Factors Influencing the Completion of Head and Neck Cancer Treatment: A Case Study of Tikur Anbessa Referral Hospital, Addis Ababa, Ethiopia

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Abstract

Cancer is a class of disease in which group of cells display uncontrolled growth, invasion that intrude upon and destroy adjacent tissues, and sometimes metastasis or spreading to other locations in the body via lymph nodes or blood. The objective of this study was to identify the risk factors that determine the completion of treatments for head and neck cancer patients at Tikur Anbessa Referral Hospital, Addis Ababa, Ethiopia. It was a retrospective study and the data from patients who were registered at the Tikur Anbessa Referral Hospital between December 2007 to January 2010. The simple random sampling method, descriptive statistics and the Kaplan-Meier survival estimator were used to estimate and compare the survival times of the patients. The Cox proportional hazard regression model was applied to model treatment follow up time and examines the association between this time with different demographic and medical variables. Result showed that among 344 head and neck cancer (HNC) patients 38.4% discontinued treatment. The survival distribution of time until treatment discontinuation was found to be significantly related to sex, age interval, region, tumor size, lymph node size, initial stage of the cancer, type of treatment, and duration for radiotherapy that the patient took as well as the aim of the prescription radiotherapy. The log rank test showed that the survival probability of patients was not statistically different among groups classified by HNC site. The study hence identifies these factors as the main reason that affects the completion of HNC treatments. It is therefore suggested that patients should be well informed about the disease so that they follow up the treatment until completion to minimize the dropout rate.

Key words: Head and Neck cancer, Tikur Ambessa, Ethiopia

Introduction

Cancer (medical term, malignant or neoplasm) is a class of disease in which group of cells display uncontrolled growth, invasion that intrude upon and destroy adjacent tissues, and sometimes metastasis or spreading to other body locations via the lymph nodes or blood. Head and neck cancer (HNC) occurs in several anatomical sites in the head and neck regions. The most common regions being the oral and nasal cavity, pharynx, larynx, salivary and thyroid glands which are diagnosed by cancer oncology using diagnosis criteria like the CT scan instrument (Tariah *et al.*, 2009). It is the sixth most common cancer in the World, and ranked seventh cause of mortality worldwide (Fan, 2004).

More than 90% of HNCs are of squamous cell histology and originate in the lip/oral cavity, nasopharynx, oropharynx, hypophaynx, and the lar ynx. During the past decade, the incidence of cancer at the base of the tongue and the tonsils has increased, especially in people younger than 45 years (Jemal et al., 2005). A study in Canada had shown that among 58 head and neck squamous cell carcinoma patients, 36 (62.1%) failed treatment while the remaining 22 patients (37.9%) were treated concurrently with no indication of failure for a period of 3 years (Tariah et al., 2009). The estimated global mortality of HNC has been put at 260, 000 deaths (Ferlay, 2000 and Min, et al., 2006) and reportedly account for approximately 12% of all cancer deaths (Gorsky, 2004). According to UICC (2005), more death from cancer had been recorded than from HIV/AIDS, malaria and tuberculosis put together, where 12.5% of all deaths each year in the world is attributed to cancer. The sad news in developing countries is the alarming rate of cancer incidence being reported. In Africa it has been estimated to be between 100 to 200/100,000 populations (ECA, 2008; UIC, 2005). Despite these facts, the study showed that cancer has not still been recognized as a priority issue in health programs of most African nations with the exception of Egypt and South Africa.

In Ethiopia, where the population was estimated to be over 73 million and service extremely health is inadequate, then cancer is the most painful, severe, and among major causes of illnesses and deaths (CSA, 2008). Although there is no cancer registry in the country, clinical records showed that there are 120,500 cancer cases per year. At Tikur Anbessa Referral Hospital, HNC is the 3rd most common cancer type next to cervical and breast cancers (ECA, 2008).

However, it is the most neglected and least prioritized health issue unlike HIV/AIDS, Tuberculosis and Malaria in Ethiopia. There is no national cancer policy, strategy, program and cancer institution. Cancer patients are practically the most neglected and underserved part of the community since cancer diagnosis and treatment facilities and trained specialists (Surgeons, Oncologists, Radiotherapists and etc) are in acute shortage. Data on cancer to convince the policy makers on the overall crisis is lacking in the country. The cancer patients and the general public have no access to information on cancer facts (CSA, 2008). So the incidence and mortality rates of HNC and all cancer types in Ethiopia were found to be more than that of all East African countries (WHO, 2005). This suggests that HNC and all cancer types have not been given adequate attention in Ethiopia (ECA, 2008). Hence, the objective of this study was to identify the risk

factors that affect the completion of treatments for head and neck cancer (HNC) patients at Tikur Anbessa Referral Hospital in Addis Ababa, Ethiopia.

Methodology

Data source

The study was retrospective in nature, which means that all the cases of exposure and the subsequent incompletion or dropout of the treatments had occurred in the past; the study merely focus on secondary data and investigated the risk of incompletion and the treatment of the disease if exposed to a particular risk factors. The source of the data used was from the patients' cards kept in record room at the Tikur Anbessa Referral Hospital from 2007 to 2010.

Study population and sample size

Three hundred and forty two HNC patients' cards from the total of 2,138 HNC patients were selected using simple random sampling method. But after collecting the data, 17 of the cards had not contained all the crucial information and they were excluded from the analysis but to compensate those with missing data, 5% of the sample size was added. This brought the final total sample size to three hundred forty four HNC patients' cards from Tikur Anbessa Referral Hospital, Ethiopia.

Variables of the study

response variable was The the "survival time" defined as the number of days from the date of enrolment of a patient in the HNC-care centre till one of the events "death", "lost to follow up" (discontinued or dropped out), "transferred out to other health centre or hospital" occurred. This meant that the survival data studied "right-censored". The here were predictor variables relate to the social, demographic, medical and clinical background of the patients having these respective classifications; age (\leq 20, 21 - 30, 31 - 40, 41 - 50, 51 - 60, 61 -70, \geq 71 years), gender, region of the patient (Addis Ababa, Oromia, Amhara, Tigray, SNNP, others), site of HNC (lip and oral cavity, nasal cavity and sinus, pharynx, larynx, salivary gland, thyroid gland), tumor size classification (size \leq 2cm was considered tumor one or T1, size greater than 2cm to 4cm, as tumor two or T₂, size above 4cm to 6cm as tumor three or T_{3} , and size > 6cm tumor four or T₄). While lymph node size was classified as; no node (N₀), node size \leq 3cm as N1, node size above 3cm to 6cm as N₂, and node size greater than 6cm as N₃, and stage of HNC (I, II, III, IV, IVC); treatment types as; surgery and radiotherapy, radiotherapy alone, and chemoradiosurgery therapy, chemo radiotherapy, chemot herapy alone. The duration of radiotherapy the patient had taken as a fraction of dose (in the number of days) and aim of the radiotherapy (palliative, radical, adjuvant).

Statistical analysis

The Survival statistical Analysis method was used in this study. The (product-Kaplan-Meier estimator limit-estimator) survival of the function was employed this for purpose according to Kaplan and Meier (1958). The log-rank test was utilized to test whether observed differences in survival experience groups between/among the was significant not. The Semior parametric regression (a multivariable) model also referred to as the proportional hazards regression (PHR) (Cox, 1972) was adopted. he model development process identifies the relevant variables following model scrutiny as discussed in (Hosmer et al., 1998). And, the analysis had been carried out using SPSS 16 version soft ware.

Results

Treatment completion

Among the 344 HNC patients in this retrospective study, 132 (38.4%) discontinued their treatments and the rest 212 (61.6%) were censored (completed or following their treatments). There are 150 female and 194 male patients, of which 44 (12.6%) and 88 (25.2%) discontinued their treatments respectively. The mean age of the patients was 44 years with a standard deviation of 16.54. A summary of the variables' are presented in Table 1.

The female patients had a better mean survival time (14.5) in months than the male patients (12). In the age category, the older group had discontinued treatments earlier and the different regions of the patients were also statistically significant. Patients from Addis Ababa city and Oromia region had the highest mean survival times of 14.6 and 13 respectively to follow up treatment of HNC. Patients with more advanced tumors (T_4) with size greater than 6 cm had lowest mean survival time of 10.424 months, this means early discontinuation of treatments. The mean survival time to complete the treatment decreased as the cancer stages increased from stage II to IVC (more advanced stage than IV). Patients who took surgery and radiotherapy treatments had better mean survival time (17.41 months) than the other treatment groups.

Table 2 showed the results based on the log-rank test. The p value indicates the differences in survival experience between two or more levels of predictors. All predictors with the exception of site of HNC manifest differences in levels of survival functions. It also showed that the mean survival time to complete

treatments by patients who took

radiotherapy was 17.33 months.

 Table 1: Socio-demographic and clinical characteristics of the HNC patients in Tikur Anbessa Referral Hospital, Addis Ababa, Dec 2007 to Jan 2010 (n=344).

Demographic	Number of	Number of	Total (%)
Variables	Drop-out (%)	Censored (%)	()
Sex Female	44(12.8)	106(30.8)	150(43.6)
Male	88(25.6)	106(30.8)	194(56.4)
Age interval ≤ 20	8(2.4)	27(7.8)	35(10.2)
21-30	13(3.7)	38(11.1)	51(14.8)
31- 40	19(5.5)	36(10.5)	55(16.0)
41- 50	33(9.6)	49(14.2)	82(23.8)
51- 60	27(7.8)	40(11.7)	67(19.5)
61- 70	21(6.1)	18(5.2)	39(11.3)
≥ 71	11(3.2)	4(1.2)	15(4.4)
Region Addis Ababa	42(12.2)	108(31.4)	150(43.6)
Oromia	29(8.4)	44(12.8)	73(21.2)
Amhara	27(7.8)	24(7.0)	51(14.8)
Tigray	5(1.5)	9(2.6)	14(4.1)
SNNP	12(3.5)	16(4.6)	28(8.1)
Other	17(4.9)	12(3.2)	28(8.1)
Site of HNC Lip & oral cavity	23(6.6)	34(9.8)	57(16.6)
Nasal cavy & sinus	16(4.6)	26(7.6)	42(12.2)
Pharynx	38(11.1)	70(20.3)	108(31.4)
Larynx	22(6.4)	31(9.0)	53(15.4)
Salivary gland	5(1.5)	15(4.3)	20(5.8)
Thyroid gland	28(8.1)	36(10.5)	64(18.6)
Tumor size T₁(≤ 2cm)	1(0.3)	10(2.9)	11(3.2)
T ₂ (2- 4cm]	6(1.7)	59(17.2)	65(18.9)
T ₃ (4- 6cm]	41(11.9)	83(24.1)	124(36.0)
T ₄ (> 6cm)	84(24.5)	60(17.4)	144(41.9)
Lymph node No(0cm)	3(1.2)	38(11.0)	/1/12 2)
	11(3.2)	81(23.5)	92(26.7)
Na(3- 6cm)	55(15.7)	71(20.6)	126(36.3)
$N_2(0 \text{ conn})$	63(18.3)	22(6.4)	85(24 7)
Initial stage	1(0.3)	11(3.2)	12(3.5)
	5(2 1)	81(23.5)	88(25.6)
IV	40(11.6)	117(34.0)	157(45.6)
IVC	84(24.4)	3(0.9)	87(25.3)
Treatment Surgery & RT	2(0.6)	35(10.2)	37(10.8)
RT alone	10(2.9)	51(14.8)	61(17.7)
Sur. RT& Chemo	5(1.5)	27(7.8)	32(9.30)
RT & Chemo	92(26.7)	97(28.2)	189(54.9)
Chemo alone	23(6.7)	2(0.6)	25(7.3)
Aim of RT Not taken RT	23(6.7)	2(0.6)	25(7.3)
Palliative	98(28.5)	72(20.9)	170(49.4)
Adjuvant	2(0.6)	8(2.3)	10(2.9)
Radical	9(2.6)	130(37.8)	10(40.4)

RT- radiotherapy, Sur- surgery and Chemo- chemotherapy

Table 2: The test of equality	and survival distributions	for HNC patients at	: Tikur Anbessa Referra	al Hospital, Addis Ababa
from 2007 to 2010	(n=344).			

Demographic variables	Mean Survival Chi-square		Log-rank	
	time		p value	
Sex Female	14.487	10.202	0.001*	
Male	12.344			
Age interval ≤ 20 21- 30	15.796	55.560	0.000*	
31- 40	14.285			
41- 50	13.887			
51-60	13.194			
61- 70	12.514			
≥71	9.702			
	4.853			
Region Addis Ababa	14.631	18.622	0.002*	
Oromia	12.963			
Amhara	10.508			
Tigray	10.758			
SŇNP	10.654			
Other	10.505			
Site of HNC Lip & Oral cavity	13.145	3.408	0.637	
Nasal cavity & Sinus	13.444			
Pharvnx	13.667			
Larvnx	12.216			
Salivary gland	15.164			
Thyroid gland	12.524			
Tumor size $T_1 (\leq 2 \text{ cm})$	14,556	65.371	0.000*	
$T_2(2-4cm)$	17.116			
T ₃ (4- 6cm]	14.131			
T_4 (> 6cm)	10.424			
Lymph node No(0em)	17 018			
	16 71/	144.64	0.000*	
$N_1(= 500)$	13 007	144.04	0.000	
N ₂ (5- 6cm)	7.015			
	7.015			
Initial stage	17.500	389.263	0.000*	
III	17.203			
IV	15.129			
IVC	5.160			
Treatment Surgery & RT	17.409	148.618	0.000*	
RT alone	15.924			
Sur, RT &Chemo	15.600			
RT & Chemo	12.151			
Chemo alone	4.640			
Aim of RT Not taken RT	4.64	198.603	0.000*	
Palliative	9.799			
Adjuvant	15.10			
Radical	17.333			

* Significant at 5% level





Figure 1. Survival and hazard function of the patients.

The estimated probability to complete treatment by the HNC patients was 0.57, in other words 57% completed their treatment during the study period (Figure 1a) while the hazard rate to discontinue the treatment increases when the treatment's time of the patient increased to 15 months (Figure 1b).

b

The Kaplan-Meier estimator survival curve for different covariates showed a pattern of one survivorship function lying above another, which indicates that the upper curve has a better survival than the lower curve. From the graph for sex, age interval, region, stage of the HNC and lymph node size of the patients had clear differences among the various groups (Figures 2 a, b, c, d, e). However, the difference was not clear among the

HNC sites of the patients (Figure 2 f).



a

b





d

e







Figure 2. The Kaplan-Meier survivor function to compare the categories of the HNC patients by a) sex type, b) age interval, c) region type, d) stage of HNC, e) lymph node size and f) sites of HNC.

Result of Cox proportional hazard regression model

The Cox model procedure that includes model selection, tests, diagnosis and fit confirmed that there was no problem with regards to interaction of main effects and confounding. Hence, the survival experience details were based on estimated crude hazard ratios (HR) shown in Table 4. It should be noted that variables with p values below 0.05 were considered statistically significant.

Uni-variate analysis of Cox proportional hazards

The uni-variate analysis between each covariates and survival time of HNC patients showed that the survival of patients was significantly related with sex, age interval, region, tumor size, lymph node size, initial stage, treatment type, and duration of RT (Table 3). The site of HNC covariate was not statistically significant at 25% significant level. However, using a modest 5% level of significance to include the multiple covariate model for further investigation of age interval, region, lymph node size, initial stage, treatment type, and duration of RT, Sex type and tumor size were not statistically significant at 5% in the multivariate analysis using forward stepwise (likelihood ratio) method.

Multiple covariates analysis

The multivariate survival analysis using Cox proportional hazards

stepwise model by forward (likelihood ratio) method identified eight covariates. The result showed that survival of patient to complete HNC treatment was significantly related with age interval, region, lymph node size, initial stage, treatment type, aim and duration of radiotherapy. However, sex and tumor size which were used in the single covariate analysis were found not significant.

After adjusting other covariates, the hazard rate to discontinue treatments by the youngest group of patients (\leq 20 years) was found to be 91.3% lower than the oldest group whose age was \geq 71 years (HR= 0.087, CI= 0.029 -0.248). The hazard rate to discontinue the treatment of the earlier initial stage II HNC patient was 92.1% lower than the highest risked stage IVC HR=0.079, patients (adjusted CI=0.017-0.338). The hazard rates to discontinue treatment of the advanced initial stages III and IV patients was 84.3% and 72.7% lower than those highest risked stage group respectively. This implied that those in the highest risk stage IVC had less probability completing of their treatment.

The result also showed that when the number of days the patient took radiotherapy was increased by a day, the danger to discontinue treatment decreased by 5.1% (adjusted HR=0.949, CI=0.924-0.975), controlling the effects of all other covariates in the model. Similarly, the other covariates; the region, treatment type, lymph

node size and aim of RT were found to be statistically significant on the survival of HNC patient to complete their treatments.

Table 3: Uni-variate analysis of Cox proportional hazards (CPH) on time to drop out of treatments by HNC patients
at Tikur Anbessa Referral Hospital, Addis Ababa, Dec 2007 to Jan 2010 (n=344).

							95% CI for HR	
Variables	β	S.E (β)	Wald	DF	Sig.	HR	Lower	Upper
Sex (Ref: Male)	0.581	0.193	9.043	1	0.003	1.787	1.224	2.609
Age int. (Ref: ≥ 71)			33.218	6	0.000			
≤ 20	-2.283	0.493	21.489	1	0.000	0.102	0.039	0.268
21- 30	-2.094	0.440	22.621	1	0.000	0.123	0.052	0.292
31- 40	-1.852	0.418	19.597	1	0.000	0.157	0.069	0.356
41- 50	-1.671	0.387	18.607	1	0.000	0.188	0.088	0.402
51- 60	-1.507	0.390	14.904	1	0.000	0.222	0.103	0.476
61- 70	-1.170	0.409	8.185	1	0.004	0.310	0.139	0.692
Region (Ref: Other)			16.905	5	0.004			
Addis Ababa	-1.062	0.302	12.387	1	0.000	0.346	0.191	0.625
Oromia	-0.440	0.312	1.991	1	0.158	0.644	0.349	1.187
Amhara	-0.249	0.323	0.591	1	0.442	0.780	0.414	1.470
Tigray	-0.466	0.512	0.827	1	0.363	0.627	0.230	1.713
SNNP	-0.407	0.382	1.132	1	0.287	0.666	0.315	1.409
Site of HNC (Ref: Thyroid			4.948	5	0.422			
gland)	-0.196	0.295	0.442	1	0.506	0.82	0.461	1.46
Lip & Oral cavity	-0.164	0.316	0.270	1	0.604	0.84	0.457	1.576
Nasal cavity & Sinus	-0.396	0.260	2.323	1	0.128	0.67	0.405	1.120
Pharynx	-0.027	0.287	0.009	1	0.926	0.97	0.554	1.710
Larynx	-0.895	0.536	2,787	1	0.095	0.40	0.143	1.168
Salivary gland	0.000			•		•••••	••••••	
Tumour size			45.36	3	0.002			
(Ref: T₄, > 6cm)	-2.212	1.007	4.827	1	0.028	0.109	0.015	0.788
T₁ (≤ 2cm)	-2.394	0.462	26.860	1	0.000	0.091	0.037	0.226
T2 (2 - 4cm]	-0.924	0.201	21.030	1	0.000	0.397	0.268	0.589
T ₃ (4 - 6cm]								
Lymph node size			73.718	3	0.000			
(Ref: N ₃ , > 6 cm)	-14.11	8.143	0.009	1	0.925	0.000	0.000	0.002
N₀ (no node)	-2.776	0.362	58.858	1	0.000	0.062	0.031	0.127
N₁ (≤ 3cm)	-1.109	0.193	33.179	1	0.000	0.330	0.226	0.481
N ₂ (3 - 6cm]				_				
Initial stage (IVC)			193.19	3	0.000			
	-14.39	10.338	0.005	1	0.942	0.000	0.000	0.001
	-4.765	0.534	/9./25	1	0.000	0.009	0.003	0.024
10	-2.976	0.238	155.76	1	0.000	0.051	0.032	0.081
Treatment type			83.041	4	0.000			
(Ref: Chemotherapy)	-15.98	12.434	0.004	1	0.951	0.000	0.000	0.002
Surgery and RT	-3.217	0.438	53.836	1	0.000	0.040	0.017	0.095
RIalone	-3.069	0.500	37.630	1	0.000	0.046	0.017	0.124
Surgery, RT & Chemo RT and Chemo	-1.737	0.244	50.765	1	0.000	0.176	0.109	0.284
Aim of RT (Ref: Radical)			81.808	2	0.000			
Palliative	-5.163	0.621	69.043	1	0.000	0.006	0.002	0.019
Adjuvant	-14.244	12.058	0.005	1	0.944	0.000	0.000	0.001
Duration of RT (in days)	-0.122	0.013	85.982	1	0.000	0.885	0.862	0.908

 Table 4: Parameters estimated by the PHR Model for HNC patients at Tikur Anbessa Referral Hospital, Addis Ababa, Dec 2007 to Jan 2010 (n=344).

Variable	DF	β	S.E (β)	Wald	Sig.	HR	95% CI for HR
Age int. (Ref: ≥ 71)	6			44.735	0.000		
≤20	1	-2.468	0.548	20.257	0.000	0.087	(0.029, 0.248)
21- 30	1	-2.619	0.495	27.963	0.000	0.072	(0.028, 0.192)
31- 40	1	-2.876	0.446	41.567	0.000	0.058	(0.023, 0.135)
41- 50	1	-2.308	0.419	30.274	0.000	0.094	(0.044, 0.226)
51-60	1	-2.062	0.432	22.825	0.000	0.124	(0.055, 0.296)
61- 70	1	-1.850	0.434	18.192	0.000	0.158	(0.067, 0.368)
Region (Ref: Others)	5			12.317	0.031		
Addis Ábaba	1	-0.976	0.318	10.515	0.002	0.377	(0.191, 0.665)
Oromia	1	-0.551	0.328	3.766	0.091	0.576	(0.278, 1.006)
Amhara	1	-0.270	0.319	0.637	0.425	0.764	(0.378, 1.428)
Tigray	1	-0.920	0.326	2.730	0.126	0.398	(0.118, 1.310)
SNNP	1	-0.787	0.338	4.762	0.047	0.455	(0.191, 0.915)
Lymph node size (Ref:N ₃	3			12.153	0.007		
, > 6 cm)							
N₀(no node)	1	-1.348	0.920	2.128	0.180	0.291	(0.042, 1.589)
N₁(≤3cm)	1	-0.408	0.506	0.638	0.328	0.610	(0.244, 1.810)
N ₂ (3- 6cm]	1	-0.692	0.210	10.780	0.001	0.490	(0.331, 0.757)
Initial stage (Ref: IVC)	3			47.837	0.000		
II -							
III	1	-1.170	0.272	46.328	0.000	0.079	(0.017, 0.338)
IV	1	-2.620	0.740	11.751	0.001	0.157	(0.092, 0.268)
	1	-1.852	1.457	0.792	0.374	0.273	(0.016, 4.756)
Treatment type	4			17.655	0.001		
(Ref: Chemo)							
Surgery and RT	1	-3.204	1.315	5.513	0.009	0.033	(0.003, 0.589
RT alone	1	-1.197	0.769	1.321	0.120	0.302	(0.086, 1.897)
Surgery, RT& Chemo	1	-2.764	0.823	11.145	0.000	0.052	(0.012, 0.319)
RT and Chemo	1	-1.544	0.648	5.628	0.010	0.188	(0.060, 0.765)
Aim of RT(Ref: Radical)	2			10.746	0.005		
Palliative							
Adjuvant	1	0.272	0.528	0.265	0.607	1.312	(0.429, 3.378)
	1	4.074	1.252	10.591	0.001	6.450	(1.921,16.152)
Duration of RT (days)	1	-0.049	0.013	13.223	0.000	0.949	(0.924, 0.975)

Discussion

The hazard rate to discontinue the trea tment of the youngest HNC patients, 7 to 20 years old, was 91.3% lower than the oldest patients whose age ranged from 71 to 86 years old (HR= 0.087, CI= 0.029 - 0.248). The confidence interval indicated that the rate may go up to 97.1% and down to 75.5%. This

result collaborates the findings of Morten (2009) from Norway, Rao *et al* (1998) from British and Rashmi *et al* (2008) from Turkey, who all reported that age was the most predictive of survival of the HNC patients, and that persons in the age group greater than 65 had high hazard rate to discontinue the treatment.

The hazard rate to discontinue treatm ent of patients whose HNC has metastasized to regional lymph node N₂ (3cm- 6 cm] was 0.497 times smaller than patients who had N_3 (> 6 cm) lymph node (HR= 0.497, CI= 0.326 - 0.743). The hazard rate to discontinue treatment at earlier initial stage II or III of the HNC was 91.1% lower than the highest risked stage IVC patients (HR= 0.079, CI= 0.022-0.36). Related findings from Egypt by Ibrahim et al (2006) and from Turkey by Rashmi et al (2008) showed that the most advanced lymph node size, and stages IV and IVC HNC patients had less survival rates from death or discontinued the treatment.

The probability to discontinue HNC treatment by patients who took the combination of surgery, RT and chemotherapy was 94.7% lower than patients who took chemotherapy alone (HR= 0.052, CI= 0.012- 0.319). Whereas the hazard rate to discontinue the treatment of the HNC patients who took RT and chemotherapy was 81.2% lower than these patients who took chemotherapy alone (HR= 0.188, CI= 0.060- 0.765). The hazard rate to discontinue the treatment of the patients who took RT by increase a unit day was decreased by 5.1% (HR= 0.949, CI= 0.924-0.975) when controlled the effects of other covariates in the model. Those results have similarity with studies from Turkey by Rashmi et al (2008) and from Ireland by Shanthim et al (2008) found that the HNC patients who took two or three combinations of treatment type had higher survival probabilities (less hazard rates).

Conclusion

This study provides evidence that the major factors that affect the completion of treatments by HNC patients are age interval, region, lymph node size, initial stage, treatment type, and the number of that days the patients took radiotherapy. Older patients (greater than 70 years) had the highest dropout rate compared to the other age groups. Patients from regions like Gambella, Afar and Benishangul-Gumuz had more advanced lymph node size (N₃), higher risked stage (IVC), took chemotherapy alone and radiotherapy for palliative purpose had lowest survival probability to complete their treatments. The study also showed that patients who took

RT for small number of days had higher dropout rate and that survival probability to complete the treatment of a patient is not significantly different among groups classified by sex and tumor size of the patients in multivariate analysis. Patients in the site of head and neck cancer categories are not significantly different in univariate analysis.

Recommendation

Based on the study findings, the main predictive factors for the survival probability to complete the treatments of HNC patients are more of clinical variables. Therefore, health workers should be cautious when a patient has more advanced lymph node size N₃ and higher stage IVC, appropriate clinical and non-clinical measures like medicine and support should be provided. Patients from distant regions, should be supported by stakeholders like government and organizations non-government to completing their treatments, once they have started. Since head and neck cancer patients can complete their prescribed treatments and HNC is a curable disease when detected early before it metastasized throughout the body, government and nongovernment health organizations, physicians and health workers should work on awareness creation to minimize the incidence of HNC in the population.

Competing interest declaration

The authors declare that they have no competing interests with regards to this study and have adhered strictly to the code of conduct and ethics required for this study.

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References

- American Cancer Society (ACS), 2004. Cancer facts and figures 2004. Atlanta.
- Amusa Y.B., Olabanji J.K and Ogundipe O.V. 2004. Pattern of HNC malignant tumors in a Nigerian teaching hospital. West Africa Journal of Medical Sciences 9: 304-310.
- Barnes L., Eveson J. and Reichart P. 2005. Pathology and genetics of tumors of the head and neck cancer. World Health Organization Classification of Tumors. 121-124 p.
- Bijan K., Jalal M. and Mohammad M. 2006. Treatment results of nasopharyngeal carcinoma. *Journal of the Egyptian National Cancer Institution* 18: 147-155.
- Brandizzi D. 2005. Epidemiological features of oral cancer in the city of Buenos Aires. *Eastern Mediterranean Journal of Health Science* 15: 372-377.
- Central Statistics Agency (CSA). 2008. Summary and statistics report of the 2007 population and housing census; population size by age and sex. Addis Ababa, Ethiopia's population census commission.
- Coatesworth A.P. and MacLennan K. 2002. Squamous cell carcinoma of the upper aero digestive tract. *America Journal of Head and Neck Cancer* 24(3): 258-261.
- Collett D. 1994. Modeling survival data in medical research. London: Chapman & Hall.
- Cox D.R. 1972. Regression models and life-tables. *Journal of Reg Stat Soc 34:* 187-220.

- Cox and Snell E.J. 1989. The analysis of binary data. 2nd edition, Chapman and Hall, Londin, UK.
- Ethiopia Cancer Association (ECA). 2008. The 2nd report, <u>www.yeeca.org</u>.
- Fan C.Y. 2004. Epigenetic alterations in head and neck cancer of prevalence, clinical significance and implications. *Current Oncology Republication 6: 152-*161.
- Ferlay J. 2000. GLOBOCAN 2000: Cancer Incidence Mortality and Prevalence Worldwide. Lyon. *IARC Cancer Base No.5.*
- Gilbar O. and De-Nour A.K. 1989. Adjustment to illness and dropout of chemotherapy of HNC patients. *Journal of Physiological Chemotherapy* 33: 1-5.
- Goldberg R.J. 1983. Systematic understanding of cancer patients who refuse treatments. Journal of Physiological Chemotherapy 39: 180-189.
- Gorsky M. 2004. Carcinoma of the tongue in a case series analysis of clinical presentation, risk factors, staging, and outcome. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontic, 98(5): 546-552.
- Gupta T., Agarwal J.P. and Laskar S.G. 2009. Radical radiotherapy with concurrent weekly cisplatin inlocoregionally advanced squamous cell carcinoma of the head and neck cancer (SCCHNC). *Head and Neck Oncology 1*: 17-22.
- Hosmer D. and Lemeshow S. 1998. Applied survival analysis: Regression Modeling of Time to Event Data. *Wiley Series in Probability and Statistics. Canada.*
- Ibrahim N.K. and Ashakar M.S. 2006. An epidemiological study on survival of head and neck cancer cases. *Egyptian Journal of Cancer* 45: 334-341.

- Jemal A., Murray T. and Ward E. 2005. Cancer statistics in Canada, 2005. *Canada Cancer Journal on Clinical* 55(1):10-30.
- Janot F., Klijanienko J. and Russo A. 2008. Prognostic value of clinic pathological data. *Journal of the National Medical Association Vol. 100, No. 6.*
- Jereczek F., Krengli M. and Orecchia R. 2006. Particle beam radiotherapy for HNC tumors: radiobiological basis and clinical experience. *HNC Journal* 28(8): 750-760.
- Kaplan E.L. and Meier P. 1958. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* 53: 457-481.
- Mehanna H., West C.M., Nutting C. and Paleri V. 2010. Head and neck cancer treatment and prognostic factors. *Biomedical journal 341: 11-16.*
- Mendenhall W.M., Parsons J.T. and Mancuso A.A. 1996. Radiotherapy for carcinoma of the super glottis larynx: *An alternative to surgery. Head and Neck Cancer 18: 24-35.*
- Min Y., Thanh N., John M.B. and Kenneth J.D. 2006. Changing failure patterns in head and neck pharyngeal cancer treated with intensity modulated radiotherapy and implications for future research. *America Journal Clinical Oncology 29: 606-612.*
- Morten B. 2009. Squamous cell carcinoma of the head and neck in the elderly. *The Open Oto-rhino-laryngologist Journal in Norway* 3:39-45.
- Murray C.L. and Lopez A.D. 1996. The Global Burden of cancer: a comprehensive assessment of mortality and disability from diseases. Cambridge: *Harvard University Press*, *the* 3rd *Report*.
- Ologe F.E., Adeniji K.A. and Busari S.S. 2005. Clinic pathological study of

head and neck cancers in Ilorin, Nigeria. West Africa Journal of Medical 35: 2-4.

- Otoh E.C., Johnson N.W. and Mandong B.M. 2006. Primary head and neckCancer in Nigeria. *West Africa Journal of Medical 25: 92-100.*
- Parkin D.M., Pisani P. and Ferlay J. 1999. Estimates of the worldwide incidence and mortality of 25 major cancers. *International Journal of Cancer 80(6):* 827-841.
- Parkin D.M. 2002. Global cancer statistics. *Cancer Journal for clinicians* 55:74–108.
- Pivot X., Niyikiza C. and Poissonnet G. 2001. Clinical prognostic factors for Patients with recurrent head and neck cancer. *Journal of Oncology 61: 197-204.*
- Rao D.N. and Dinshaw K.A. 1998. Survival analysis of 5595 HNC results of conventional treatment in a highrisk population. *British Journal of Cancer* 77(9): 1514-1518.
- Rashmi K., Arbind D., Aziz B., James B. and Andrew C. 2008. Prognostic factors depicting overall survival in HNC tumors. *Turkish Journal of Cancer 38*(4):159-166.
- Rowley H., McRae R.D. and Cook J.A. 1995. Lymphoma presenting to a Head and Neck Cancer. *Journal of Clinical Otolaryngology* **20**(2): 139-144.
- Shanthi M. and Arlene A.F. 2008. Changing epidemiology, diagnosis,

and treatment of HNC. *Mayor (from Ireland) Journal of Clinical Processing* **83**(4):489-501.

- Sobin L.H. and Wittekind C. 2002. TNM Classification of Malignant Tumors. *Hoboken National Journal, 6th edition.*
- Tariah O.B., Somefun A. and Adeyemo W.L. 2009. Current evidence on the burden of head and neck cancers. *Head and neck Cancer Oncology* 1: 14.
- Tedros B., Richard N. and Paul K. 2005. Prediction of Treatment Response in HNC by Magnetic Resonance Spectroscopy. *America Journal of Neuroradiology* 26:2108–2113.
- Thephamongkhol K., Browman G., Hodson I., Oliver T. and Zuraw L. 2004. Treatments of chemotherapy with radiotherapy for head and neck cancer. A Clinical Practice Guideline Evidence Based Series in Toronto 2004.
- Union International Cancer Cases (UICC). 2005. The 4th report, <u>www.uicc.org</u>.
- Yu P.C., Ngan M.T., Chen K.T. and Shinn Y.L. 2000. Cause of interruption of treatments for HNC patients in Taiwan. Japan Journal of Clinical Oncology 30(5): 230-234.
- World Health Organization (WHO). 2005. Head and neck health issues, the 4th and 5th reports.