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CLINICAL ARTICLE

Gynecology

Impact of HIV infection on access to cancer care and survival among women with invasive cervical cancer in Côte d'Ivoire: A prospective cohort study

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Abstract

Objective: To assess the impact of HIV on access to invasive cervical cancer (ICC) care and overall survival (OS) in a time of universal access to antiretroviral therapy (ART).

Methods: A cohort of women prospectively diagnosed with ICC was consecutively recruited from 2018 to 2020 in public/private cancer centers in Côte d'Ivoire. Follow-up data were collected through facility- and phone-based approaches. Logistic and Cox regression models allowed analysis of factors associated with access to cancer care and OS, respectively.

Results: Overall, 294 women with ICC aged 50 years (interquartile range [IQR] 43–60) were enrolled, including 21.4% of women living with HIV (WLHIV), 87% being on ART. An advanced ICC clinical stage (III–IV) was less frequent in WLHIV (63.5% vs. 77.1% in HIV-uninfected women; $P=0.029$). Cancer care was initiated in 124 (42.2%) women (54.0% in WLHIV; 39.0% in HIV-uninfected; $P=0.030$). Factors independently associated with access to cancer care were International Federation of Gynecology and Obstetrics (FIGO) stage I–II (adjusted odds ratio [aOR] 3.58, 95% CI 2.01–6.38) and no treatment by traditional healers prior to ICC diagnosis (aOR 3.69, 95% CI 1.96–6.96). The 2-year OS was 37.9% (95% CI 30.0–47.9). HIV status was not predictive of mortality (adjusted hazard ratio [aHR] 0.98, 95% CI 0.60–1.69). An advanced clinical stage was the only measured predictor of death (aHR 1.59, 95% CI 1.02–2.47).

Conclusion: In a time of universal access to ART, HIV infection was not associated with OS among women with ICC in Côte d'Ivoire. Higher access to cancer care in WLHIV might be mediated by enhanced access to ICC screening services, supporting the need to expand these services to other types of healthcare facilities.

KEYWORDS
access to care, Côte d'Ivoire, HIV, invasive cervical cancer, overall survival

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1 | BACKGROUND

Invasive cervical cancer (ICC) is the second most common cancer and the leading cause of cancer death in women in sub-Saharan Africa.[1] In Côte d'Ivoire, in 2020, the standardized incidence was 31.2/100000 women.[1] ICC is one of the forms of cancer with the highest rates of treatment and potential for cure if detected and treated early.[2] However, access to quality care among women with ICC is a major challenge in low- and middle-income countries.[3] Significant effort to make cancer treatments available and to build practitioners' capacity in cancer surgery and radiotherapy have been made in most of these countries in recent decades.[4] National oncologists and radiotherapists were trained, and technical platforms for cancer management have been recently improved with the creation in 2018 of the first radiotherapy center in Côte d'Ivoire, which adds to the existing surgery and chemotherapy strategies.[5] Although the demand for radio-chemotherapy and surgery is increasing, their actual accessibility remains globally poorly documented.

HIV infection is a known risk factor for ICC[6,7] which has been classified as an AIDS-defined malignancy.[8] In sub-Saharan Africa where over 70% of the world's number of women living with HIV (WLHIV) are found, WHO predicts a 99% increase in ICC-related deaths by 2040.[1,9] The effect of HIV infection on access and completion of radio-chemotherapy remains poorly documented.[10] Although antiretroviral therapy (ART) is widely available, the increasing burden of non-communicable diseases, including malignancies, could mitigate the gains already achieved in survival of WLHIV.[11] The impact of HIV status on survival after ICC in sub-Saharan Africa is also poorly studied and seems conflictual. Studies conducted in eastern and southern Africa, in a context of limited access to ART, reported poorer survival among WLHIV.[12–14] In the era of universal access to ART, knowing the determinants of access to cancer care and predictors of mortality could help to direct resources more appropriately and effectively facilitate the care pathway from detection to ICC management. We investigated the impact of HIV infection on access to cancer care and overall survival (OS) among women with ICC in Côte d'Ivoire.

2 | MATERIALS AND METHODS

2.1 | Study design and population

A prospective multi-center cohort study was conducted and all women diagnosed with ICC between July 2018 and June 2020 in Abidjan, Côte d'Ivoire, were enrolled. Comprising around one-quarter of the whole national population, Abidjan is the most populated city of Côte d'Ivoire. The city concentrates major health and administrative services and represents the only referral center for many infectious and non-communicable diseases in the country. Women were consecutively recruited in public/private cancer centers of Abidjan, the unique urban area in the country providing diagnostic services and delivering cancer care during the study period. During that period, all women who presented for suspicion of ICC in the gynecology departments from the three university hospitals of Treichville, Cocody and Yopougon, the Oncology Department of the University Hospital of Treichville, as well as the only comprehensive chemotherapy and radiotherapy center in the country (Alassane Ouattara National Center of Oncology and Radiotherapy) were systematically proposed a cervical biopsy. All women with a histologically confirmed ICC were proposed to participate in the present study. In Côte d'Ivoire, all oncologists and gynecologists from the private sector are also practising in the public sector. We have therefore asked all these practitioners to refer all women diagnosed in private centers for enrolment in the study. Recruitment in the private sector was mainly from the largest private oncology center of Treichville ("Clinique COBA") and the "Groupe medical du Plateau." Women diagnosed in smaller private clinics were consecutively enrolled during their attendance at the national radiotherapy center. Full information on the study was provided to all women by the oncologists/gynecologists or research assistants in their comfortable language (French or local language). To prevent any missed ICC cases, histopathology laboratory databases were matched with women registered through the facility-based system. Women with ICC not previously identified through the facility-based approach were subsequently called by cancer registry investigators and proposed to be enrolled in the present study.

2.2 | Data collection

Data were collected by trained research staff using a combination of face-to-face interviews and patient medical record review. A 2-day training session for gynecologists, oncologists, and cancer registry investigators was performed prior to enrolments, encompassing study protocol review, validation, and administration of case report forms (CRFs); review of standard operating procedure was done using theoretical and practical training. At enrolment, demographics and economic variables including educational level, residency, professional status, monthly income, health insurance, and clinical and histopathological characteristics as well as data on HIV infection and clinical stage (International Federation of Gynecology and Obstetrics [FIGO] classification) were collected using a standardized baseline CRF. HIV status was documented using the national algorithm. A nationally approved rapid HIV test (Determine® HIV-1/2; Abbott Diagnostics) was systematically proposed to women after counseling conducted by the cancer specialist. A capillary blood sample was collected by fingerprick

test at the time of interview. A positive result indicated the collection of a venous blood sample for confirmation purposes, by enzyme-linked immunosorbent assay, at the referral laboratory (CeDReS), University Hospital of Treichville. Those who were already in HIV care were asked to provide additional information on their HIV care pathway. Their HIV follow-up data (date of first HIV diagnosis, ART use, last known CD4 count, and last known HIV viral load measure) were subsequently extracted from their HIV medical record. Of note, HIV status did not impact the ICC care pathway, ICC treatment protocol being standardized across all facilities regardless of HIV status.

A mixed approach was used to collect follow-up data from participants during their routine medical visits ("facility-based approach") and through regular phone calls ("phone-based approach"). A standardized follow-up CRF was completed by research investigators at each patient visit to the participating facility. Data on the purpose of the follow-up visit (scheduled follow-up/treatment, complications management), clinical assessment, nature of administered treatment, and inter-cure toxicity were monitored by oncologists/gynecologists. In addition, all enrolled women and/or their relatives were traced through phone calls every 3 months to collect additional post-ICC-diagnosis data, especially information on access to care and vital status. In the event of death, close relatives were asked to provide information on the date of death (which appears on the death certificate or from a landmark date in the calendar). Before classifying women as lost to follow-up, their close relatives were contacted using contact information (phone number essentially) shared with investigators at enrolment. For practical reasons, we were not able to ensure a systematic follow-up for women who did not receive cancer treatment within our research project. Indeed, most women who did not receive treatment left the care system early and were mostly unreachable during phone call tracing.

2.3 | Outcome definition

"Access to cancer care" was defined as the initiation of a prescribed cancer treatment, comprising the three pillars of cervical cancer care: surgery, external beam radiotherapy, and chemotherapy administered alone or in combination with radiation (concurrent chemo-radiation therapy [CCRT]), whether as palliative or curative intent. Comprehensive staff meeting with oncologists, gynecologists and other specialists ensured low diversity in treatment pathways among the women enrolled, irrespective of HIV status.

Overall survival was computed from the day of cervical biopsy or cervical surgical piece collection until death from any cause (event), or until the date of the latest news, in women who have initiated cancer care. Patients still alive on December 20, 2021 or lost to follow-up were right-censored. Loss to follow-up was defined as patients who did not come to their treatment center for at least 3 months and who did not respond to phone calls after a fortnightly follow-up of 3 months. The OS probability at 12 and 24 months and their 95% confidence intervals (95% CIs) were computed.

2.4 | Statistical analysis

Prior to data analysis, missing data were completed using patient medical records or histopathological reports, and interviews with women who were still alive or their relatives in case of death, conducted by oncologist/gynecologists. Categorical variables were described as proportions and continuous variables as medians and their interquartile ranges (IQRs). Comparisons were made using Pearson χ^2 test or Fisher exact test when appropriate for categorical variables, and Student *t*-test or Wilcoxon rank-sum test for continuous variables. Kaplan–Meier estimator was used to compute time to cancer care initiation following the ICC diagnosis. A logistic regression model following a stepwise-descending procedure was performed to determine factors associated with access to cancer care. Odds ratio (OR) and 95% CI were calculated for the crude and adjusted models. All variables with a *P*-value less than 0.25 were initially entered into the adjusted model. The Hosmer–Lemeshow test was performed to assess the overall fit of the final model. For predictors of OS, the log-linearity hypothesis was systematically verified for quantitative variables. Variables that had a plausible linear effect were included in the model in categorical form (using empirical quartiles or thresholds previously reported in the literature). The OS was estimated using the Kaplan–Meier estimator. The survival curves were compared using the log-rank test or the Gehan–Wilcoxon test when appropriate at the threshold $\alpha = 5\%$. Factors associated with the instantaneous risk of death were assessed through unadjusted and adjusted Cox proportional hazards regression models. Results were displayed as hazard ratio (HR) with 95% CI. The proportionality of the instantaneous HR hypothesis was checked through Schönefeld residuals. HIV status was forced into the models. Variables with *P* less than 5% were considered statistically significant. Analyses were conducted using R studio 4.0.4 software.

2.5 | Ethical consideration

This research has been performed in accordance with the Declaration of Helsinki. The National Ethics Committee of Côte d'Ivoire approved this study (no. 041-18/MSHP/CNESVS-kp). All enrolled women provided informed and written consent. Participants were able to withdraw their consent at any time during follow-up.

3 | RESULTS

3.1 | General characteristics

During the study period, 353 ICC cases were recorded through both a facility-based approach (272 cases) and histopathological laboratory databases (81 cases). We were not able to link to cancer care facility for 56 (15.9%) women after their biopsy, as they were living a long way from Abidjan. In total, 297 (84.1%) women

diagnosed with ICC were surveyed. Three (1%) were subsequently excluded after withdrawal of consent during the tumor extension assessment stage.

The remaining 294 women had a median age of 52 years (IQR 43.0–60.0), including 46 (IQR 40.5–51.0) years among WLHIV and 54 (IQR 44.5–62.0) years among HIV-uninfected women ($P < 0.001$). Regarding their economic status, 105 (35.7%) had no formal income and 171 (58.2%) received less than US$268 monthly (Table 1). Eighteen (6.1%) women reported having health insurance. Regarding HIV status, 63 (21.4%) were WLHIV, including 55 (87%) on ART prior to ICC diagnosis and eight (13%) newly diagnosed for HIV at ICC diagnosis. Among those who were aware of their HIV status, the median time since ART initiation was 4 (IQR 1–10) years; CD4 counts at HIV diagnosis and last known measure were 372 cells/μL (IQR 194–510) and 492 cells/μL (IQR 378–750), respectively.

A diagnosis of ICC was done according to symptoms in 280 (95.2%) women, and through systematic screening in 14 (4.8%) women, the latter being more frequent in WLHIV (15.9%) than in HIV-uninfected women (1.7%) ($P < 0.001$). At ICC diagnosis, a FIGO stage III–IV was retrieved in 218 (74.1%) women, but this was less common in WLHIV than in HIV-uninfected women (63.5% vs. 77.1%, $P = 0.029$). Squamous cell carcinoma was identified in 259 (88.1%) ICC patients (Table 2).

TABLE 1 Demographic, economic, socio-behavioral, and reproductive health characteristics among women with invasive cervical cancer (ICC) according to HIV status in Abidjan, Côte d'Ivoire, from 2018 to 2020 ($N = 294$).

	Total ($N = 294$)		HIV-uninfected ($N = 231$)		HIV-infected ($N = 63$)		*P*-value
Characteristics	***n***	**(%)**	***n***	**(%)**	***n***	**(%)**	
Age at ICC diagnosis (year) (median [IQR])	52.0 (43.0–60.0)		54.0 (44.5–62.0)		46 (40.5–51.0)		<0.001
25–45	86	(29.3)	58	(25.1)	28	(44.4)	0.002
45–60	129	(43.9)	102	(44.2)	27	(42.9)	
60–91	79	(26.9)	71	(30.7)	8	(12.7)	
Place of residence							
Rural/semi-urban	235	(79.9)	181	(78.4)	54	(85.7)	0.196
Urban	59	(20.1)	50	(21.6)	9	(14.3)	
Educational level							
No formal education	143	(48.6)	118	(51.0)	25	(39.7)	0.387
Primary level	88	(29.9)	66	(28.6)	22	(34.9)	
Secondary level	55	(18.7)	42	(18.2)	13	(20.6)	
University	8	(2.7)	5	(2.2)	3	(4.8)	
Professional status							
Employed	140	(47.6)	105	(45.5)	35	(55.6)	0.360
Unemployed	131	(44.6)	108	(46.7)	23	(36.5)	
Retired	23	(7.8)	18	(7.8)	5	(7.9)	
Monthly income (USD[a])							
No resource	105	(35.7)	86	(37.2)	19	(30.2)	0.321
<268	171	(58.2)	133	(57.6)	38	(60.3)	
≥268	18	(6.1)	12	(5.2)	6	(9.5)	
Health insurance coverage (yes)	18	(6.1)	14	(6.1)	4	(6.3)	0.933
Parity (median [IQR])	5 (3–7)		6 (3–7)		3 (2–5)		<0.001
<5	125	(42.5)	82	(35.5)	43	(68.3)	
≥5	169	(57.5)	149	(64.5)	20	(31.7)	
History of using contraceptives[b] (yes)	44	(15.0)	35	(15.2)	9	(14.3)	0.864
Tobacco use							
No use	255	(86.7)	197	(85.3)	58	(92.1)	0.160
Current or former use	39	(13.3)	34	(14.7)	5	(7.9)	

Abbreviation: IQR, interquartile range.

[a]1 USD = 0.0018 FCFA (exchange rate at August 20, 2021).

[b]Oral or injectable contraceptives, or implants or intrauterine device.

TABLE 2 Clinical, histological, and pre-diagnosis care characteristics according to HIV status among women with invasive cervical cancer (ICC) in Abidjan, Côte d'Ivoire, from 2018 to 2020 ($N = 294$).

	Total ($N = 294$)		HIV-uninfected ($N = 231$)		HIV-infected ($N = 63$)		*P*-value
Characteristics	***n***	**(%)**	***n***	**(%)**	***n***	**(%)**	
BMI	22.3 (19.8–25.7)		23.1 (20–26)		20.8 (19.1–35.5)		0.012
WHO performance status							
0–2	273	(78.6)	218	(94.4)	55	(87.3)	0.053
3–4	21	(7.1)	13	(5.6)	8	(12.7)	
How ICC was discovered							
Through ICC symptoms	280	(95.2)	227	(98.3)	53	(84.1)	<0.001
Through regular screening	14	(4.8)	4	(1.7)	10	(15.9)	
Symptoms of ICC							
Vaginal discharge[a]	268	(91.2)	215	(93.1)	53	(84.1)	0.028
Pelvic pain	186	(63.3)	151	(65.4)	35	(55.6)	0.178
Weight loss	145	(49.3)	107	(46.3)	38	(60.3)	0.120
Leucorrhea	113	(38.4)	90	(39.0)	23	(36.5)	0.682
Primary health facility							
Primary or secondary level	197	(67.0)	165	(71.4)	32	(50.7)	0.002
Tertiary health level	46	(15.7)	35	(15.2)	11	(17.5)	
NGOs or Private health facilities	51	(17.3)	31	(13.4)	20	(31.7)	
Pre-diagnosis delay[b] (median [IQR])	150 (60–270)		150 (60–300)		90 (15–255)		0.061
≤30 days	71	(24.1)	48	(20.8)	23	(36.5)	0.010
>30 days	223	(75.9)	183	(79.2)	40	(63.5)	
Patient delay[c] (median [IQR])	88.5 (25–244.8)		82 (22–239.5)		90 (31.5–282)		0.423
≤15 days	85	(28.9)	69	(29.1)	16	(25.4)	
>15 days	209	(71.1)	162	(70.1)	47	(74.6)	
Primary care interval[d] (median [IQR])	40	(0–153)	45	(0–150)	21	(0–177)	0.542
≤40 days	149	(50.7)	90	(39.0)	27	(42.9)	
>40 days	145	(49.3)	141	(61.0)	36	(57.1)	
ICC histologic type							
Squamous cell carcinoma	259	(88.1)	202	(87.4)	57	(90.5)	0.510
Adenocarcinoma/sarcoma/other[e]	35	(11.9)	29	(12.6)	29	(9.5)	
FIGO stage							
I–II	76	(25.9)	53	(22.9)	23	(36.5)	0.029
III–IV	218	(74.1)	178	(77.1)	40	(63.5)	
Access to traditional healer prior to ICC diagnosis							
Yes	79	(26.9)	63	(27.3)	16	(25.4)	0.766
No	215	(73.1)	168	(72.7)	47	(74.6)	

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).

[a]Spontaneous hemorrhage from cervix, outside menstruation.

[b]Time between first symptom recognition and first attendance at health facility.

[c]Time between first attendance at the referral center and cervical biopsy.

[d]Including non-specific carcinoma.

[e]Time between first attendance and first visit to the health specialist (gynecologist or oncologist).

3.2 | Access to cancer care and associated factors

Of the 297 women, 294 (99.0%) considered accessing cancer care, of whom 124 (42.2%) effectively initiated it. Reasons for no access to care were lack of economic resources for 150 (91.2%), refusal of care with no further explanation for 9 (5.3%), and hemodynamic instability at the time of cancer diagnosis with death soon thereafter for 6 (3.5%).

Cancer treatment initiation was retrieved in 34 (54.0%) WLHIV and in 90 (39.0%) HIV-uninfected women ($P=0.030$). The overall treatment completion rate was 65.3%, with rates of 76.4% for WLHIV and 61.1% for HIV-uninfected women ($P=0.050$). Cancer treatment included 18 (14.5%) women undergoing hysterectomy, 31 (25.0%) having chemotherapy alone and 75 (60.5%) having CCRT. The median time to treatment initiation was 8.7 months (IQR 4.43–14.10). Times to initiation of chemotherapy, surgery, and CCRT were 5.80, 13, and 8.50 months, respectively (Figure 1).

No significant difference between the income levels and treatment initiation was found ($P=0.122$). In multivariate analysis, factors associated with access to cancer care were FIGO stage I–II (adjusted odds ratio [aOR] 3.58, 95% CI 2.01–6.38) and no treatment by traditional healers prior to ICC (aOR 3.69, 95% CI 1.96–6.96) (Table 3).

3.3 | Overall survival

Of the 124 women who were followed up for a median time of 18.7 (IQR 11.8–27.5) months, 86 (69.4%) experienced death from any cause, including 22 WLHIV and 64 HIV-uninfected women. The 24-month OS rates in WLHIV (37.7%, 95% CI 28.7–49.6) and HIV-uninfected women (38.4%, 95% CI 24.6–60.0) were not significantly different ($P=0.231$) (Figure 2). In crude analysis, OS was influenced by treatment modalities (38.9%, 76.6%, and 28.1% for chemotherapy alone, hysterectomy, and CCRT, respectively [$P=0.003$]) and FIGO stage (46.6% and 31.5% for stages I–II and III–IV, respectively [$P=0.041$]). In univariate analysis, FIGO stage (III–IV vs. I–II), treatment modalities (chemotherapy and CCRT vs. surgery) and treatment completion were associated with risk of mortality. In adjusted analysis, HIV status was not predictive of OS (aHR 0.98, 95% CI 0.60–1.69) and FIGO stage III–IV was only predictive of death (aHR 1.59, 95% CI: 1.02–2.47) (Table 4).

4 | DISCUSSION

While women diagnosed with ICC in Côte d'Ivoire are facing major financial barriers and delays in accessing cancer care, a higher access

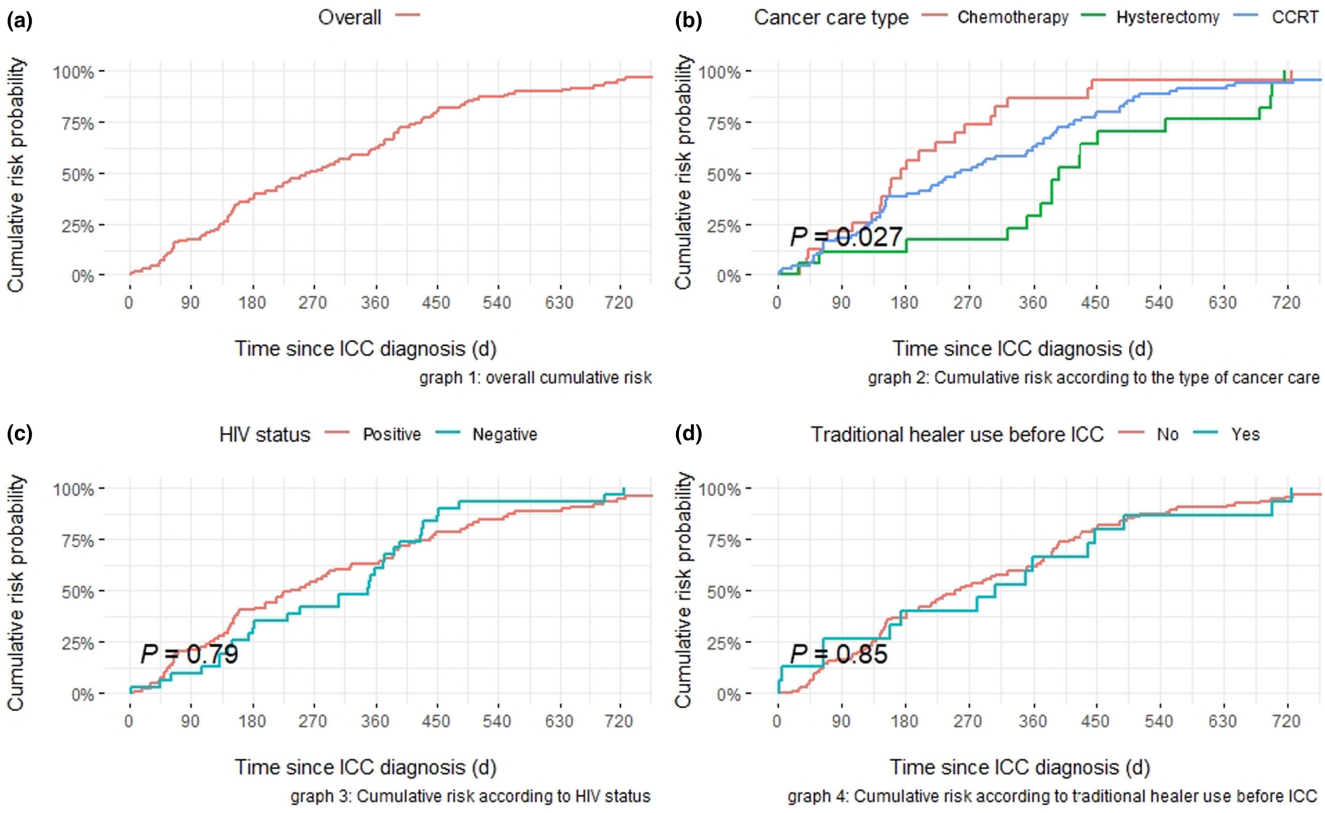

FIGURE 1 Time to cancer care initiation among women with invasive cervical cancer (ICC) in Abidjan, Côte d'Ivoire, from 2018 to 2020 ($N=110$). (a) Overall cumulative risk; (b) cumulative risk according to type of cancer care; (c) cumulative risk according to HIV status; (d) cumulative risk according to treatment by traditional healer prior to ICC. CCRT, concurrent chemo-radiation therapy. *, date of cancer care initiation was not clearly specified for 14 women; these 14 women were successfully contacted by telephone, the specific anti-cancer treatment was done but the date of initiation was not confirmed, as the medical record was not found in the care unit.

TABLE 3 Factors associated with access to cancer care among women with invasive cervical cancer (ICC) in Abidjan, Côte d'Ivoire, from 2018 to 2020 ($N = 294$).

	Access to cancer care (yes)		Univariate analysis			Multivariate analysis (final model)		
Characteristics	***N*** [a]	***n* (%)** [a]	**OR**	**95% CI**	***P***	**aOR**	**95% CI**	***P***
HIV status								
Uninfected	231	90 (39.0)	1			1		
Infected	63	34 (54.0)	1.84	(1.05–3.22)	0.030	1.65	(0.89–3.05)	0.112
Age at ICC diagnosis (year)								
60–91	79	26 (32.9)	1		0.092			
45–60	129	55 (42.6)	1.52	(0.82–2.74)				
25–45	86	43 (50.0)	2.0	(1.0–3.81)				
Monthly income (USD[b])								
No resource	105	36 (34.3)	1		0.122			
<268	171	80 (46.8)	1.68	(1.02–2.78)				
≥268	18	8 (44.4)	1.53	(0.56–4.22)				
Place of residence								
Rural/semi-urban	235	95 (40.4)	1					
Urban	59	29 (49.2)	1.42	(0.80–2.53)	0.231			
Parity								
≥5	169	64 (37.9)	1					
<5	125	60 (48.0)	1.46	(0.92–2.44)	0.079			
FIGO stage at presentation								
III–IV	218	73 (33.5)	1			1		
I–II	76	51 (67.1)	4.10	(2.30–7.10)	<0.001	3.58	(2.01–6.38)	<0.001
Use of a traditional healer before the ICC diagnosis								
Yes	107	33 (30.8)	1			1		
No	187	95 (50.8)	4.01	(2.22–7.34)	<0.001	3.69	(1.96–6.96)	<0.001

[a]*N*, number in each category; *n* (%), number and percentage of access to cancer care per group for a given variable.

[b]1 USD = 0.0018 FCFA (exchange rate at August 20, 2021).

to care was reported in WLHIV. After adjusting to HIV status, access to cancer care was associated with early diagnosis and no treatment by traditional healers prior to diagnosis. Mortality was mainly predicted by a late (II–IV) FIGO staging and HIV status did not impact OS in our present analysis.

In sub-Saharan Africa, recent publications tend to report higher access to cancer care in recent years, with up to 80% of diagnosed patients compared with less than 20% in prior reports before 2010.[15,16] Access to cancer care was higher among WLHIV, but there was no effect of HIV status after adjusting for socioeconomic and diagnostic factors. Higher access to ICC care was reported in WLHIV in Botswana and Uganda.[12,16] In a general context of poverty and limited access to education, HIV infection itself cannot significantly impact access to cancer care, especially as there is not yet a support mechanism for the ICC management apart from rare research projects in Côte d'Ivoire. One hypothesis would rely on an enhanced access to ICC screening in WLHIV resulting in lower advanced disease at ICC diagnosis, leading to more curative treatment. Aside from economic considerations, most WLHIV were already receiving HIV care in comprehensive health services and were therefore more accustomed to accessing healthcare than women from the general population, who might be less used to accessing healthcare for other conditions.[17] The scattering of cancer care centers in Abidjan, with varying availability of diagnostic capacity and therapeutic options, results in long delays in initiating treatment and a high risk of being lost to care. This could also partly explain the suboptimal rate of completeness of CCRT in our cohort (66.7%), corroborated by previous studies.[18,19] However, the relatively high rate of treatment completion among WLHIV found in our cohort is at odds with the low completeness reported in South Africa.[18,20] WLHIV have a higher awareness of ICC and this is reflected in their journey in seeking prediagnostic and therapeutic care. They are more likely to use testing services, and to seek and remain in care, probably also due to follow-up by community counselors supported by implementing partners.[17] Promoting the early detection of ICC should be supported by a policy to ease access to healthcare services through universal health coverage. Further studies should be done to measure progress toward the last 90% WHO cervical cancer elimination target, by evaluating the effect of social and flexibility measures (i.e., delaying radiation and oncology care fees, staggering payment overtime).

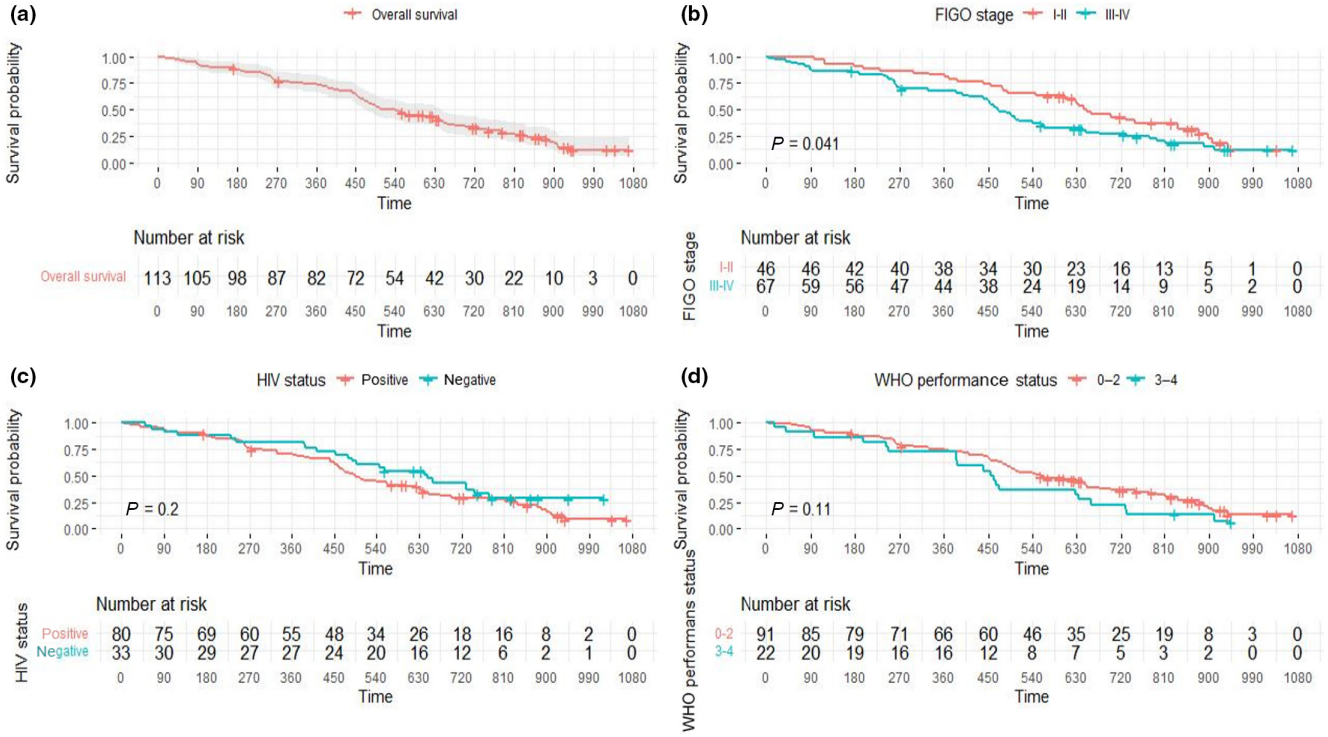

FIGURE 2 Overall survival according to HIV status, FIGO stage, and WHO performance status at invasive cervical cancer (ICC) diagnosis among women in Côte d'Ivoire.

The literature reports conflicting results with regard to the impact of HIV infection on the risk of death after an ICC diagnosis. Indeed, some studies mainly conducted prior to the universal treatment era reported a 1.5- to 2-fold higher effect in WLHIV.[14,18] Our findings were consistent with those reported from Uganda and Botswana,[16,21] as well as a recent systematic review that found no significant effect of HIV on survival after an ICC diagnosis.[10] The implementation of the universal access to ART approach as early as possible has improved the prognosis of HIV infection and the life expectancy of WLHIV.[11] In addition, ART may have a positive effect on prognosis in WLHIV receiving cancer treatment.[22] WLHIV also have access to better follow-up for their health, which, far from being holistic, includes psychosocial support in certain HIV clinics, as recommended by national HIV care guidelines in Côte d'Ivoire.[23] ICC screening uptake by nearly 60% of WLHIV in Abidjan demonstrates its appropriation by WLHIV and healthcare workers in HIV clinics.[24] This high participation in the cervical screening program has probably led to early-stage ICC detection which is already known as a predictive factor for OS.[21,25] The lack of a significant difference in OS rates reported in our study could be explained by the residual gap in life expectancy between WLHIV and the general population as well as the early onset of comorbidities, and aging-related diseases faced by WLHIV. Overall, a long delay in starting cancer treatment (including radical hysterectomy) as well as the poor completion rate are major barriers to survival that should be addressed. Further studies should assess innovative interventions to reduce delays in access to care as well as support mechanisms to enhance treatment initiation and completion.

The present study is among one of the first conducted in West Africa that prospectively investigate the effect of HIV on ICC outcomes in the context of universal access to ART. However, our study has some limitations. The studied population only reflects women with ICC who effectively accessed the healthcare system. An undocumented but surely significant number of women presenting with ICC have never been identified, especially when living in rural/semi-urban settings far from the economic capital of the country. The small number of women included in the survival analysis limits our ability to conclude that HIV infection has no impact on OS. The low survival rate reported after 24 months of follow-up limited the relevance of a longer follow-up (3- or 5-year OS), usually reported in the literature. Beyond the HIV infection issue, this study provides a comprehensive overview of outcomes and challenges facing women in low- and middle-income countries in seeking care after an ICC diagnosis. The findings are, in light of the availability of care at the national level, generalizable to all women in Côte d'Ivoire and could serve as a reference for West African decision-makers who are opening or planning to open cancer centers. Additional qualitative research will help researchers to understand better the interplay between HIV infection and treatment-seeking and mortality after an ICC diagnosis in sub-Saharan Africa.

5 | CONCLUSION

In a period of increased access to ART, OS does not appear to be significantly impacted by HIV infection among women with ICC in

TABLE 4 Predictors of mortality among women with invasive cervical carcinoma (ICC) in Abidjan, Côte d'Ivoire, 2018–2020 ($N = 124$).

	Unadjusted analysis				Adjusted analysis[a]		
Characteristics	***n/N*[b]**	**HR**	**95% CI**	***P***	**aHR**	**95% CI**	***P***
HIV status				0.612			
Uninfected	64/90	1			1		0.977
Infected	22/34	0.88	(0.54–1.43)		0.98	(0.60–1.69)	
Age at ICC diagnosis (y)				0.245			0.181
<40	19/25	1			1		
41–60	47/74	0.69	(0.41–1.18)		0.63	(0.37–1.08)	
60–85	20/25	1.0	(0.53–1.88)		0.90	(0.47–1.71)	
Place of residence				0.383			
Rural/semi-urban	65/95	1					
Urban	21/29	1.30	(0.8–2.0)				
ICC histological figure				0.098			
Adenocarcinoma and others	7/16	1					
Squamous carcinoma	79/108	1.92	(0.89–4.16)				
FIGO stage				0.045			0.036
I–II	33/51	1					
III–IV	53/73	1.50	(1.01–2.32)		1.59	(1.02–2.47)	
Time from symptoms to ICC diagnosis				0.201			0.217
≤30 days	16/28	1			1		
>30 days	70/96	1.41	(0.82–2.43)		1.41	(0.80–2.49)	

Note: Proportionality of the instantaneous hazard ratios hypothesis was checked by the Schönefeld residuals, $P = 0.2$.

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio.

[a]Only adjusted variables are presented.

[b]*n/N*, number of deceased women/number of women diagnosed with ICC for a given variable category.

Côte d'Ivoire. Higher access to cancer care among WLHIV might be mediated by enhanced access to ICC screening services through HIV clinics, supporting the need to expand access to ICC screening services across other healthcare facilities. The reported barriers in access to cancer care and the gap in OS highlight the need to improve specific cancer therapy availability and the ability to pay for it in West Africa. Implementing comprehensive strategies involving conventional health professionals and traditional healers is also critical in the context of eliminating cervical cancer as a public health problem by 2030.

AUTHOR CONTRIBUTIONS

Antoine Jaquet designed the study, which was planned by Simon P. Boni, Innocent Adoubi, François Dabis, Apollinaire Horo, and Boris K. Tchounga. Data were collected under the supervision of Innocent Adoubi, Apollinaire Horo, Jean-Claude Comoe, Judith Didi-Kouko-Coulibaly, Aristophane Tanon, Raoul D. Moh, Patrick A. Coffie, and Boris K. Tchounga. Analysis and first interpretation were done by Simon P. Boni, who wrote the first draft of the manuscript. All the authors revised the manuscript for the final version, which was written by Simon P. Boni and Antoine Jaquet.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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