Gynecologic Oncology 151 (2018) 215–220

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Five-year overall survival following chemoradiation among HIV-positive and HIV-negative patients with locally advanced cervical carcinoma in a South African cohort

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HIGHLIGHTS

- HIV-positive patients with locally-advanced cervical carcinoma were less likely to complete chemoradiation.
- Outcomes showed comparatively lower 5-year overall survival in HIV-positive patients.
- Total dose of radiation was not found to affect overall survival.
- Factors linked to poor outcomes included HIV status and inability to receive chemotherapy

ARTICLE INFO

Article history:
Received 15 July 2018
Received in revised form 21 August 2018
Accepted 27 August 2018
Available online 5 September 2018

Keywords:
Cervical cancer
HIV
Chemoradiation
Radiotherapy
Survival

ABSTRACT

Objectives. In South Africa, where HIV prevalence among adults is 18.9%, cervical carcinoma is the second most common malignancy in women. However, oncology services are considerably more accessible in South Africa than in many neighbouring countries.
This study reports five-year overall survival in a cohort of HIV-positive and -negative cervix carcinoma patients undergoing primary radiotherapy at a single institution in South Africa.

Methods. Prospective cohort study of all locally advanced cervix carcinoma patients referred for radiotherapy (EBRT) from July 2007 to November 2011. Overall survival (OS) was the primary end-point.

Results. A total of 492 patients commenced treatment with radical intent, including 71 HIV-positive patients (14.4%) and 421 HIV-negative patients (85.6%). Of the 433 who were prescribed standard fractionation EBRT, 384 were prescribed concurrent platinum-based chemotherapy (88.7%). Fewer HIV-positive than HIV-negative patients (58.5% *vs.* 76.1%; $p = 0.007$) completed ≥4 cycles. The OS of HIV-negative patients was 49.5% (95%CI; 44.6%–54.4%) at 5 years. The OS of HIV-positive patients was significantly lower, 35.9% (95% CI; 23.9%–48.0%) at 5 years ($p = 0.002$). In our Cox models, factors affecting outcome were HIV infection, stage IIIB disease, presence of hydronephrosis, and delivery of concurrent chemotherapy.

Conclusion. In our large cohort, HIV-positive patients had poorer survival than HIV-negative patients, however nearly 40% survived 5 years, justifying provision of the best standard of care to HIV-positive patients with cervical carcinoma.

1. Introduction

Cervical carcinoma is the second most common malignancy among women in South Africa; the overall age-standardised incidence rate (ASR) is 22.06/100,000, and among black women it is 25.90/100,000 [1]. Rates are similar in most sub-Saharan African countries and other low- or middle-income countries (LMICs), but no high-income country (HIC) has an ASR above 10/100,000. The LMICs also have higher cervical carcinoma mortality rates, due in part to inadequate healthcare.

Infection with the human papilloma virus (HPV), which causes cervical carcinoma, is highly prevalent in sub-Saharan Africa, and human

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https://doi.org/10.1016/j.ygyno.2018.08.038
0090-8258/

immunodeficiency virus infection (HIV) is also highly prevalent [2]. Women with HIV and HPV infections are more likely than women with HPV alone to develop persistent HPV infections, high grade cervical intra-epithelial lesions, and ultimately cancer [3].

Since 2004, national guidelines regarding antiretroviral therapy (ART) for HIV have been available in South Africa [4]. Until 2011, only those patients with a CD4 < 200 cells/μl or WHO stage 4 were eligible for ART, but current local guidelines now support commencement of cART at a CD4 cell count <500 cells/μl [5]. In 2014, South Africa introduced a school-based national HPV vaccination program for girls aged 9–10 years [6]. However, this program has yet to influence the prevalence of HPV in the South African population at risk for cervical cancer.

Unlike many of its neighbors, South Africa is an upper middle-income country with large academic medical centres that can provide cervical cancer treatment on a par with the best practice in many HIC facilities. South Africa's public tertiary care hospitals have multidisciplinary gynaecological oncology units and can offer LINAC (linear accelerator) based 3-dimensional radiotherapy, high-dose rate brachytherapy, and chemotherapy agents.

The management of cervical cancer in HIV-positive women has, thus far, been based on best practice for HIV-negative women, while seeking to optimize combination antiretroviral therapy (cART) so as to maintain adequate CD4 counts and to suppress the viral load [7]. Little is known about the long-term survival of patients with cervical cancer and HIV [8–10].

We therefore analyzed overall five-year survival in a prospective cohort of HIV-positive and -negative cervix carcinoma patients undergoing radiotherapy, from a single institution in South Africa providing access to high quality oncology services.

2. Methods

2.1. Patient records

For this prospective cohort study, we collected a patient registry for all cervix carcinoma patients attending for primary radiotherapy during the time period July 2007 to November 2011 in the Division of Radiation Oncology, Tygerberg Hospital. Patients were entered into the registry at the start of treatment. The patients included in this analysis had stage IB1 to stage IIIB cancers and commenced external beam radiotherapy (EBRT) prescribed to a minimum of 40 Gray (Gy) with radical intent. Patients who were excluded from the analysis were those who did not start radiotherapy as planned and those who had undergone a hysterectomy, or had radical surgery for cervical cancer.

Ethical approval was obtained from the University of Stellenbosch Human Research Ethics Committee and Tygerberg Academic Hospital.

Data collected included demographic and clinical characteristics of the patients. For HIV-positive patients, we determined whether they had commenced cART before, or during, treatment of cervix cancer, and we recorded their initial CD4 cell count. During the time period of this study, viral load was not routinely tested in the oncology clinic. Cervical cancer treatment details, including EBRT dose, high-dose-rate (HDR) brachytherapy dose, and chemotherapy cycles, were documented. The total doses of EBRT and HDR brachytherapy were calculated using equivalent dose in 2Gy fraction (EQD_2) formulas [11].

2.2. Treatment

At our institution, patients with cervix carcinoma are routinely tested for HIV during diagnostic work-up. Many patients were diagnosed as HIV-positive incidentally during their work-up for suspected cervix carcinoma. Patients who tested HIV-positive started receiving cART either just before, or as soon as possible after commencing radiation treatment. At the time of the study, cART included triple therapy with lamivudine, efavirenz, and tenofovir, unless the creatinine clearance was low, in which case the patient received stavudine instead of tenofovir. Every HIV-positive patient commencing radiation or chemoradiation received concurrent cotrimoxazole prophylaxis. Because many patients receive their routine HIV care in local clinics, we have limited access to information on their adherence to cART therapy.

Diagnostic work-up included laboratory investigations, chest X-ray and abdominal ultrasound. In our institution, PET-CT was not available for the assessment of nodal and distant metastases until 2012. In addition, the evaluation of nodal cancer is challenging because HIV-positive patients often have reactive nodes.

Patients with IB1 cancers who were not fit for surgery or locally advanced IB2-IIIB disease received 45 to 52.5 Gy external beam radiation (EBRT) in 23 to 28 fractions, 1.8–2 Gy per fraction. Patients with anaemia and hydronephrosis were included if they were medically fit and had adequate renal function. During the study period, the lower dose per fraction was prescribed for HIV-positive patients or patients with previous abdominal surgery, due to theoretical concerns regarding gastrointestinal toxicities. Due to pressure on the radiotherapy waiting list, some patients with stage IIIB disease, including the elderly and those with severe medical co-morbidities, poor performance status, or poor renal function, received a hypofractionated regimen of 40.05 Gy in 15 fractions, or 42.72 Gy in 16 fractions, and no chemotherapy.

Table 1
Demographic and clinical characteristics of patients with cervical carcinoma, by HIV status.

Variable	HIV-negative	HIV-positive	Total	p-Value
	n = 421 (85.6%)	n = 71 (14.4%)	n = 492	
Median age years (interquartile range)	50 (43–58)	40 (35–49)	49 (41–57)	0.001*
Age groups				
39 years or less	65 (15.4%)	33 (46.5%)	98 (19.9%)	<0.001*
40–59 years	266 (63.2%)	37 (52.1%)	303 (61.6%)	
60 years or more	90 (21.4%)	1 (1.4%)	91 (18.5%)	
Histology				
Squamous cell carcinoma	391 (92.9%)	67 (94.4%)	458 (93.1%)	0.65
Adenocarcinoma	15 (3.6%)	2 (2.8%)	17 (3.5%)	
Other	15 (3.6%)	2 (2.8%)	17 (3.5%)	
Stage				
Stage IB1-IIA	12 (2.9)	0	12 (2.4%)	
IIB	120 (28.5%)	15 (21.1%)	135 (27.4%)	
IIIA	3 (0.7%)	0	3 (0.7%)	
IIIB	286 (67.9%)	56 (78.9%)	342 (69.5%)	0.06
Hydronephrosis present (stage IIIB)	58 (20.3%)	14 (25.0%)	72 (21.1%)	0.43
Node positive (ultrasound)	67 (15.9%)	14 (19.7%)	81 (16.5%)	0.42

* $p < 0.05$ regarded as significant.

Table 2
Treatment characteristics by HIV status.

Variable	HIV-negative	HIV-positive	Total	p-Value
	n = 421	n = 71	n = 492	
Standard fractionation	369 (87.6%)	64 (90.1%)	433 (88.0%)	0.55
Hypofractionation	52 (12.4%)	7 (9.9%)	59 (12.0%)	
Median EQD2 Gy (interquartile range)	77.7 Gy (75.0–80.8)	76.3 Gy (69.3–81.5)	77.7 Gy (75.0–80.9)	0.94
≥69.25 Gy EQD_2 total dose	356 (84.6%)	54 (74.1%)	410 (83.3%)	0.08
≥20 Gy HDR[a]	333 (90.3%)	51 (79.7%)	384 (88.5%)	0.02*
Chemo 4 or more cycles[b]	252 (76.1%)	31 (58.5%)	283 (73.7%)	0.007*
1–3 cycles	79 (23.9%)	22 (41.5%)	101 (26.4%)	
Transfusion given[c]	173 (42.3%)	45 (66.2%)	218 (45.7%)	<0.001*

[a] If prescribed 1.8–2 Gy per fraction (n = 433).
[b] If prescribed 1.8–2 Gy per fraction and chemotherapy (n = 384).
[c] Missing data 15 patients.
* $p < 0.05$ significant.

Full treatment details have been described in our previous paper [12]. We used conformal 3-dimensional planning and a 6–18 MV (megavoltage) energy, 4-field arrangement. We then delivered 20 to 26 Gy Ir^{193} HDR intracavitary brachytherapy in 4 to 5 fractions. During the time period of this study, no image-guided brachytherapy was available. The absolute minimum total dose considered adequate for the purpose of this study was 69.25 Gy EQD_2 (45 Gy EBRT and 20 Gy in 4 fractions HDR brachytherapy). After 2009, we increased the brachytherapy dose to 25Gy in 5 fractions in keeping with international recommendations that total dose EQD_2 should be >80 Gy [13] (Higher doses per fraction are not suitable for the straight source HDR technique). Treatment is scheduled to be completed within 55 days.

Most patients also received cisplatin 40 mg/m^2 weekly, but if their calculated glomerular filtration rate or ethylenediaminetetraacetic acid (EDTA) glomerular filtration rate was <50 ml/min, they received carboplatin area-under-the-curve 2 (AUC2) weekly. We did not modify the dose for patients with a low CD4 cell count unless it fell below 200, in which case chemotherapy was omitted. Patients whose haemaglobin (Hb) fell below 10 g/dl received a red cell concentrate transfusion (resource constraints limit the use of blood transfusions).

2.3. Follow-up

Follow-up is scheduled routinely at 6 weeks post treatment, every three months in year 1, every six months in years 2 to 5, and annually to 10 years. Due to the poor socio-economic situation of many patients, and the distance they must travel from home to the cancer centre, many do not adhere to the follow-up program. Consequently, we could not determine local recurrence rates and progression- or disease-free survival at five years. Therefore, the primary end-point of this study was overall survival, measured from the start of EBRT to date of death or last recorded visit. Patient data were censored on 1 December 2016, 5 years after the last patient commenced EBRT in the cohort. We obtained mortality data from the South African Medical Research Council's national population register (NPR), which can provide a date of death for those patients who have a national identity number. We right-censored those without a national identity number at their last recorded date of follow-up. For most patients, we could not establish cause of death because we lacked access to death certificate information; we had in-patient records of pre-terminal events for only a few patients. For the purposes of this study, therefore, we analyzed all-cause mortality or overall survival.

2.4. Statistics

We evaluated the statistical significance of differences in demographic factors and clinical parameters between HIV-positive and HIV-negative patients by means of *t*-tests for continuous variables and χ^2 tests for categorical variables. Overall survival was computed using the Kaplan-Meier method. We developed Cox multivariable logistic regression models for the associations of HIV status, stage, total dose of radiation, and prescription of chemotherapy with mortality, expressing results as hazard ratios (HRs) with 95% confidence intervals (CIs). All tests were 2-sided, and p values of 0.05 or less were considered

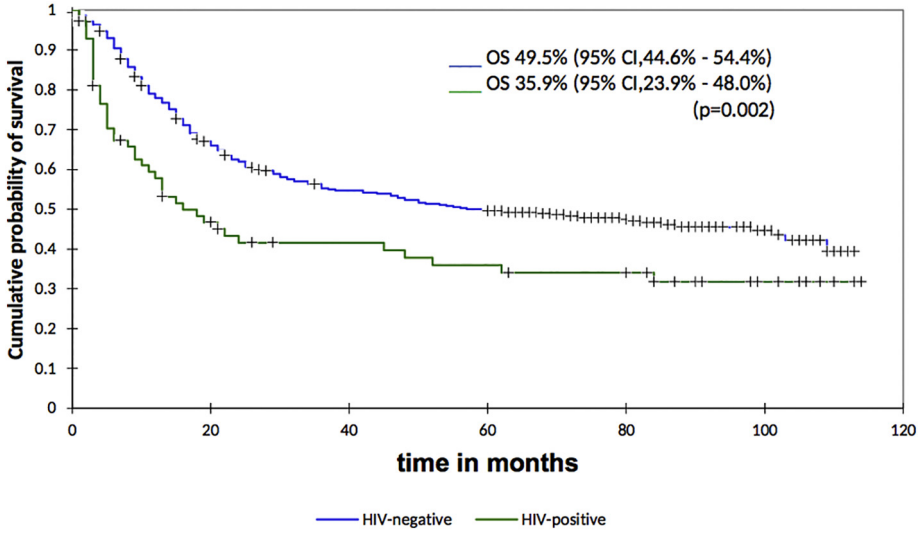

Fig. 1. 5-Year overall survival by HIV status.

Table 3
Predictors of all-cause mortality.

Variable	Hazard ratio	95% CI	p-Value
HIV status			
Negative	Referent		
Positive	1.45	1.01–2.08	0.04*
Stage			
IB1-IIIA	Referent		
IIIB	1.50	1.10–2.05	0.01*
Hydronephrosis			
Absent	Referent		
Present	1.70	1.12–2.59	0.01*
Total EQD_2 dose			
>69.25 Gy	Referent		
<69.25	1.01	0.65–1.57	0.96
Chemotherapy			
≥4 cycles	Referent		
1–3	1.18	0.84–1.65	0.34
0	1.86	1.26–2.76	0.02*

* $p < 0.05$

significant. Data were analyzed using the SPSS Statistics software program (version 25.0; SPSS, Inc., Chicago, IL).

3. Results

From May 2007 to November 2011, 525 cervical carcinoma patients stage IB1 to IIIB commenced primary radiotherapy treatment. Of these, 33 patients received palliative treatment of 8–30 Gy and were excluded from this analysis. The remaining 492 patients were prescribed >40 Gy EBRT and were included.

3.1. Demographic and clinical characteristics

The cohort included 71 HIV-positive patients (14.4%) and 421 HIV-negative patients (85.6%) (Table 1). Their median age was 49 years, but the HIV positive group was younger at 40 years than the HIV-negative group at 50 years ($p = 0.001$). Most of the patients (69.5%) were diagnosed in stage IIIB, 78.9% of the HIV group and 67.9% of the uninfected group ($p = 0.06$). The vast majority of cases were pathologically defined as squamous cell carcinoma (93.1%).

Among the HIV infected patients, the median CD4 count was 386 cells/μl (iQR 256–450); 43 (60.6%) of the HIV-infected patients were on cART at the time of cervical cancer diagnosis, with a median CD4 of 366 cells/μl (iQR 276–458). The remaining 28 patients commenced treatment before or during EBRT, with a median CD4 of 324 cells/μl (iQR 209–407). Eleven patients had a recorded CD4 < 200, 7 of whom were not on cART.

3.2. Treatment parameters

Overall, 433 (88.0%) patients (87.6% of HIV-positive and 90.1% of HIV-negative patients) were prescribed standard fractionation EBRT (Table 2).

The median EQD_2 to point A was 77.7 Gy (iQR 75.0–80.9), for both groups. A large proportion of the cohort received a minimum of 69.25 Gy (83.3%); more of the HIV-negative patients (84.6%) than the HIV-positive patients (74.1%) completed the total prescribed radiotherapy ($p = 0.08$). Of those who were prescribed 1.8–2 Gy per fraction, 90% of the HIV-negative patients but only 80% of the HIV-positive patients completed brachytherapy ($p = 0.012$).

Of the 433 patients in the standard fractionation group, 384 (88.7%) were prescribed platinum-based chemotherapy. Fewer HIV-positive than -negative patients were able to complete 4 or more cycles. In addition, more HIV-positive than -negative patients required a red blood cell transfusion to maintain a hemoglobin over 10 g/dl, 66.2% ($p < 0.001$).

3.3. Survival

The median follow-up for the 492-patient cohort was 30.5 months (0–114 months) and 22,367 person-months. Two-year and five-year survival data were not available for 35 (7.1%) and 44 (8.9%) of the total cohort, respectively. The overall survival for the whole cohort was 59.1% (median not reached) at 2 years and 47.6% (median, 4.2 years; 95%CI, 27.1–72.9 months) at 5 years. Among patients who were prescribed chemoradiation and completed at least one cycle, the OS was 51.8% at 5 years.

HIV-negative patients had an OS of 62.0% (95%CI; 57.2%–66.7%) at 2 years and 49.2% (95%CI; 44.6%–54.4%) at 5 years. HIV-positive patients had poorer OS, 41.6% (95% CI; 29.5%–53.7%) at 2 years and 35.9% (95%CI; 23.9%–48.0%), at 5 years ($p = 0.002$) (Fig. 1). Within two years, 38 HIV-positive patients had died; only three more patients died in the next three years. The difference in survival remained significant when patients with a CD4 cell count of 200 or less were excluded from the analysis. Within the HIV-positive cohort, 5-year OS of those established on cART was similar to that of patients newly diagnosed with HIV, 38.4% *vs.* 31.4% ($p = 0.322$). The difference between the 5-year survival of the HIV negative group and that of HIV-positive patients established on cART was not quite statistically significant, 49.5% *vs.* 38.4% ($p = 0.063$).

The two- and five-year survival for Stage IB1-IIIA patients was 74.3% and 61.5% overall. For the Stage IIIB patients, 2- and 5-year OS was 52.2% and 41.3% overall. Survival was significantly lower for HIV-positive patients (Supplementary Table 1, S1).

In bivariate analysis, survival was not influenced by age, nodal status, histological subtype or transfusion status. The presence of hydronephrosis did, however, impact survival significantly.

With respect to total radiotherapy dose delivered, those who received 69.25 Gy EQD_2 or more fared better, with a 5-year OS of 50% *vs.* 36.9% ($p = 0.002$). HIV-status again conferred a lower OS even on those receiving adequate radiation (Supplementary Table 1).

In the standard fractionation cohort, survival was strongly associated with chemotherapy but was adversely affected by HIV-positivity. Among patients who received 4 or more cycles of platinum chemotherapy and complete radiotherapy >69.25 GY, 5-year OS was significantly better in the HIV-negative patients at 57.0% [Stage IB1-IIIA 71.9%; IIIb 48.2%] than at 35.2% in the HIV-positive patients [Stage IB1-IIIA 66.8%; IIIB 25.2%] ($p = 0.009$).

Those who received no chemotherapy, due to their comorbidities and poor performance status, fared worst of all; 5-year OS was 36.2% and 20.2% in the HIV-negative and -positive patients, respectively.

We developed Cox regression models for the 433 patients who had been deemed fit for radical standard fractionation radiotherapy, with or without chemotherapy (Table 3). The models included all factors found to be significant on bivariate analysis: stage at diagnosis, HIV status, presence of hydronephrosis, completion of EQD_2 69.25 Gy radiotherapy and any chemotherapy. Red cell transfusion status was not associated with poor survival. Factors that were significantly associated with poor overall survival were HIV infection, Stage IIIB disease, the presence of hydronephrosis and ineligibility for chemotherapy.

4. Discussion

This study is one of the first to report the 5-year overall survival of a prospective cohort of HIV-positive cervical carcinoma patients. The overall 5-year survival of the 492 patients in the cohort, including patients with risk factors that are frequently reasons for exclusion from clinical trials, such as HIV infection and hydronephrosis, was 47.8%. Demographic and clinical factors adversely affecting outcome in the 433 patients treated with standard fractionation external beam radiotherapy were HIV positivity, advanced stage (stage IIIB) disease, and, in particular, hydronephrosis. Those who were unfit to receive chemotherapy fared worse.

The adherence of the cohort to prescribed external beam radiotherapy and brachytherapy was high; >80% received the prescribed minimum dose. In addition, 76% of the HIV-negative patients were able to tolerate at least 4 cycles of the prescribed concomitant platinum-based chemotherapy.

HIV-positive patients were less likely than HIV-negative patients to complete prescribed radiotherapy and even less likely to complete chemotherapy. However, approximately 75% of HIV-positive patients received adequate radiotherapy, and 58% completed the prescribed minimum cycles of chemotherapy.

In this observational study, patients who were not prescribed chemotherapy or were prescribed hypofractionated regimens were more likely than others to have a poor performance status, inadequate renal function, or other co-morbidities, such as active tuberculosis, which is common in the Western Cape Province of South Africa.

In a subset of HIV-negative patients without hydronephrosis, who completed chemoradiation, the 5-year overall survival was 58.4% (stage IIB 71.9% and stage IIIB 49.7%). These results are similar to those of a recent chemoradiation trial from Tata Memorial Hospital in India, with arguably a comparable, though highly selected, treatment population [14]. The 1243-patient United Kingdom audit of outcomes for chemoradiation reported a 5-year OS of 55% for the chemoradiation group, 61% for stage IIB and 44% for the stage IIIB patients [15]. Overall survival among our HIV-negative patients who were prescribed chemoradiation was therefore consistent with both developing and developed world data.

We could find no other prospective cohort study reporting 5-year survival for an HIV-positive cohort with an HIV-negative comparison group and complete demographic and treatment data. Coghill et al. reported on associations between HIV status and cancer deaths based on cancer registry data in the United States [8]. Among cervix carcinoma patients in the period 1996–2010, those who were HIV-positive had an all-cause mortality hazard ratio of 2.50, but a cancer-specific hazard ratio of 1.27 that was not statistically significant. In our sample, we could not tell whether the deaths we identified were AIDS-related or cancer-specific because we receive only limited death notice information. Most of the HIV-positive patients who died in our study did so within the first 2 years after diagnosis. We can speculate that HIV makes cervical carcinoma more biologically aggressive than it would otherwise be, or that cancer therapy adversely affects HIV control. With inadequate clinical follow-up, it is unclear which scenario is more likely.

Two HIV-positive cohort studies from Botswana, Dryden-Petersen et al. and Grover et al., presented conflicting results at their 2-year follow-up point [16,17]. In the former, HIV infection nearly doubled the risk of death (HR 1.95, 95% CI 1.2–3.17; $p = 0.007$), and median overall survival was 21.7 months. In the latter, the HR 1.12 was not statistically significant, the median OS was not reported, and the 2-year OS was 66% among HIV-positive patients, >20% higher than that of our HIV-positive patients. The differences between the two Botswana studies, noted by Grover et al., were partially explained by the inclusion of patients who were prescribed only palliative care in the Dryden-Petersen cohort, a lower CD4 cell count, and missing treatment data. In our unit, unlike that in the two Botswana studies, very few patients with early-stage disease are treated with chemoradiation. At our institution, gynaecological oncology surgeons manage active screen-and-treat programs and provide radical surgery for all early-stage disease. The patient population in our unit probably consists mainly of women who did not access the screening program. As a result, most of them present with locally advanced disease; nearly 80% of the HIV-positive patients in our study sample were stage IIIB, potentially accounting for the low survival of the cohort as a whole. In addition, our HIV-positive patients had a lower median CD4 cell count than those in the Grover study, probably because many of them were referred in the era prior to universal cART coverage.

Ferreira et al. performed a matched retrospective cohort study of all cervix cancer patients treated at a single institution in Brazil over a 12-year period [9]. The cohort included 87 HIV-positive patients. Of the subset who underwent radiotherapy, the HIV-positive patients were more likely to relapse within 2 years.

In a study of outcomes among 228 stage IIB patients, 13 of whom were HIV-positive, in South Africa, Jemu et al. found that HIV infection did not affect survival [18]. In Ethiopia, a cohort study of 1655 cervix cancer patients, of whom 139 were HIV-positive, also found that HIV status did not impact survival [10]. However, 789 patients were listed as HIV status unknown, and the study did not categorize patients by therapy received, although it noted that 71% of patients who received radiotherapy were treated with palliative intent. Finally a small matched cohort study of 50 HIV-positive patients undergoing adjuvant, radical and palliative radiotherapy in South Africa found that HIV infection adversely affected the ability to complete treatment and led to poor overall survival [19].

The strengths of our study include the prospective collection of demographic and treatment data. Although a number of patients were lost to clinical follow-up, access to the national registry ensured that vital status was available for over 90% of the cohort at 5 years. All patients were managed within a multi-disciplinary team environment, and high quality oncological and infectious disease interventions were available at no or minimal cost to the patients. Our sample included only patients treated with primary radiotherapy with curative intent. Adherence to planned radiotherapy was 98%, as we noted in our previous paper [12]. Most patients who failed to complete radiotherapy did so because of medical complications.

Limitations of the study include the use of paper records prior to the introduction of an electronic patient management system in radiotherapy; as a result, some subjects may have been missed. Information on acute toxicity was not reported in this study because it was available only for a subset of the cohort and had been previous reported [20]. Lack of data on late toxicity, local recurrence, distant metastases and cause of death is a limitation but one that is common among survival studies conducted in low resource settings, where many patients find it difficult to attend for frequent follow-up. The proportion of HIV-positive patients in our sample was 14.4%, relatively low compared to that of other centres in sub-Saharan Africa, but consistent with HIV prevalence in our institution's catchment area. The HIV-positive patients in our sample had a moderately low median CD4 count, probably because many of our patients were diagnosed and treated prior to the full cART rollout. A new cohort study in the 'modern' era is needed to see if cervical cancer patients whose HIV is well controlled have better survival than the HIV-positive patients in this study. Finally, our cohort included both patients who were deemed fit for radical therapy and patients who had co-morbidities that limited prescription of chemotherapy.

5. Conclusions

This cohort study of nearly 500 patients with locally advanced cervical cancer found that among women eligible for curative treatment for cervical cancer, HIV-positive patients had poorer overall survival than HIV-negative patients. Additional factors affecting outcome were cervical cancer stage and concurrent chemotherapy. A number of HIV-infected patients were able to tolerate adequate chemoradiation (58.5%), or radiation alone (74.1%), and nearly 40% were alive at 5 years. The outcomes of the HIV-negative cohort were comparable to data from the developed world. Despite their lower survival, we conclude that HIV-positive patients should be provided access to antiretroviral therapy, an effective screening program, and the best standard of care both in surgical and non-surgical oncology therapy in order to optimize outcomes. In addition, including HIV-positive patients in clinical trials will assist in answering questions that cohort studies cannot.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2018.08.038.

Author contributions

Hannah M Simonds - conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing - original draft, and writing - review and editing.

Matthys H Botha - conceptualization, funding acquisition, methodology, supervision, validation, visualization, writing - review and editing.

Alfred I Neugut - conceptualization, supervision, visualization, writing - review and editing.

Frederick H Van der Merwe - conceptualization, investigation, visualization, writing - review and editing.

Judith S Jacobson - conceptualization, formal analysis, methodology, supervision, validation, visualization, writing - review and editing.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Acknowledgements

We thank the staff and patients at Tygerberg Hospital. In addition we thank Laurence Court, Francis Papier, Richard Pitcher and Ria Laubscher for data collection and advice.

Financial disclosures

Supported with grant funding from CANSA (The Cancer Association of South Africa). Any opinion, findings and conclusions or recommendations expressed in this material are those of the author(s) and CANSA does not accept liability in regard thereto.

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