3	0.0404	0.3700	0.5430
as.factor(stage)4	0.0153	0.0481	0.8263
as.factor(initial.treat)2	-0.1102	2.4703	0.1160
as.factor(initial.treat)3	-0.0691	0.8954	0.3440
as.factor(initial.treat)4	-0.0208	0.0782	0.7798
as.factor(treat.take)2	0.0872	1.4718	0.2251
as.factor(treat.take)3	0.0121	0.0330	0.8560
as.factor(treat.take)4	-0.0295	0.1944	0.6593
as.factor(treat.take)5	0.0677	0.7849	0.3756
as.factor(treat.take)6	0.0484	0.3935	0.5305
HIV.status	-0.0437	0.3696	0.5432
place	0.0693	0.9276	0.3355
GLOBAL	NA	15.2439	0.4340

Chisq= chi-squared., p= p-value

4. Conclusion and Recommendation

4.1. Conclusion

This study used the survival time of cervical cancer patients' dataset of those patients who started their cancer treatment from January 2015 up to March 2017 with the aim of modeling the determinant of time-to-recurrence of cervical cancer patients in TASH. Out of the total 952 women who started cancer medicine (treatments), about 40.5% revealed the recurrence of cervical cancer at the end of the study.

In assessing the significant risk factors, the log rank test revealed that age, smoking of cigarettes', stage of disease, initial treatment that patients took, type of treatment that the patient took, HIV status, and place had a significant effect on the survival probability of patients with cervical cancer. It also showed that the aim of radiotherapy, the number of cycles of chemotherapy that patients took, and tumor size were not significant for the survival probability of patients with cervical cancer.

4.2. Recommendations

Since cervical cancer infection is the most deadly illness in the world, modeling the disease's survival time aids in identifying the key risk variables that influence the effectiveness of therapy. By taking these factors into account, new vaccines or medications can be developed. In order to include additional factors (social, economic, behavioral, nutritional, environmental, viral load, and the like) that may impact the recurrence of cervical cancer, more research in the field should be conducted utilizing this recently established and most flexible technique.

Based on the findings of the study, the following recommendations are made for the ministry of health, policymakers, the community at large, Tikur Anbessa Specialized Hospital, and researchers.

1) The ministry of health and legislators should focus on increasing public awareness of cervical cancer by informing people about its risk factors, making it mandatory for them to finish their prescribed treatment without viewing it as an incurable condition, monitoring their cancer status to reduce the chance of a recurrence, acknowledging cervical cancer as a serious health issue, and establishing screening programs and early detection guidelines for the most vulnerable populations.
2) In addition, it will be important to open cancer diagnostic and treatment centers in each region of the country, and awareness has to be given to society about the causes of cervical cancer.
3) Tikur Anbessa is an expert in Hospitals should include comprehensive patient characteristics in the cancer registry data and work to raise public and professional knowledge of early detection, quick treatment utilizing workable, successful regimens, and early being diagnosed. The WHO worldwide coding system has to be integrated with this older hospital-based cancer registry.

Abbreviations

ACS	American Cancer Society.
AFT	Accelerated Failure Time
AIC	Akaike Information Criterion
AIDS	Ac uired Immune Deficiency Syndrome
ANC	Antenatal Care
CC	Cervical Cancer
CSA	Central Statistical Agency
DHS	Demographic and Health Survey
DNA	Deoxyrebose Nucleic Acid
ECA	Ethiopian Cancer Association
HDI	Human Development Index
HIV	Human Immune Virus
HPV	Human Pappiloma Viruses
NHS	National Health Service
PH	Proportional Hazard
PO	Proportional Odds
TASH	Tikur Anbessa Specialized Hospital
WHO	World Health Organization

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Author Contributions

Demelash Lemmi Ettisa is the sole author. The author read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Appendix

Table 4. *Frequency distribution for Baseline characteristics of recurrence of cervical cancer patients at TASH based on the variables under study and log-rank test results, (January, 2015- march 2017).*

Covariate	Category	recurrent	censored	Total percent	p-value
Age	≤ 50 *or*	38	16	47.6%	0.000
	> 50	132	72	52.6%	
Smoking	Non-smoker	120	242	86.2%	0.000
	Smoker	50	16	13.8%	
Stage of disease	stageI	10	128	6.2%	0.000
	StageII	46	15	32.6%	
	StageIII	89	10	51.7%	
	Stage IV	25	214	9.5%	
Initial treatment	Surgery	5	4	2.1%	0.002
	Chemotherapy	3	10	3.1%	
	Radiotherapy	152	214	87.1%	
	Chemo-radiation	10	22	7.6%	
	No chemo	90	144	55.7%	
Number of cycles	First cycle	54	73	30.0%	0.912
	Second cylce	26	33	14.2%	
Aim of radiother-apy	No RT	4	2	1.4%	0.636
	Palliative	112	151	62.6%	
	Radical	17	97	36.0%	
Tumor size	≤ 4	126	191	75.5%	0.255

Covariate	Category	recurrent	censored	Total percent	p-value
Types of treatment	>4	44	59	24.5%	0.001
	Surgery	4	0	1.0%	
	Chemotherapy	2	3	1.2%	
	Radiotherapy	127	189	75.2%	
	Chemo-radiation	34	53	20.7%	
	Surgery-chemotherapy	2	10	0.7%	
	Surgery-radiotherapy	1	4	1.2%	
HIV status	no	113	180	69.8%	0.041
	yes	57	70	30.2%	
Place	Urban	68	127	46.4%	0.003
	rural	102	123	53.6%	

Table 5. *The estimated mean survival time and 95% confidence interval for recurrence of cervical cancer patients with different covariates characteristics.*

Age of patients	Mean			
	Estimate	Std.Error	95% confidence interval	
			Lower Bound	Upper Bound
Less than or equal to 50	22.363	.526	21.329	23.397
Greater than 50	16.437	.526	15.406	17.467
Stage of disease				
Stage I	16.344	1.619	13.172	19.517
Stage II	20.007	.709	18.620	21.395
Stage III	19.612	.535	18.563	20.662
Stage IV	13.745	1.176	11.443	16.050
Smoking habit of patients				
Non-smoker	20.217	.424	19.387	21.047
Smoker	12.919	.883	11.189	14.649
Initial treatment of patients took				
Surgery	16.351	.932	14.534	18.178
Chemotherapy	19.884	.679	18.552	21.215
Radiotherapy	18.591	.655	17.307	19.215
Comnbination	21.974	1.144	19.733	24.216
Number of cycles patients took				
No chemo	19.16	.546	18.089	20.230
First cycles	19.082	.730	17.652	20.512
Second cycles	18.539	1.117	16.35	20.729
Aim of radiotherapy				

Age of patients	Mean		95% confidence interval	
	Estimate	Std.Error	Lower Bound	Upper Bound
No RT	19.400	3.276	12.979	25.821
Palliative	18.839	.504	17.851	19.828
Radical	19.387	.703	18.003	20.757
Tumor size of cervical cancer				
Less than or equal to 4	19.282	.466	18.368	20.195
Greater than 4	18162	.822	16.551	19.773
Types of treatment patients took				
Surgery	11.929	2.010	7.989	15.868
Chemotherapy	20.706	1.743	17.290	24.122
Radiotherapy	19.052	.483	18.105	19.999
Chemoradiation	19.952	.894	18.193	21.679
Surgery and chemotherapy	16.667	5.004	6.859	26.474
Surgery and radiotherapy	13.000	.000	13.000	13.000
HIV status of patients				
No	19.567	.471	18.646	20.493
Yes	17.695	.786	16.155	19.234
Place where patients come				
Urban	20.369	.576	19.241	21.497
Rural	17.87	.557	18.962	18.962

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