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Contribution of HIV infection to mortality among cancer patients in Uganda

Anna E. Coghill[a,b,c], **Polly A. Newcomb**[a,b], **Margaret M. Madeleine**[a,b], **Barbra A. Richardson**[a,b], **Innocent Mutyaba**[d], **Fred Okuku**[d], **Warren Phipps**[a,b,d], **Henry Wabinga**[e], **Jackson Orem**[a,d], and **Corey Casper**[a,b,d]

[a]Fred Hutchinson Cancer Research Center, Seattle, Washington [b]University of Washington, Seattle, Washington [c]National Cancer Institute, Bethesda, Maryland, USA [d]UCI/Hutchinson Cancer Center Alliance, Uganda [e]Kampala Cancer Registry, Kampala, Uganda

Abstract

Objective—HIV infection is associated with cancer risk. This relationship has resulted in a growing cancer burden, especially in resource-limited countries where HIV is highly prevalent. Little is known, however, about how HIV affects cancer survival in these settings. We therefore investigated the role of HIV in cancer survival in Uganda.

Design—Retrospective cohort (N = 802).

Methods—Eligible cancer patients were residents of Kyadondo County, at least 18 years of age at cancer diagnosis, and diagnosed between 2003 and 2010 with one of the following: breast cancer, cervical cancer, non-Hodgkin's lymphoma, Hodgkin's lymphoma, or esophageal cancer. Patients were classified as HIV-infected at cancer diagnosis based on a documented positive HIV antibody test, medical history indicating HIV infection, or an HIV clinic referral letter. The primary outcome, vital status at 1 year following cancer diagnosis, was abstracted from the medical record or determined through linkage to the national hospice database. The risk of death during the year after cancer diagnosis was compared between cancer patients with and without evidence of HIV infection using Cox proportional hazards regression.

Results—HIV-infected cancer patients in Uganda experienced a more than two-fold increased risk of death during the year following cancer diagnosis compared to HIV-uninfected cancer patients [hazard ratio 2.28; 95% confidence interval (CI) 1.61–3.23]. This association between HIV and 1-year cancer survival was observed for both cancers with (hazard ratio 1.56; 95% CI 1.04–2.34) and without (hazard ratio 2.68; 95% CI 1.20–5.99) an infectious cause.

Conclusion—This study demonstrates the role of HIV in cancer survival for both cancers with and without an infectious cause in a resource-limited, HIV-endemic setting.

Correspondence to Anna E. Coghill, Infections and Immunoepidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 6120 Executive Boulevard, Rockville, MD 20892, USA., Tel: +1 240 276 7184; anna.coghill@nih.gov.

Conflicts of interest
There are no conflicts of interest.

Keywords

cancer in Africa; cancer survival; HIV; immunosuppression; Uganda

Introduction

Introduction of HAART in 1996 led to marked improvements in immune status and life expectancy for HIV-infected individuals in the US and Europe [1]. Although HIV treatment rollout has been delayed in resource-limited settings such as East Africa, a 2010 report demonstrated greater than 65% reductions in overall mortality for HIV-infected Ugandan patients after the introduction of antiretroviral therapy (ART) [2]. Recent evidence demonstrates that patients who initiate ART can in fact achieve life expectancy comparable to the Ugandan general population [3].

This increased life expectancy exposes HIV-infected patients to the risk of developing chronic diseases, including cancer. HIV infection and cancer risk have been linked in the US since the beginning of the HIV epidemic [4–11]. Importantly, cancer is a complication of HIV infection that is increasingly recognized to impact not just resource-rich but also resource-limited regions [12–14]. One Ugandan study utilized data from the Kampala Cancer Registry (KCR) to compared cancer rates in patients from a large HIV clinic to those in the general population, and observed significantly elevated cancer risk associated with an AIDS diagnosis [15]. Data from Uganda and Kenya have also recently demonstrated declines in individual Kaposi sarcoma (KS) risk in HIV-infected patients after ART treatment [16]. However, the association between successful HIV treatment and declining KS incidence on a population level in Uganda is not as clear as the dramatic declines observed after the introduction of ART in the US [13,17–22]. KCR trend data report that KS incidence has only begun declining [annual percentage change: −4.5%; 95% confidence interval (CI) −5.6%, −3.4%] for men under the age of 50, with no significant declines observed for either men aged greater than 50 or any subset of women [13,23].

As expected, increased HIV treatment uptake in resource-limited settings has increased HIV-infected patient life expectancy. Against this backdrop, the consistently elevated risk for cancer in this ageing population will result in a growing number of patients diagnosed with both diseases over time. Therefore, the question of whether and how HIV plays a role in cancer outcomes is of public health importance.

Little is known, however, about the role HIV plays in cancer survival in either resource-rich or resource-limited settings. Since the introduction of ART in Uganda in the early 2000s, results from only one cancer survival study have been reported. In that study, 154 non-Hodgkin lymphoma (NHL) patients were ascertained from the Uganda Cancer Institute (UCI), and the study found that HIV-infected NHL patients not receiving HIV treatment experienced significantly poorer 1-year cancer survival than both HIV-uninfected NHL patients and HIV-infected NHL patients receiving appropriate HIV treatment [24]. The growing importance of the role of immunosuppression in cancer patient outcomes and the lack of data specific to resource-limited settings motivated us to investigate the role of HIV in survival after a cancer diagnosis in Uganda.

Methods

Eligibility

Eligible cancer patients were residents of Kyadondo County, Uganda, at least 18 years of age at the time of cancer diagnosis, and diagnosed from 2003 to 2010 with one of the following: breast cancer, cervical cancer, NHL, Hodgkin lymphoma (HL) or esophageal cancer. Patient residence, age at diagnosis, and year of diagnosis were abstracted from the medical record. For men, we selected two cancers with (NHL, HL) and one without (esophageal) an established infectious cause. For women, we selected the two most common cancers: one with (cervical) and one without (breast) an infectious cause. Patients with a prior malignancy noted in the medical record were excluded.

Case ascertainment

Eligibility criteria were used to generate lists of cancer patients using the KCR database, a population-based cancer registry that has performed cancer registration in Kyadondo County since the 1950s, with the exception of selected years in the 1970–1980s due to political turmoil [14,25]. Cases are ascertained for the KCR primarily from the Pathology Department at Mulago Hospital, the largest tertiary referral hospital in Uganda, as well as the four main hospitals in Kampala and the national hospice system. Patient lists were then transferred to the UCI, the only comprehensive cancer treatment facility for Uganda, where record departments facilitated medical record retrieval. Lists were also provided to appropriate clinics at Mulago Hospital in order to survey for records for cancer patients who may not have presented to the UCI. To achieve more complete case ascertainment, eligibility criteria were also given directly to the record officers at the UCI and Mulago to check against the clinic log books used for patient registration and to aid in the identification of patients meeting eligibility criteria who may not have been included in the KCR database listing.

Exposure assessment

A cancer patient was classified as HIV-infected at the time of cancer diagnosis if he/she met any of the following criteria: documented positive HIV antibody test, indication of HIV infection in the medical history, or evidence of treatment at a local HIV clinic. If a cancer patient did not have specific evidence of HIV infection, the patient was classified as HIV-uninfected.

Outcome assessment

The primary outcome was vital status at 1 year following cancer diagnosis, with death from any cause classified as an event. Three possible vital status outcomes existed for each cancer patient: alive – medical record included a clinic visit dated at least 1 year after cancer diagnosis; dead – medical record noted the patient died during the year following cancer diagnosis; and unknown/lost – last clinic visit date in the medical record was less than 1 year after cancer diagnosis and medical record did not specifically note the patient died.

Cancer patients at the UCI and Mulago are often transferred to the national hospice system (Hospice Africa Uganda) for palliative care, and the national hospice system conducts active

follow-up for enrollees. Therefore, for any cancer patient with unknown vital status at 1 year, linkage to the national hospice system database was conducted.

Survival time for each cancer patient was calculated beginning at the earlier of: date of first presentation, listed on the medical record intake form, or biopsy result date, listed on the pathology report confirming a histological diagnosis. The survival time end date was date of death listed in the medical record for deceased cancer patients. Survival time was censored on the last date of clinical contact listed in the medical record or last date listed in the national hospice system database for cancer patients who were not deceased. For 1-year survival analyses, cancer patients with survival time greater than 1 year were administratively censored at 1 year, and for 2-year survival, patients with survival time greater than 2 years were administratively censored at 2 years.

Covariates and extent of disease assessment

Patient characteristics at cancer diagnosis were abstracted directly from the medical record, including age, sex, duration of symptoms, history of smoking, family history of cancer, and prior medical conditions (diabetes, tuberculosis, cardiovascular disease). Reproductive history, including parity, contraception, menarche, and menopausal status, was generally recorded in the clinical notes for female patients. Information on BMI, measured for the purpose of chemotherapy dosage, was available for lymphoma patients, and hemoglobin was noted for lymphoma and cervical cancer patients.

Cancer stage was abstracted from the medical chart. If an initial clinical stage was not specifically noted, a consulting physician reviewed the medical record and adjudicated stage based on available data. If stage was assigned based on the TNM Classification of Malignant Tumors system, the T, N, and M values were used to assign a categorical value ranging from stage I to IV, with stages I and II considered early disease and stages III and IV considered advanced disease.

Statistical analysis

Kaplan–Meier product-limit survival estimates were generated comparing differences in time to death in the year following cancer diagnosis according to HIV infection using the log-rank test. Cox proportional hazards regression was utilized to evaluate the association between HIV infection at cancer diagnosis and 1-year cancer survival. Multivariable regression models included the following covariates selected *a priori*: age, calendar year of cancer diagnosis, and cancer stage.

Etiologically meaningful subgroups of cancers were defined as: cancers with an infectious cause (NHL, HL, cervical) and cancers without an established infectious cause (breast, esophageal). Regression models were evaluated among NHL and cervical cancer patients with further adjustment for variables with *P*-values less than 0.10 in Kaplan–Meier analyses, including BMI (NHL) and hemoglobin (NHL, cervical cancer).

HIV-infected patients were subdivided according to year of cancer diagnosis, which served as a surrogate for estimated ART availability in Uganda: 2003–2005 (ART coverage: 5–25%), 2006–2008 (ART coverage: 30–45%), and 2009–2010 (ART coverage ≥50%) [26].

Risk of death during the year after cancer diagnosis was compared between HIV-uninfected cancer patients and HIV-infected cancer patient subgroups. To avoid over-adjustment, year of diagnosis was not included in this model.

Results

The cohort (N = 802) included the following cancer diagnoses: breast cancer (n =220), cervical cancer (n = 316), NHL (n = 134), HL (n = 63), and esophageal cancer (n = 69) (Table 1, Fig. 1). Approximately one-third of cancer patients were HIV-infected at cancer diagnosis, although the proportion differed by cancer type. Among patients diagnosed with a cancer without an established infectious cause, HIV prevalence was much lower (breast: 11%; esophageal: 6%) than among patients diagnosed with infection-related cancers (NHL: 57%; cervical: 42%; HL 56%).

Only 322 of the 802 cohort members were alive 1 year after cancer diagnosis. Among those who died in the year following cancer diagnosis (n=152), more than two-thirds died in the first 6 months. For patients with unknown vital status (n = 328), over half were lost to follow-up by 3 months, indicative of loss occurring almost immediately after cancer diagnosis. Risk of death was significantly related to specific cancer type (log rank P-value <0.01), regardless of HIV status. Breast cancer patients had the best prognosis, with nearly two-thirds confirmed as alive at 1 year, whereas 1-year survival ranged from 33 to 35% for cancers with an infectious cause (Table 2). Only 16% of esophageal cancer patients were confirmed as alive at 1 year, although most patients (70%) were lost to follow-up in that first year.

The majority of cohort members were women due to inclusion of breast and cervical cancer diagnoses; among lymphoma and esophageal cancer patients, approximately 45–55% were females. HIV-infected cancer patients were significantly younger than HIV-uninfected patients. For example, 41% of HIV-infected cervical cancer patients were 18–35 years old at diagnosis, compared to only 13% for HIV-uninfected cervical cancer patients.

Esophageal cancer, the malignancy with the lowest proportion of HIV-infected cases, was the only cancer for which the majority of patients (64%) were 56–86 years old at diagnosis. The stage of disease at presentation also varied according to HIV status (Fig. 2). HIV-infected cervical cancer patients were uniformly diagnosed at earlier stages: 38% of HIV-infected cervical cancer cases were diagnosed with stage I–II disease, compared to 21% of HIV-uninfected cervical cancer patients. In contrast, HIV-infected HL patients were diagnosed with advanced disease more often than HIV-uninfected patients. There was no substantive difference observed for NHL or breast cancer patients, who were uniformly diagnosed with advanced disease, regardless of HIV status. Stage at presentation was undetermined for 56 of the 69 esophageal cancer patients.

HIV-infected cancer patients were more than twice as likely to die during the year following cancer diagnosis compared with HIV-uninfected cancer patients (hazard ratio 2.28; 95% CI 1.61–3.23) (Table 2). Importantly, this association between HIV infection at cancer diagnosis and poorer 1-year cancer survival was observed for both cancers with and without

an infectious cause. Specifically, HIV-infected patients diagnosed with infection-related cancers had greater than 50% higher risk of death during the year following cancer diagnosis (hazard ratio 1.56; 95% CI 1.04–2.34), and HIV-infected patients diagnosed with cancers without an infectious cause also experienced significantly higher risk of death (hazard ratio 2.68; 95% CI 1.20–5.99). Risk of dying with NHL was not different from the results shown in Table 2 after further adjustment for sex, hemoglobin, and BMI, and risk of dying with cervical cancer was not different after adjustment for hemoglobin.

Although most deaths occurred in the first year after cancer diagnosis, an additional 42 patients died during the second year. Utilizing this additional follow-up showed 2-year outcomes consistent with those reported for 1 year (Supplemental Table 1, http://links.lww.com/QAD/A389). To investigate the impact of HIV therapy on 1-year cancer survival, we compared HIV-uninfected to HIV-infected cancer patients diagnosed during different periods of estimated ARTavailability in Uganda [26]. HIV-infected cases diagnosed prior to widespread ART availability (2003–2005) experienced the poorest 1-year cancer survival compared to HIV-uninfected patients (hazard ratio 2.75; 95% CI 1.43–5.28) (Fig. 3). Risk of death during the year after cancer diagnosis remained elevated in HIV-infected patients diagnosed in more recent years.

Approximately 40% of patients classified as HIV-uninfected lacked direct confirmation of HIV-uninfected status in the medical record, defined as either a negative HIV antibody test result or HIV-uninfected status recorded in clinical notes. However, no differences in 1-year cancer survival were observed between confirmed and unconfirmed HIV-uninfected cases (hazard ratio 0.87; 95% CI 0.54–1.40). Results for 1-year cancer survival comparing only confirmed HIV-uninfected to HIV-infected cancer patients were consistent with results shown in Table 2 (hazard ratio 2.18; 95% CI 1.50–3.18).

Discussion

This is the largest and most comprehensive study of the association between HIV and cancer survival in sub-Saharan Africa to date. We observed that HIV-infected cancer patients in Uganda experienced a more than twofold increase in risk of death in the year following cancer diagnosis compared to HIV-uninfected cancer patients. This association between HIV status at cancer diagnosis and poorer cancer survival was observed for both cancers with and without an infectious cause, regardless of stage at diagnosis. These findings extend the established relationship between HIV and excess cancer risk to include a role for HIV in cancer outcomes.

Only one prior cancer survival study has been reported after the introduction of ART in Uganda. The UCI-based study observed that HIV-infected NHL patients receiving ART experienced comparable 1-year cancer survival to HIV-uninfected patients with NHL [24]. One pre-ART study examined outcomes 3 years after cervical cancer diagnosis and reported marginally poorer survival for HIV-infected women at 1 year, although differences according to HIV status did not persist among women surviving 3 years after cervical cancer diagnosis [27].

Our findings are consistent with the limited data available from the US on HIV-related immunosuppression and cancer survival. The largest study to date, a New York-based registry study, observed that the survival disadvantage after cancer diagnosis in HIV-infected relative to HIV-uninfected cancer patients decreased with the introduction of HAART [28]. However, the inclusion of data from 1980 to 2000 complicates interpretation of these results since cancer patient mortality could have been largely influenced by drastic changes in the rate of AIDS-related deaths across different HIV therapy decades. Only one large US cancer survival study to date has been conducted using data solely from the HAART era [29]. After accounting for cancer stage and cancer treatment among HIV-infected patients treated with combination ART, researchers observed lower risk of death after cancer diagnosis for HIV-infected patients with higher levels of immune competence and well controlled HIV viremia.

It is accepted that immunosuppression is associated with increased cancer risk, corroborated by observations in both organ transplant recipients [30–34] and HIV-infected patients [11,20,35]. Specifically, cancers attributable to infectious agents are most commonly elevated in immunosuppressed individuals [36–40]. We observed that a relationship between HIV infection and cancer survival exists not only for infection-related cancers but also for cancers without an established infectious cause. This suggests that once a tumor is present, mechanisms may exist whereby immunosuppression can alter tumor growth for cancers with distinct causes.

For infection-related cancers, immune dysfunction results in an inability to control oncogenic viruses. Both the number and functional capacity of antiviral, Epstein-Barr virus (EBV)-specific $CD8^+$ T cells are impaired in AIDS patients who progress to NHL [41–43], providing a biologically plausible mechanism for the association between HIV-related immunosuppression and NHL risk. Antiviral immunity can also influence tumor progression; studies have observed that HIV-infected KS patients with clinical improvement had lower levels of replicating human herpesvirus 8 (HHV8), the causative agent for KS in the peripheral blood and superior $CD8^+$ T-cell responses specific to HHV8 [44,45].

$CD8^+$ T-cell dysfunction is a hallmark of HIV pathogenesis that occurs as a result of the destruction of $CD4^+$ T cells by HIV and chronic immune activation that stems from persistent, long-term HIV infection and prevalent co-infections such as cytomegalovirus [46–51]. A key implication of chronic immune activation is premature ageing of the immune system, known as immune senescence [52–55]. This immune dysfunction has implications for antitumor surveillance among all cancer diagnoses since $CD8^+$ T cells can develop cytotoxic responses to proteins on the surfaces of tumor cells, and both experimental and population studies have illustrated the importance of these lymphocytes in the prevention of tumor formation and in altering tumor prognosis [56–67].

Another direct implication of persistent immune activation in the context of HIV is chronic inflammation [68,69]. Levels of pro-inflammatory cytokines are significantly higher in HIV-infected versus HIV-uninfected individuals, and population studies have consistently found that inflammation correlates with the degree of HIV disease severity [70–73]. Elevated inflammatory signaling could alter tumor promotion since inflammation is considered to be

an underlying hallmark of cancer [74–77]. Ultimately, the tumor environment may be affected by the presence of HIV infection, regardless of tumor cause. The exhaustion of key lymphocyte populations could diminish the capacity of the immune system to control the metastatic potential of that tumor, whereas high levels of inflammation can promote tumor growth.

Our findings also highlight clinically relevant differences between HIV-infected and HIV-uninfected cancer patients. The results of this study suggest that vigilance is indicated in the management of HIV-infected cancer patients as they often present at a high stage of disease. Interestingly, among cervical cancer patients, HIV-infected women were actually diagnosed at earlier stages of disease at twice the rate of HIV-uninfected women, suggesting that women currently in the HIV care system may be under increased surveillance.

In agreement with earlier findings from the UCI for NHL patients [24], we also observed evidence that management of HIV-infected cancer patient immunosuppression is important for 1-year cancer outcomes. Although individual calendar year did not impact cancer survival among all study participants, HIV-infected patients diagnosed in the subset of years with limited ART availability in Uganda had a more pronounced risk of death after cancer diagnosis compared to HIV-infected patients diagnosed after more widespread ART rollout. Future studies that collect sensitive information on immunosuppression, including cancer patient $CD4^+$ T-cell counts, are needed to confirm these clinically relevant findings in this patient setting.

Strengths of this study include restriction of eligibility to recent years, avoiding vast differences that would be expected across different decades in overall survival because of changes in patterns of deaths due to AIDS. In addition, data on stage at presentation were collected, decreasing the potential for confounding bias in survival comparisons. The inclusion of HIV-uninfected cancer patients provided a true unexposed comparison group, and we were able to enroll adequate numbers of cancer patients to estimate type-specific effects for certain cancers. Future studies could combine data from extant cancer registries across sub-Saharan Africa and include additional years of cancer registration in order to increase event numbers and improve statistical power to detect differences for rarer malignancies. This study is not without limitations, including significant loss to followup. Approximately 40% of cancer patients were lost from vital status follow-up prior to 1 year. Reassuringly, however, the difference in loss to follow-up did not differ by HIV status. Another limitation was the lack of specific ART information. We examined the data by year of cancer diagnosis as a proxy for HIV treatment availability and found that survival appeared somewhat improved in more recent years. It is possible that cancer diagnostics and treatment improved with increasing calendar years, making it impossible to directly attribute the increased survival in more recent calendar years to availability of ART alone. Future studies should consider individual ART data over time across a range of baseline $CD4^+$ T-cell counts to confirm that improved immune status is associated with altered cancer patient survival.

Uganda does not have nationwide death registration to provide cause of death information. This precluded an examination of cancer-specific survival. Instead, overall survival during

the year following cancer diagnosis was used as a verifiable outcome. Our confidence that the survival differences observed reflected not just HIV-related causes of death but also cancer-specific death is strengthened by the proximity of the majority of events to the date of cancer diagnosis, a trend consistent irrespective of HIV status. We were also unable to ensure complete case ascertainment; cases lost to follow-up prior to histological diagnosis or with lost medical records were not available. Although this limitation does not threaten internal validity of the study, it may limit generalizability.

The study demonstrated a role for HIV in cancer patient survival for cancers with and without an infectious cause in a resource-limited, HIV-endemic setting. To extend our findings, future investigations should include prospective evaluation of cancer-specific outcomes and active mortality follow-up. The collection of more sensitive, longitudinal, HIV-related measures such as HIV RNA level and $CD4^+$ T-cell counts may identify characteristics of HIV-infected cancer patients that could explain observed survival differences. The question of the role of immunosuppression in cancer patient outcomes will become increasingly important as the number of HIV-infected patients diagnosed with cancer continues to grow in both resource-rich and resource-limited settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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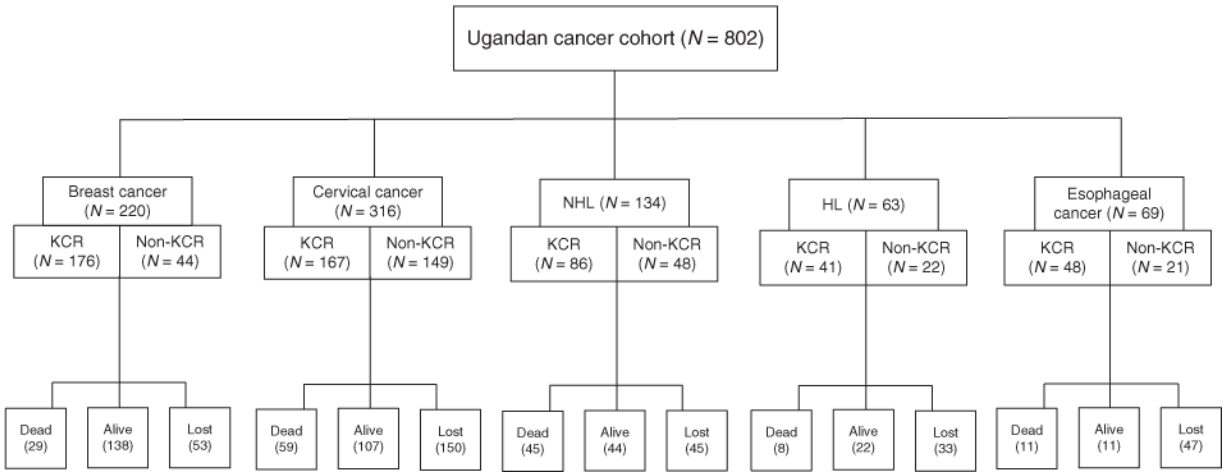

Fig. 1. Ascertainment source and vital status at 1 year of cohort patients, according to cancer diagnosis

Ascertainment sources include KCR: medical records retrieved by providing the list of names from the KCR database to the records officers, and non-KCR: medical records retrieved by the records officers scanning clinic log books for additional cases who met eligibility criteria. KCR, Kampala Cancer Registry.

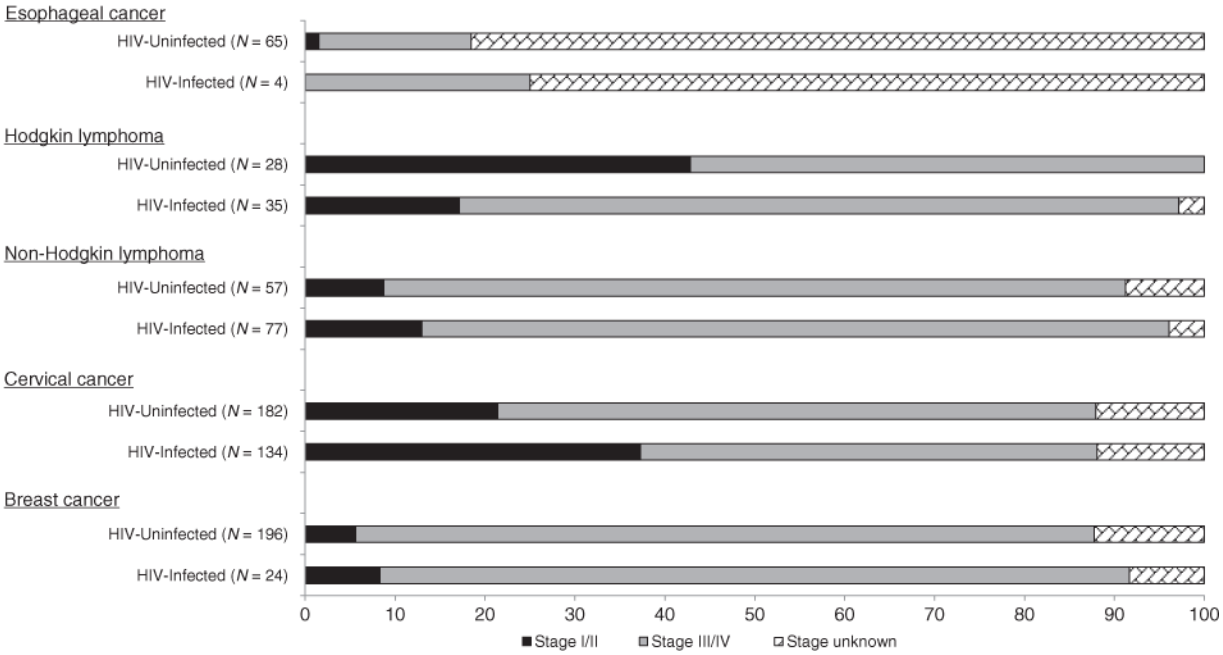

Fig. 2.

Percentage distribution of stage of disease at presentation, according to cancer diagnosis and HIV status.

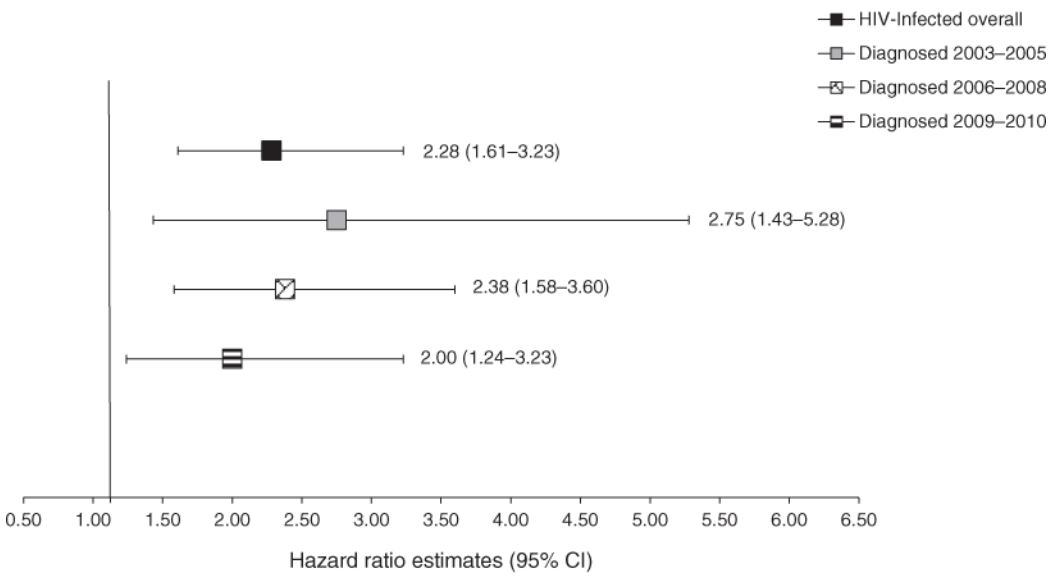

Fig. 3. Association between HIV and 1-year cancer survival, according to HIV treatment availability

Estimated HIV treatment availability in Uganda [26]: 2003–2005: 5–25%; 2006–2008: 30–45%; 2009–2010: assumed to have increased above 50%.

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Table 1

Cancer patient cohort characteristics.

	Total cohort (*N* = 802)		**HIV-negative (*n* = 528)**		**HIV-positive (*n* = 274)**		
	N	**%**	***n***	**%**	***n***	**%**	**Chi-square *P*-values[a]**
Cancer type							
Breast cancer	220	27.4	196	37.1	24	8.8	
Cervical cancer	316	39.4	182	34.5	134	48.9	
Non-Hodgkin lymphoma	134	16.7	57	10.8	77	28.1	
Hodgkin lymphoma	63	7.9	28	5.3	35	12.8	
Esophageal cancer	69	8.6	65	12.3	4	1.5	<0.01
Sex of patient[b]							
Female	125	47.0	62	41.3	63	54.3	
Male	141	53.0	88	58.7	53	45.7	0.04
Age (years)							
18–35	211	26.3	103	19.5	108	39.4	
36–44	188	23.4	93	17.6	95	34.7	
45–55	210	26.2	159	30.1	51	18.6	
56–86	185	23.1	169	32.0	16	5.8	<0.01
Year of cancer diagnosis							
2003–2005	120	15.0	81	15.3	39	14.2	
2006–2008	367	45.8	244	46.2	123	44.9	
2009–2010	315	39.3	203	38.5	112	40.9	0.78
BMI[c]							
<18.5	73	37.2	34	40.5	39	34.8	
18.5–24.99	66	33.7	23	27.4	43	38.4	
25.0–29.99	19	9.7	11	13.1	8	7.1	
30+	7	3.6	4	4.8	3	2.7	0.32
Missing	31	15.8	12	14.3	19	17.0	
Anemia at presentation[d]							
No	126	24.6	77	28.8	49	19.9	

	Total cohort (*N* = 802)		HIV-negative (*n* = 528)		HIV-positive (*n* = 274)		
	N	**%**	***n***	**%**	***n***	**%**	**Chi-square *P*-values[a]**
Yes: ≤12 g/dl	221	43.1	100	37.5	121	49.2	
Severe: ≤7 g/dl	70	13.6	32	12.0	38	15.4	0.01
Missing	96	18.7	58	21.7	38	15.4	
Tumor stage							
Stage I	31	3.9	19	3.6	12	4.4	
Stage II	105	13.1	49	9.3	56	20.4	
Stage III	377	47.0	262	49.6	115	42.0	
Stage IV	160	20.0	94	17.8	66	24.1	<0.01
Missing	129	16.1	104	19.7	25	9.1	
Parity							
Nulliparous	31	4.7	19	4.4	12	5.4	
Parous	535	81.4	348	79.8	187	84.6	0.67
Missing	91	13.9	69	15.8	22	10.0	
Menopausal status[e]							
Post-menopausal	183	27.9	165	37.8	18	8.1	
Pre-menopausal	369	56.2	190	43.6	179	81.0	<0.01
Missing	105	16.0	81	18.3	24	10.9	
Vital status at 1 year							
Alive	322	40.2	234	44.3	88	32.1	
Dead	152	19.0	79	15.0	73	26.6	
Lost to follow-up	328	40.9	215	40.7	113	41.2	<0.01

[a] Chi-square *P*-values for difference according to HIV infection status for each covariate of interest.

[b] Numbers and percentages for sex restricted to lymphoma and esophageal cancer patients (*n*=266).

[c] Numbers and percentages for BMI restricted to lymphoma patients (*n*=197).

[d] Numbers and percentages for anemia restricted to lymphoma and cervical cancer patients (*n*=513).

[e] Numbers and percentages for parity and menopausal status restricted to female patients (n=657).

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Table 2

Association between HIV and 1-year cancer survival.

	Total/deaths	Percentage alive at 1 year	Model 1[a]		Model 2[b]	
			HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
All cancer patients (*N* = 802)						
HIV-uninfected	528/79	44.3	1.00		1.00	
HIV-infected	274/73	32.1	2.08 (1.47–2.94)	<0.01	2.28 (1.61–3.23)	<0.01
Cancers with infectious cause (*n* = 513)						
HIV-uninfected	267/48	36.7	1.00		1.00	
HIV-infected	246/64	30.5	1.52 (1.01–2.28)	0.04	1.56 (1.04–2.34)	0.03
NHL (*n* = 134)						
HIV-uninfected	57/19	42.1	1.00		1.00	
HIV-infected	77/26	26.0	1.16 (0.63–2.14)	0.65	1.33 (0.71–2.47)	0.37
HL (*n* = 63)						
HIV-uninfected	28/3	35.7	1.00		1.00	
HIV-infected	35/5	34.3	1.71 (0.36–8.07)	0.50	1.74 (0.36–8.33)	0.49
Cervical cancer (*n* = 316)						
HIV-uninfected	182/26	35.2	1.00		1.00	
HIV-infected	134/33	32.1	1.59 (0.88–2.85)	0.12	1.71 (0.96–3.04)	0.07
Cancers without infectious cause (*n* = 289)						
HIV-uninfected	261/31	52.1	1.00		1.00	
HIV-infected	28/9	46.4	2.64 (1.19–5.86)	0.02	2.68 (1.20–5.99)	0.02
Breast cancer (*n* = 220)						
HIV-uninfected	196/23	63.8	1.00		1.00	
HIV-infected	24/6	54.2	1.98 (0.74–5.28)	0.17	2.04 (0.76–5.47)	0.16
Esophageal cancer (*n* = 69)						
HIV-uninfected	65/8	16.9	1.00		1.00	
HIV-infected	4/3	0.0	4.63 (0.95–22.6)	0.06	4.09 (0.80–20.86)	0.09

CI, confidence interval; HL, Hodgkin lymphoma; HR, hazard ratio; NHL, non-Hodgkin lymphoma.

[a]Model includes: age, year of cancer diagnosis.

[b]Model includes: Model 1 + stage at presentation (categorical: stage I/II, stage III/IV, stage unknown).