Outcomes of cervical cancer among HIV-infected and HIV-uninfected women treated at the Brazilian National Institute of Cancer

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INTRODUCION

Human immunodeficiency virus (HIV) infection increases the risk of some malignancies. In people infected with HIV, cancer occurs at a younger age and in many cases at advanced stages at the time of diagnosis. The most common cancers in this population are AIDS-defining cancers, such as Kaposi's sarcoma, non-Hodgkin's lymphoma, and cervical cancer. With the introduction of HAART in 1996, there was a significant increase in the life expectancy of people living with HIV. These individuals, who have died relatively young, are now aging and therefore the risk of developing diseases due to the aging process has become increasingly evident in this population. Cervical cancer (UCC) is an important cause of morbidity and mortality in HIV infected women. As HIV infected people are living longer. Many HIV infected women diagnosed with CCU will not die of AIDS and therefore it is important to understand the impact of HIV on the prognosis of cancer in patients who have received treatment for it. Objective: We evaluated mortality, response to treatment and relapse among HIV-infected and HIV-uninfected women with cervical cancer in Rio de Janeiro, Brazil.

METHODS

Cohort study of 87 HIV-infected and 336 HIV-uninfected women with cervical cancer. Patients at the Brazilian National Institute of Cancer (2001–2013) were matched on age, calendar year of diagnosis, clinical stage, and tumor histology. Staging and treatment with surgery, radiotherapy, and/or chemotherapy followed international guidelines. We used a Markov model to assess responses to initial therapy, and Cox models for mortality and relapse after complete response (CR).
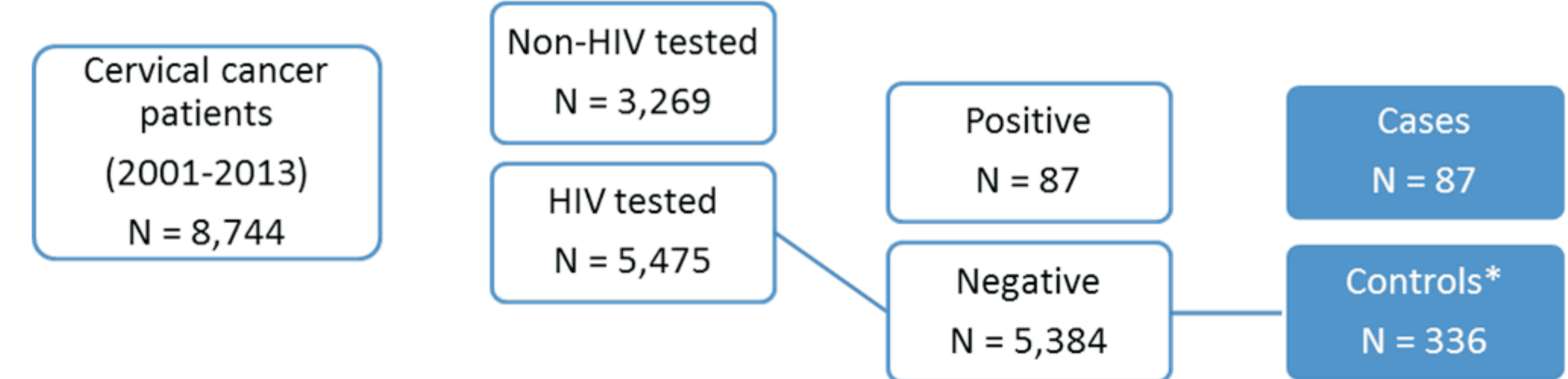

Figure 1. Flowchart of the study population. *There were four HIV-uninfected women matched to each HIV-infected woman, except three HIV-infected women had only three matches, three had two matches, and one had one match

RESULTS

Table 1. Characteristics of HIV-infected and HIV-uninfected patients with cervical cancer treated at INCA (2001-2013)

Characteristic	HIV-infected patients Number (%)		HIV-uninfected patients Number (%)[a]		p-value
Total	87	(100)	336	(100)	
Age at registration, years					0.71
<35	22	(25.3)	74	(22.0)	
35-49	53	(60.9)	206	(61.3)	
50+	12	(13.8)	56	(17.7)	
Calendar year of registration					0.51
2001-2005	32	(36.8)	124	(36.9)	
2006-2009	31	(35.6)	101	(30.1)	
2010-2013	24	(27.6)	111	(33.0)	
Race					0.25
White	38	(43.7)	169	(50.3)	
Non-white	49	(56.3)	165	(49.1)	
Clinical stage					1.00
Stage IA	12	(13.8)	48	(14.3)	
Stage IB1	12	(13.8)	47	(14.0)	
Stage IB2	4	(4.6)	16	(4.8)	
Stage II	14	(16.1)	56	(16.7)	
Stage III	35	(40.2)	134	(39.9)	
Stage IVA	4	(4.6)	16	(4.8)	
Stage IVB	6	(6.9)	19	(5.7)	
Histology					0.86
Squamous cell carcinoma	81	(93.1)	311	(92.6)	
Adenocarcinoma	6	(6.9)	25	(7.4)	
First course of cancer therapy					0.99
Surgery	24	(27.6)	95	(28.3)	
Radiation	20	(23.0)	77	(22.9)	
Radiation and chemotherapy	25	(28.7)	100	(29.8)	
None	18	(20.7)	64	(19.1)	
Body mass index, kg/m^{2}					0.002
<25.0	33	(82.5)	110	(52.1)	
25.0-29.9	5	(12.5)	58	(27.5)	
30.0+	2	2 (5.0)	43	(20.4)	
Missing*	47		125		
Education					0.58
Incomplete primary school	48	(55.2)	165	(49.4)	
Primary school	25	(28.7)	102	(30.5)	
Secondary school	14	(16.1)	67	(20.1)	
Marital status					0.003
Married/with partner	20	(23.0)	142	(42.6)	
Divorced/widowed	16	(18.4)	54	(1621)	
Single	51	(58.6)	137	(41.1)	
Missing*	0		3		
Tobacco use					0.25
Current/former	39	(48.8)	137	(41.6)	
None	41	(51.2)	192	(58.4)	
Missing*	7		7		
Alcohol use					0.41
Current/former	24	(30.8)	84	(26.2)	
None	54	(69.2)	237	(73.8)	
Missing*	9		15		

a There were four HIV-uninfected women matched to each HIV-infected woman, except three HIV-infected women had only three matches, three had two matches, and one had one match. * Missing values were not included in the calculations of the percentages or in the chi-square test P values.

Table 3. Associations of HIV infection with overall mortality and cancer-specific mortality, overall and in patient subgroups

Patient group	Overall mortality HR (95%CI)	Cancer-specific mortality HR (95%CI)
All patients, unadjusted	1.38 (1.02-1.87)	1.31 (0.94-1.82)
All patients, adjusted for clinical stage	1.29 (0.95-1.75)	1.18 (0.85-1.65)
Patients treated with surgery, unadjusted	8.70 (1.59-47.5)	--
Patients treated with radiation, adjusted for clinical stage and brachytherapy	1.22 (0.82-1.82)	0.96 (0.62-1.48)
Models s tratified by follow-up time, adjusted for clinical stage[a]		
Early follow-up	0.97 (0.65–1.45)	0.99 (0.69–1.42)
Late follow-up	2.02 (1.27–3.22)	4.35 (1.86–10.2)

Adjustment for clinical stage was accomplished using categories defined as stage IA/IB1, IB2/II, III, or IVA/IVB. CI, confidence interval; HR, hazardratio. [a]For overall mortality, follow-up time was divided at 1 year after cancer diagnosis. For cancer-specific mortality, follow-up time was divided at 2 years after cancer diagnosis.
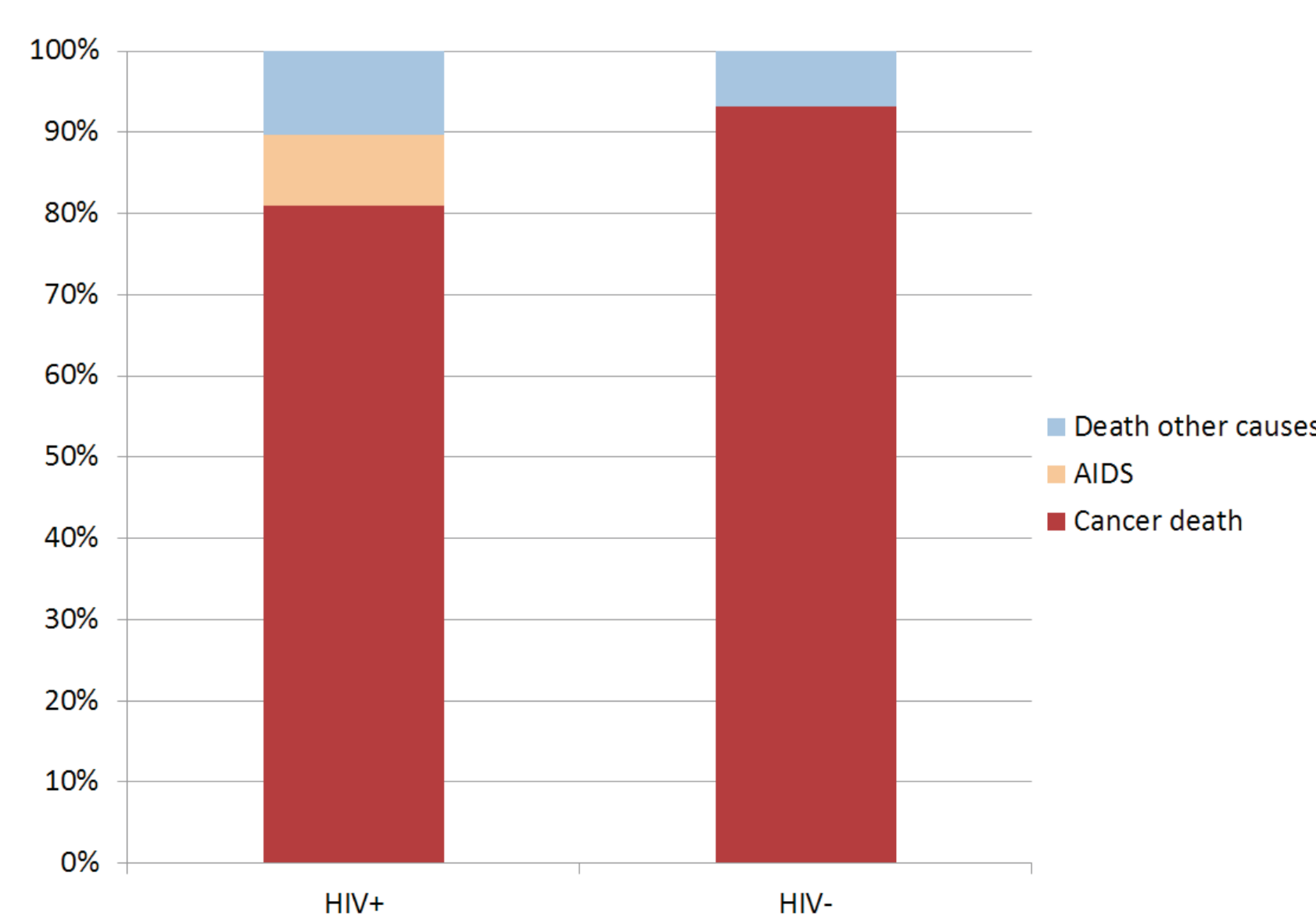

Figure 2. Causes of death by HIV status.

Table 2. Univariate associations of patient characteristics with overall mortality and cancer-specific mortality

Characteristic	Deaths, N	Overall mortality HR (95% CI)		Cancer deaths, N	Cancer-specific mortality HR (95% CI)	
HIV status						
Infected	56	1.38	(1.02-1.87)	46	1.31	(0.94-1.82)
Uninfected	171	1.00	Reference	159	1.00	Reference
Age at registration, years						
<35	54	1.00	Reference	47	1.00	Reference
35-49	142	0.97	(0.71-1.33)	132	0.98	(0.70-1.37)
50+	31	0.71	(0.46-1.11)	26	0.67	(0.42-1.09)
Calendar year of registration						
2001-2005	71	0.74	(0.53-1.03)	61	0.71	(0.50-1.01)
2006-2009	87	1.24	(0.90-1.70)	79	1.26	(0.90-1.74)
2010-2013	69	1.00	Reference	65	1.00	Reference
Race						
White	109	1.00	Reference	101	1.00	Reference
Non-white	117	1.02	(0.79-1.33)	103	0.99	(0.75-1.30)
Clinical stage						
Stage IA-IB1	6	0.08	(0.04-0.20)	1	0.02	(0.00-0.12)
Stage IB2-II	42	1.00	Reference	36	1.00	Reference
Stage III	134	2.75	(1.94-3.89)	123	2.91	(2.00-4.22)
Stage IV	45	5.01	(3.27-7.68)	45	5.46	(3.50-8.52)
Histology						
Squamous cell carcinoma	221	4.13	(1.84-9.31)	200	4.48	(1.85-10.9)
Adenocarcinoma	6	1.00	Reference	5	1.00	Reference
Body mass index, kg/m^{2}						
<25.0	85	1.00	Reference	78	1.00	Reference
25.0-29.9	27	0.57	(0.37-0.88)	24	0.55	(0.35-0.86)
30.0+	13	0.37	(0.21-0.67)	13	0.39	(0.22-0.71)
Missing	102	0.98	(0.73-1.30)	90	0.96	(0.71-1.30)
Education						
Incomplete primary school	128	1.00	Reference	118	1.00	Reference
Primary school	61	0.72	(0.53-0.97)	55	0.70	(0.50-0.96)
Secondary school	37	0.65	(0.45-0.94)	31	0.61	(0.41-0.91)
Marital status						
Married/with partner	77	0.77	(0.58-1.04)	70	0.76	(0.56-1.03)
Divorced/widowed	40	1.00	(0.70-1.44)	36	0.99	(0.68-1.45)
Single	110	1.00	Reference	99	1.00	Reference
Tobacco use						
Current/former	106	1.46	(1.12-1.91)	99	1.51	(1.14-1.99)
None	114	1.00	Reference	101	1.00	Reference
Alcohol use						
Current/former	55	0.83	(0.61-1.12)	47	0.77	(0.56-1.08)
None	160	1.00	Reference	148	1.00	Reference
CD4 count status, among HIV-infected women						
Available	23	0.51	(0.30-0.86)	20	0.51	(0.29-0.92)
Not available	33	1.00	Reference	26	1.00	Reference

CI, confidence interval; HR, hazard ratio

We found a trend (p = 0.056) in the association of HIV infection with overall survival; 35% and 49% of HIV + and HIV- women, respectively, were alive in 5 years. However, when we adjusted for clinical stage, the odds of dying associated with HIV lost significance (HR 1.29, 95% CI 0.95-1.75). We observed a strong association (p <0.001) of HIV infection with the risk of recurrence after complete treatment for cancer (HR 3.60, 95% CI, 1.86-6.98), and this association even maintained after adjustment by clinical stage of the tumor. HIV infected patients had a less disease-free survival compared to HIV-, 47% and 88%, respectively.
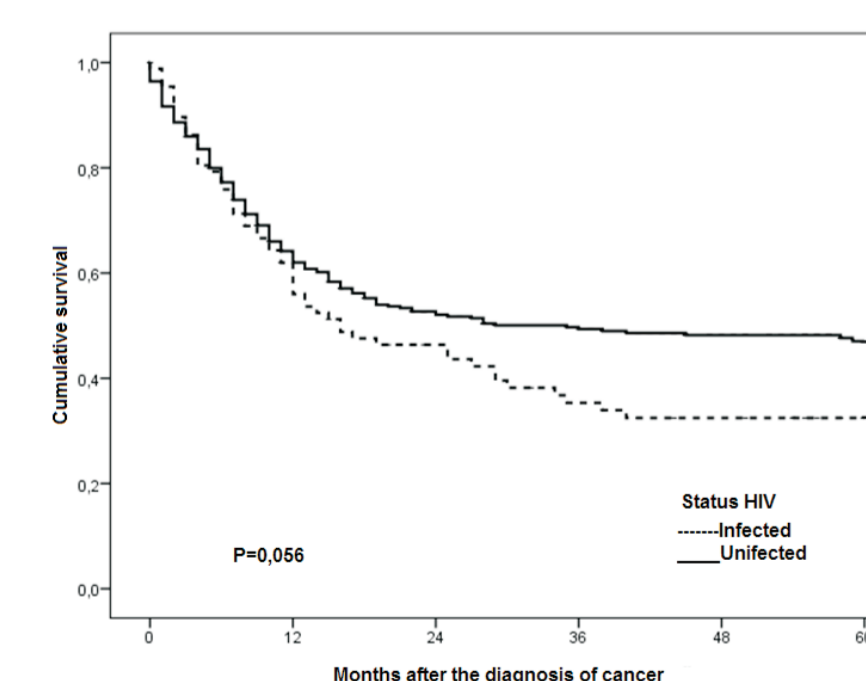

Figure 3. Kaplan-Meier analysis of overall survival between HIV-positive and HIV-negative patients.
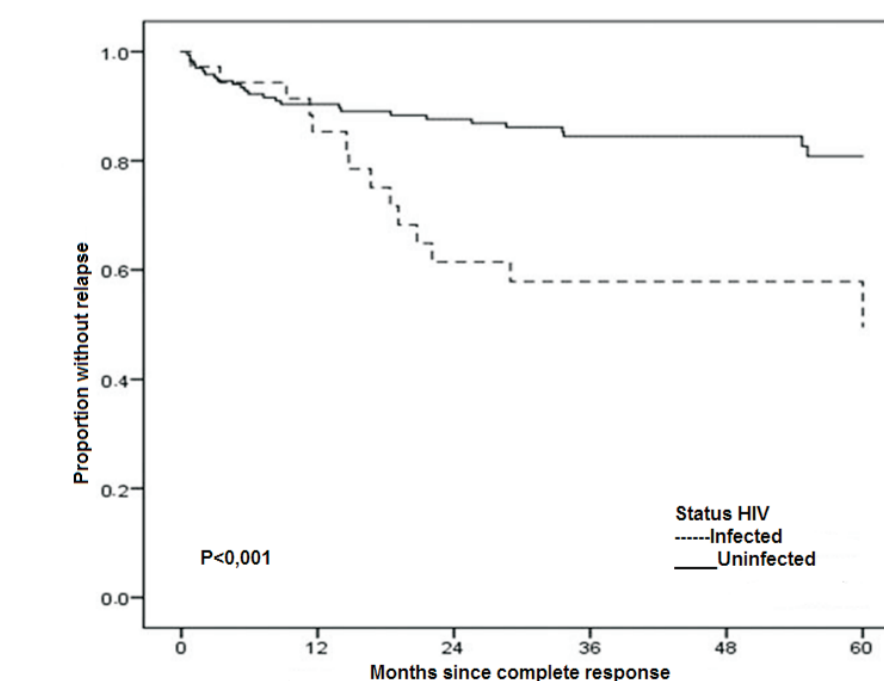

Figure 4. Kaplan-Meier analysis of disease-free survival between HIV-positive and HIV-negative patients with complete initial response to cancer therapy

CONCLUSION

Among women with cervical cancer, HIV infection was not associated with initial treatment response or early mortality, but relapse after attaining a complete response and late mortality were increased in those with HIV. These results point to a role for an intact immune system in control of residual tumor burden among treated cervical cancer patients.

Projeto Gráfico: Área de Edição e Produção de Materiais Técnico-Científicos / INCA

MINISTÉRIO DA SAÚDE