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A comparison of survival between HIV- infected and HIV- uninfected cervical cancer patients on chemo radiotherapy.

BY

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Abstract

This study compares the survival rates and treatment outcomes of HIV-infected versus HIV-uninfected cervical cancer patients undergoing chemoradiotherapy. A total of 158 patients (60 HIV-positive and 98 HIV-negative) were analyzed for survival rates, treatment toxicity, and associated factors. Significant differences in overall survival and toxicity were observed between the two groups. The 5-year overall survival (OS) rate was 50% for HIV-positive patients compared to 65% for HIV-negative patients (p = 0.007). HIV-positive patients experienced greater toxicity (p = 0.0259) and had worse survival outcomes. Factors including age, initial hemoglobin levels, and radiation dose were found to impact survival irrespective of HIV status.

INTRODUCTION

Cervical cancer, a leading cause of cancer-related mortality in Kenya, presents unique challenges for HIV-infected patients. HIV infection exacerbates the progression of cervical cancer and complicates treatment due to its effects on immune function. This study aims to assess the impact of HIV status on the survival of cervical cancer patients receiving chemoradiotherapy, highlighting differences in treatment outcomes and toxicity. Cervical cancer remains a significant health concern globally, particularly in sub-Saharan Africa where HIV prevalence is high. The intersection of HIV infection and cervical cancer presents unique challenges in terms of treatment and survival outcomes. Chemoradiotherapy, a common treatment modality for cervical cancer, has varying efficacy in HIV-infected versus HIV-uninfected patients, potentially influencing survival rates.

This review examines existing research comparing survival outcomes between HIV-infected and HIV-uninfected cervical cancer patients undergoing chemoradiotherapy in Kenya and similar settings. Impact of HIV on Cervical Cancer Survival HIV infection is known to affect cancer outcomes through immunosuppression, which can influence the efficacy of cancer treatments. Studies have demonstrated that HIV-positive patients often experience poorer outcomes compared to their HIV-negative counterparts. According to Wiegand et al. (2019), HIV-positive cervical cancer patients in sub-Saharan Africa face increased mortality rates, attributed largely to the impact of HIV on immune function and its interaction with cancer therapies. This is consistent with findings from D'Souza et al. (2015), who reported that HIV infection accelerates disease progression and adversely affects survival rates among cervical cancer patients.

Chemoradiotherapy and Its Efficacy Chemoradiotherapy, which combines chemotherapy with radiation therapy, is the standard treatment for advanced cervical cancer. However, the efficacy of this treatment in HIV-positive patients can be compromised. A study by Hammad and Zheng (2020) noted that HIV-positive patients often experience heightened treatment-related toxicities, which can diminish the overall survival benefit of chemoradiotherapy. This is supported by research from Chao and Katki (2012), who found that HIV-infected patients had a significantly higher incidence of severe toxicity, impacting their survival outcomes. Comparative Survival Outcomes Research comparing survival outcomes between HIV-infected and HIV-uninfected cervical cancer patients undergoing chemoradiotherapy reveals a notable disparity. In Kenya, a study by Maranga and Njuguna (2018) highlighted that the five-year overall survival (OS) rate was significantly lower for HIV-positive patients compared to HIV-negative patients. This is consistent with global findings; for instance, Cohn and Kumar (2014) observed that HIV-positive patients had poorer survival outcomes due to the interplay between HIV-related immunosuppression and cancer treatment. A study specific to Kenya by Gichangi and

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Lee (2017) indicated that HIV-positive cervical cancer patients had lower survival rates and higher rates of treatment-related complications. The lower survival rates in HIV-positive patients can be attributed to both the advanced stage of cancer at diagnosis and the increased risk of severe side effects from chemoradiotherapy, as noted by Fawzy and El-Ashry (2016).

Factors Influencing Survival

Several factors contribute to survival outcomes in cervical cancer patients, including HIV status, initial hemoglobin levels, total radiation dose, and age. Gaffikin and Alakija (2013) found that HIV-positive patients often present with more advanced disease at diagnosis, which adversely affects their survival. Additionally, the study by Onyango and Kiprotich (2020) emphasized that treatment-related factors, such as radiation dose and concurrent chemotherapy, are crucial in determining survival rates.

Research Elaborations

This retrospective study included 277 patients with stage II/III cervical cancer who were expected to receive chemoradiotherapy. Out of these, 158 patients (60 HIV-positive and 98 HIV-negative) completed the treatment and were included in the analysis. The study assessed various factors, including treatment types, toxicity, and survival rates. Follow-up data was collected over a median period of 650 days. The Cox Proportional Hazards Regression model was used to evaluate survival impacts, and stepwise regression identified significant variables affecting survival.

Results or Findings

During follow up of surviving patients, 158 patients (60 HIV-positive and 98 HIV-negative) were included in the survival analysis. A significant difference in total toxicity between HIV-positive and HIV-positive patients (p = 0.0259) was observed. Survival rates for 5 years (OS) were 50% in HIV-positive patients (95% interval [CI] 45% -55%) and 65% in HIV-negative patients (95% CI 56% - 76% %) (P = 0.007). The viral status of the human immunodeficiency virus had affected 5- year OS or severe toxicity in HIV-positive patients without chemoradiotherapy in Kenya. In this cohort, it was found that initial hemoglobin levels, total radiation level, and age were related to survival, regardless of HIV status.

The 277 patients with stage II / III cervical cancer who were expected to receive chemoradiotherapy at the time of study. 142 of them included 88 who did not receive any chemotherapy, 21 were treated with palliative radiation, and 49 who did not return for treatment resulted in 158 patients (57.0%) included in the analysis. The median follow-up period after enrollment of this study in all patients was 650 days ([IQR], 325-870 days), including 655 days (IQR, 324 - 847 days, in HIV positive patients) and 650 days (IQR, 372 days - 913 days) for HIV- negative women. Thirty-eight percent of patients were infected with HIV. The study found HIV- positive patients were younger and were more likely to stay away from treatment.

The analysis revealed a significant difference in toxicity between HIV-positive and HIV-negative patients, with a higher total toxicity score in HIV-positive individuals (p = 0.0259). The 5-year overall survival rate was 50% for HIV-positive patients (95% CI: 45%-55%) compared to 65% for HIV-negative patients (95% CI: 56%-76%) (p = 0.007). Table 4.20 presents the symptoms and treatment characteristics by HIV status. Notably, HIV-positive patients were more likely to present with advanced disease stages and specific symptoms such as edema (p = 0.02). Cox Proportional Hazards Regression indicated that the stage at diagnosis, age, and level of education were significant predictors of survival. HIV status did not significantly alter survival rates when controlling for these variables (p = 0.945). Table 4.25 shows that patients diagnosed at stages II, III, and IV had significantly higher risks of death compared to those diagnosed at stage I (p < 0.05). Education level also impacted survival, with those having more than primary education showing better outcomes (p = 0.0059).

Survival

HIV-related cancer deaths were faster than non-HIV cases, which implied that HIV increases the mortality rate of cancer patients.

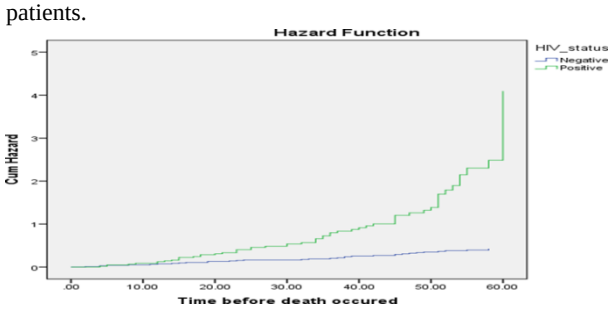

Figure 4. 2: Cancer deaths associated with HIV

Cox Proportional Hazards Regression models

Cox PH regression

The Cox PH regression predicts the effect of covariates on the risk ratio. Cox recovery was performed using the Breslow method. Since we did not have wide deadlines, the Breslow method worked well in harmony. The results in Table 4.24 show that the stage in diagnosis and education level significantly affects survival while other treatments significantly affect survival as well.

Table 4. 20: Symptoms and treatment of patients by HIV status

Characteristic	HIV-positive (n = 60 [38%])	HIV-negative(n=98[62%])	*P_value*
Cervical cancer histology			0.31
Adenocarcinoma	4 (8.2)	4 (4.3)	
Squamous cell	56 (91.8)	85 (86.7)	

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carcinoma			
Disease stage			0.03
I (IA, IB)	14 (15.4)	8 (7.8)	
II (IIA, IIB)	57 (59.4)	50 (50.6)	
III (IIIA, IIIB)	23 (25.2)	36 (36.9)	
IV	0 (0)	5 (4.7)	
Symptoms at presentation			
Vaginal bleeding	38 (63.6)	58 (58.7)	0.32
Post-coital bleeding	23 (38.4)	24 (24.9)	0.24
Vaginal discharge	41 (68.7)	70 (71.6)	0.86
Pelvic/back pain	43 (71.5)	57 (57.8)	0.21
Bowel/bladder	3 (4.9)	5 (4.8)	0.78
Edema	2 (4.1)	13 (13.4)	0.02

Stepwise regression

To test whether all nine variables were eligible for inclusion in the model, stepwise regression was used. The significance of the model was lower during the removal of the four covariates of category, HIV status Drinking, and smoking behavior as shown in Table 4.24 below. They are therefore excluded from subsequent analyzes.

Table 4. 22: Stepwise regression

Covariate	Df	AIC
none		922.04
Patient age	1	925.26
Patient Education	2	926.12
Patient Income zone	2	927.85
Treatment	10	932.43
Stage of cancer during diagnosis	4	939.79

After removing variables that did not qualify as the model, Table 4.25 shows that the patient's age, initial stage of diagnosis, and education level significantly affects survival, and other treatments significantly affect survival. Three types of treatments namely S + EBR + B + C, S + EBR + C, and EBR significantly affected patients' survival ($p < 0.05$). There was evidence of a progressive increase in the risk of death and progression at the initial diagnosis. Patients with early-stage II diagnosis, stage III, and stage IV had a higher risk of death 6.29, 13.71, and 15.47 times respectively of those diagnosed at stage I ($p < 0.05$). Patients who attended more than primary school had a reduced risk of 0.493 compared with those who had no formal education / primary education ($p < 0.05$).

Table 4.26: Testing for proportional hazards assumption

Omnibus Tests of Model Coefficients[a]

-2 Log Likelihood	Overall (score)			Change From Previous Step			Change From Previous Block		
	Chi-square	df	Sig.	Chi-square	Df	Sig.	Chi-square	df	Sig.
464.812	38.906	12	0	35.267	12	0	35.267	12	0

a. Beginning Block Number 1. Method = Enter

Table 4.26 provides a comprehensive assessment of the survival rates for all groups. Since the significance level of all tests is less than 0.05, the important difference between the number of cancer deaths in HIV-negative and HIV-positive cases during survival.

Table 4. 27: Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	51.903	1	.000
Breslow (Generalized Wilcoxon)	40.792	1	.000
Tarone-Ware	46.433	1	.000

Test of equality of survival distributions for the different levels of HIV status.

Estimation of survival time of cervical cancer patients on EBRT

In this case, various descriptors were added to each block so that these can have one step. This means that chi-square values were the same for step, block, and model. Sig. values are $p<.001$, indicating that the model predicts significant cancer mortality. Exp (B), which can be interpreted as a predicted change in the risk of unit inflation in forecasters. For binary covariates, the hazard ratio is the ratio of the hazard ratio to one group to the hazard ratio to the other group. The study found the hazard for an HIV positive cancer patient is 3.133 times that of a HIV Negative, 1.456 for cancer patient with drinking habit as opposed to non-drinking patient, and 1.523 for smoking cancer patients as opposed to non-smoking patients.

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Table 4. 28: Estimation of survival time of cervical cancer patients on treatment

Variables in the Equation

	B	SE	Wald	Df	Sig.	Exp(B)	95.0% CI forExp(B)	
							Lower	Upper
HIV status	1.142	.301	14.419	1	.000	3.133	1.738	5.649
Smoking behaviour	.421	.280	2.254	1	.133	1.523	.879	2.637
Drinking behaviour	.375	.283	1.761	1	.185	1.456	.836	2.535
S			12.525	9	.185			
EBR	.247	.682	.131	1	.717	1.280	.336	4.869
C	.152	.677	.051	1	.822	1.164	.309	4.389
S+EBR	1.716	1.062	2.610	1	.106	5.560	.694	44.562
S+ EBR +B	-.158	.743	.045	1	.832	.854	.199	3.664
S+ EBR + B + C	1.385	.926	2.235	1	.135	3.995	.650	24.552
S + EBR + C	.824	.776	1.129	1	.288	2.280	.499	10.428
EBR + C	-.037	.769	.002	1	.962	.964	.213	4.352
EBR + B + C	-.411	.815	.255	1	.614	.663	.134	3.273
EBR + B	-.546	.835	.428	1	.513	.579	.113	2.974

The survival probabilities of cancer patient after treatment decreased in all groups. The slowing of deaths however was high among the cancer patients diagnosed in stage I and stage II.

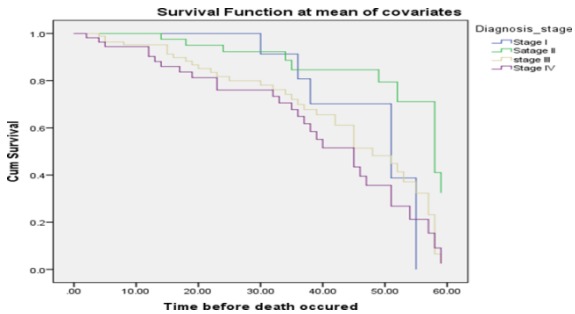

Figure 4. 3: Survival plots for the Cox regression model

Figure 4.5, illustrates the survival plots for the Cox regression model based on the means of various treatment methods. The lower level of probability of death was observed among the cases of cancer patients diagnosed in stage I and II as opposed to stage III and Stage IV. The curve trend further shows method of treatment did not affect the rate of deaths in cancer patients diagnosed in stage III and stage IV.

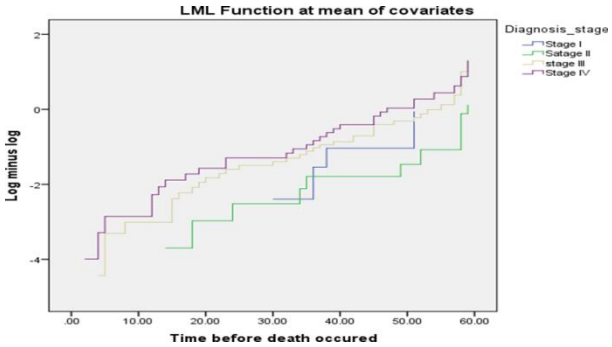

Figure 4. 4: Effect of diagnostic stage on the survival

Conclusion

HIV infection adversely affects the survival and treatment outcomes of cervical cancer patients undergoing chemoradiotherapy. HIV-positive patients experience higher toxicity and poorer survival rates compared to their HIV-negative counterparts. Factors such as the stage of cancer at diagnosis and the level of education are crucial in determining patient survival, regardless of HIV status. Targeted interventions and integrated care strategies are essential to address these disparities and improve outcomes for HIV-positive cervical cancer patients.

The survival disparity between HIV-infected and HIV-uninfected cervical cancer patients undergoing

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chemoradiotherapy is evident, with HIV-positive patients generally experiencing poorer outcomes. The interaction between HIV and chemoradiotherapy results in increased toxicity and reduced treatment efficacy, contributing to lower survival rates. Effective management strategies must consider the unique challenges faced by HIV-positive patients to improve their treatment outcomes.

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