FACTORS INFLUENCING RECEIPT OF RADIATION TREATMENT IN WOMEN WITH CARCINOMA OF THE CERVIX IN GHANA.

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Abstract

Objective: We evaluated the influence of demographic and clinical features on access to radiotherapy among women with cervical cancer.

Methodology: A cross-sectional analytical study design was used to review hospital records of women diagnosed with cervical cancer from 1st January 2010 and 31st December 2013 at Ghana's two largest public cancer treatment centres. Basic demographic and clinical data were captured from the records. Multivariate logistic regression was used to determine the odds of receiving radiotherapy in women with carcinoma of the cervix.

Results: One thousand seven hundred twenty-five (1725) women with cervical cancer were studied, of which 955 (57.7%) women received radiotherapy. The likelihood of receiving radiotherapy increased with increasing age (OR: 2.2; 95% confidence interval, CI, 1.5-3.1, 70-79, versus ≤39 years. The indigenous semi-urban dwellers (unadjusted OR: 2.4; 95% CI: 1.6-3.5), and foreign nationals (unadjusted OR: 4.1; 95% CI: 2.5-6.9), were more likely to receive radiation treatment relative to those who resided in the metropolis. Women with three or more comorbidities (unadjusted OR: 0.2; 95% CI: 0.1-0.5), those recruited at the gynaecology unit (unadjusted OR: 0.01; 95% CI: 0.002- 0.01) and subjects with no histological diagnosis (unadjusted OR: 0.004; 95% CI: 0.002-0.01) were likely not to receive radiation treatment. After controlling for other variables, recruitment from the gynaecologic units was significantly associated with a probability of receiving radiation treatment (Adjusted OR: 0.1; 95% CI: 0.01-0.3).

Conclusion: Women diagnosed with cervical cancer at the gynaecologic departments were less likely to access radiation treatment.

Keywords: *Ghana, Gynaecologic Oncology; Radiation treatment; Treatment Default; Cervical cancer.*

Introduction

Cervical cancer is the second most common cancer in Ghanaian women.[1] Human papillomavirus (HPV) infection is established as the cause of cervical cancer, and vaccines such as Cervarix, Gardasil and Gardasil-9, have been developed and are widely available in high-income countries (HICs). The screening for pre-cancer cervical conditions has also been implemented in HICs for the secondary prevention of the disease. In Ghana, just about a quarter (26.94%) of women aged 18 years or above have had Pap smear tests.[2] Although HPV vaccination programs exist, participation by the target population remains low.[3] These factors have led to the majority (65.9-70.8 %) of women with cervical cancer presenting with late disease.[4,5]

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The mainstay of treatment for women with locally advanced disease (International Federation of Gynaecologist and Obstetricians Stage, FIGO Stage, IB3-IVA) has changed over the years from radiotherapy alone to concurrent chemoradiation.[6] Several studies have demonstrated the survival advantage of cisplatin-based chemotherapy.[7–9] Primary radiotherapy is also indicated in women with early diseases, but are not good candidates (morbidly obese women with attendant detrimental anaesthetic risk, uncontrolled hypertension, or diabetes mellitus) for radical surgical treatment. The recommended treatment for women with FIGO stage 1A2, 1B1, 1B2 and 2A1 disease is radical hysterectomy and pelvic lymph node dissection, with or without radiotherapy. Post-operative adjuvant radiotherapy (PORT) is considered after surgery, when histopathologic findings suggest lymph node involvement, positive parametrial or surgical margins among other factors.

Like most low- and middle-Income Countries (LMICs), Ghana is faced with a significant resource deficit in the diagnosis and treatment of cervical cancer. In other jurisdictions, geographical variation in access to radiotherapy has been reported in cancer care, while in

others, attendant comorbidities also prevent the receipt of recommended radiation protocol.[10] Where services are available, the cost of treatment often prevents access. Out-of-pocket cost for procedures, investigations, and treatment for women receiving a standard radiation regimen range from US$ 1,525 to US$ 2,129 in a country where the minimum wage is US$ 1.96.[1]

In Ghana, access to radiation services and actual receipt of the treatment in women with cervical cancer is largely unknown. Where radiation services are available, understanding the factors that influence access to treatment can help identify areas where improvement in care is needed, especially considering the poor survival for women with cervical cancer in Ghana.[11] We evaluated the influence of demographic and clinical features on receipt of radiotherapy among women with cervical cancer.

Materials and Methods

The methods for the study have previously been described elsewhere (Nartey et al 2018).[12]

Study design

A cross sectional study design in which hospital records were reviewed.

Study sites and patient navigation

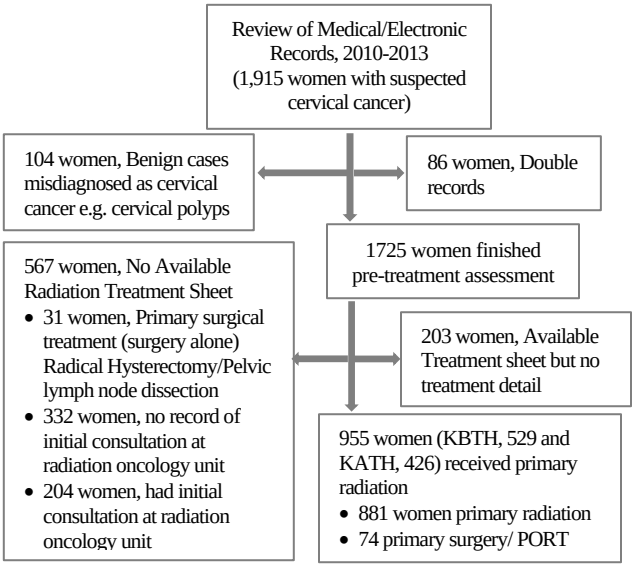
There are two public cancer treatment centres which offer radiotherapy services in Ghana, located in two tertiary hospitals: Korle Bu Teaching Hospital (KBTH), Accra and Komfo Anokye Teaching Hospital (KATH), Kumasi. We excluded the Ghana Swedish Medical Centre (GSMC), a private cancer treatment centre situated in Accra. The study population consisted of all histologically and clinically confirmed cervical cancer cases diagnosed at the Gynaecology and Oncology Units from January 1, 2010, to December 31, 2013.

As per practice, each patient is given an individualized schedule for pre-treatment assessment, definitive treatment, and post-treatment surveillance.[2] Women with signs and symptoms suggestive of cervical cancer undergo pre-treatment assessment at the Gynaecology or Oncology Units. Haematology, serum biochemistry, ultrasonography (USG), histopathology, cystoscopy, sigmoidoscopy, intravenous urography (IVU), computerized tomography (CT) and magnetic resonance imaging (MRI) assessments form the core of investigations done in the pre-treatment assessment of cervical cancer. This evaluation process also seeks to stabilize existing chronic conditions (anaemia, hypertension, diabetes, and others). Image-guided drainage of hydro- and pyometra, insertion of nephrostomy tubes and the application of ancillary surgical and medical protocols are also undertaken when necessary.

All patients are reminded of their appointments a day or two before the due dates. A patient who cannot honour a scheduled visit is often counselled on compliance and given a new date. The patient is labelled as "defaulted treatment" if she failed to honour two or more scheduled visits during pre-treatment assessment or definitive treatment. Treatment default can occur at any stage, up to the completion of the radiation regimen. Early treatment default describes default before treatment initiation. The activities prior to treatment initiation include pre-treatment assessment, simulation for 2-D radiotherapy, or planning for 3-D conformer radiotherapy. The first and second review visits are scheduled at two and four weeks, respectively, after treatment. Subsequently, the patient is seen at three-month intervals for the first year and then every 6 months for the next few years.

Patient record selection

We reviewed paper-based and electronic medical records (including pathology results) at the Oncology and Gynaecology units of the two hospitals and collected information on all newly diagnosed women with invasive cervical cancer within the period (Figure 1). Out of 1725 women with newly diagnosed cervical cancer, 995 (57.7%) received radiation treatment at the two public cancer treatment centres between 1st January 1, 2010, and 31st December 2013. One hundred and five (105), 6.1%, women received radical surgical treatment with or without post-operative radiotherapy (PORT) as treatment for cervical cancer.



[1] Average cost of treatment for locally advanced cervical cancer. An estimate from Gynaecologic Oncology Unit, Department of Obstetrics & Gynaecology, Komfo Anokye Teaching Hospital, 2020.

[2] Departmental protocol on patient navigation during cancer treatment (treatment default and loss-to-follow up), Department of Oncology, Komfo Anokye Teaching Hospital.

Note KATH: Komfo Anokye Teaching Hospital KBTH: Korle Bu Teaching Hospital; PORT: Post-operative adjuvant radiotherapy. Flow chart of the data source of women diagnosed and treated for cervical cancer between January 1, 2010, and December 31, 2013, at the two tertiary hospitals in Ghana is displayed in **Figure 1**.

Data collection

For each unit, available information for women with cervical cancer were extracted from paper-based and electronic medical records onto a standard data collection sheet. The data were reviewed for accuracy and the following variables were used to link the cases between the units: histology report number, unique identification (ID), age, and telephone number. After linking the data from the units and removing duplicates, the data were stripped of all identifiers.

Basic demographic and clinical features, and treatment information were obtained for all cervical cancer patients within the period. A patient recruitment hospital was defined as the hospital where the patient information was obtained. Receipt of radiotherapy was defined by a record of initiation, default or completion of radiation treatment evidenced by the treatment regimen detailed on the radiotherapy sheet. Women with missing treatment information were designated as not having received radiotherapy, similar to the method used by Baldwin et al.[13]

Statistical analysis

STATA version 14.1 (StataCorp, Texas) software was used in all data analyses. We calculated the proportion of various demographic and clinical features according to the recruitment hospitals. The socio-demographic and clinical characteristics were compared using Pearson's chi-square and Fisher's exact tests. We calculated the proportion of women who received radiotherapy in each hospital and then used logistic regression to estimate the bivariate and multivariate odds of receiving radiotherapy for patients with different characteristics. The test for statistical significance did not include missing responses.

Ethical Approval

The study obtained ethical approval from the University of Otago Ethics (Health) Committee, Ghana Health Service Ethical Committee, Committee on Human Research and Publication and Ethics, Kwame Nkrumah University of Science and Technology (CHRPE, KNUST) and KATH.

Results

One thousand seven hundred twenty-five (1725) women with cervical cancer were studied, of which 955 (57.7%) women received radiotherapy. Women seen at KBTH were younger, single, fewer numbers had formal education, and resided in the metropolis or the urban area ($p<0.001$) (Table 1). Data on educational status was missing in 533 (51.0%) and 411 (60.4%) women in KBTH and KATH, respectively. About one out of five women diagnosed with cervical cancer received no formal education (20.8%).

Table 1: Distribution of key demographic features by hospital of recruitment

Characteristic	KBTH (N=1045)	KATH (N=680)	χ^2 (p-value)
	n (%)	n (%)	
Age group (years)			
≤39	123 (11.8)	63 (9.3)	
40-49	215 (20.6)	149 (22.0)	
50-59	287 (27.5)	161 (23.8)	
60-69	207 (19.9)	109 (16.1)	
70-79	157 (15.1)	148 (21.9)	
≥80	53 (5.1)	47 (6.9)	=0.001
Missing	3	3	
Place of residence			
Metropolis	512 (49.9)	428 (63.7)	
Urban	406 (39.5)	103 (15.3)	
Semi-urban	12 (1.2)	137 (20.4)	
Overseas	96 (9.4)	4 (0.6)	<0.001*
Missing	19	8	
Marital status			
Single	207 (24.4)	6 (1.0)	
Married	447 (52.7)	307 (50.2)	
WDS	194 (22.9)	299 (48.8)	<0.001
Missing	197	68	
Formal education			
NFE	206 (40.2)	152 (56.5)	
Primary	85 (16.6)	38 (14.1)	
High school	182 (35.6)	67 (24.9)	
Tertiary	39 (7.6)	12 (4.5)	<0.001
Missing	533	411	
Employed			
No	209 (24.8)	108 (16.3)	
Yes	635 (75.2)	553 (83.7)	<0.001
Missing	201	19	
Parity			
0-2	209 (20.5)	70 (10.8)	
3-4	263 (25.9)	127 (19.6)	
5+	545 (53.6)	451 (69.6)	<0.001
Missing	28	32	

Note: Number and percentage excludes missing data.
OR: Odd ratio; χ^2: Chi square *Fisher's exact test;
KATH: Komfo Anokye Teaching Hospital
KBTH: Korle Bu Teaching Hospital;

WDS: Widowed/Divorced/Separated**, NFE**: No formal education.

Table 2 illustrates the key clinical features of the hospital of recruitment. The proportion of women with clinically diagnosed cervical cancer was higher in KBTH (27.8%) than in KATH (14.4%) (p<0.001). For 203 (11.7%) women, we could not obtain information on the receipt of radiotherapy. Receiving radiotherapy (p=0.951), chemotherapy (p=0.890), and having a significant past medical history did not vary significantly by the recruitment hospital. Compared with women seen at KATH (101, 14.9%), more women diagnosed at KBTH had missing data on the FIGO stage (313; 30.0%) (p < 0.001). The percentage of women with FIGO stage IV disease was 13.7% at KBTH and 10.7% at KATH. A total of 955 (57.7%) women with cervical cancer received radiotherapy, of which 529 (55.4%) were from KBTH.

Table 2: Key clinical features by hospital of recruitment

Characteristic	KBTH (N=1045)	KATH N=680	χ^2 (p-value)
	n (%)	n (%)	
Basis of diagnosis			
Clinical	291 (27.8)	98 (14.4)	
Histology of primary	754 (72.2)	582 (85.6)	<0.001
Missing	0	0	
Grade of differentiation			
Well	125 (16.6)	47 (8.1)	
Moderately	284 (37.6)	308 (52.9)	
Poorly/ Undifferent-iated	345 (45.8)	227 (39.0)	<0.001
Missing	291	98	
Histological subtype			
SCC	606 (85.2)	513 (89.8)	
ADC/ Adenosquam-ous	95 (13.4)	57 (10.0)	
Other	10 (1.4)	1 (0.2)	=0.002
Missing	334	109	
FIGO Stage			
Stage I	50 (6.8)	40 (6.9)	
Stage II	267 (36.5)	161 (27.8)	
Stage III	315 (43)	316 (54.6)	
Stage IV	100 (13.7)	62 (10.7)	<0.001
Missing	313	101	
Any comorbidity			
No	492 (55.4)	421 (61.9)	
Yes	396 (44.6)	259 (38.1)	=0.010
Missing	157	0	
Any medical history			
No	835 (94.2)	640 (94.1)	
Yes	51 (5.8)	40 (5.9)	=0.916
Missing	159	0	
Received radiotherapy			
No	315 (37.3)	252 (37.2)	
Yes	529 (62.7)	426 (62.8)	=0.951
Missing	201	2	
Received chemotherapy			
No	22 (7.5)	7 (7.9)	
Yes	271(92.5)	81 (92.1)	=0.890
Missing	192	20	

Note: Number and percentage excludes missing data.
FIGO: International Federation of Gynaecology and Obstetrics.
KATH: Komfo Anokye Teaching Hospital; Korle Bu Teaching Hospital;
OR: Odd ratio; χ^2: Chi square*Fisher's exact text

Age at diagnosis, place of residence, marital status, ethnicity, recruitment unit and the basis of diagnosis all showed independent associations with receipt of radiotherapy. The likelihood of receiving radiotherapy increased with increasing age (OR: 2.2; 95% confidence interval, CI, 1.5-3.1) for the age group, 70-79 versus the youngest group (≤39 years) as shown in **Table 3**.

Among women diagnosed with cervical cancer, the indigenous semi-urban dwellers (unadjusted OR: 2.4; 95% CI: 1.6-3.5), and foreign nationals (unadjusted OR: 4.1; 95% CI: 2.5-6.9), were more likely to receive radiation treatment relative to those who resided in a metropolis. Women with three or more comorbidities (unadjusted OR: 0.2; 95% CI: 0.1-0.5), being recruited at the gynaecology unit (unadjusted OR: 0.01; 95% CI: 0.002-0.01) and subjects with no histological diagnosis (unadjusted OR: 0.004; 95% CI: 0.002-0.01) were all less likely to receive radiotherapy. These relationships were not statistically significant after adjusting for all variables in the analyses except for patients recruited from the gynaecology unit (adjusted OR: 0.1; 95% CI: 0.01-0.3). A separate analysis was performed excluding women with unknown information on radiotherapy treatment which reduced the ORs (see additional file 1, **Table S1**).

Additional file 1:
Table S1 presents an overview of the unadjusted and adjusted ORs of having radiotherapy by patients features excluding women with unknown information on radiation therapy. Restricting the analyses to women with information on receipt of radiotherapy reduces both the crude and adjusted ORs in some analysis. For example, the OR for women not residence in Ghana reduces from 4.1 (95% CI: 2.5-6.9) to 3.2 (95% CI: 1.9-5.4). However, some ORs for some variables did not change after inclusion of women with unknown information on receipt of radiotherapy.

Table S1: Results of logistic regression examining the influence of various features on receipt of radiotherapy (excluding women with unknown radiotherapy treatment information)

Characteristics	Received radiotherapy	No radiotherapy	OR *	95% CI	OR †	95% CI
	N (%)	N (%)				
Age group (years)						
≤39	84 (8.8)	64 (11.3)	1.0		1.0	
40-49	172 (18)	142 (25.1)	0.9	0.6-1.4	0.4	0.2-1.2
50-59	259 (27.2)	143 (25.3)	1.4	0.9-2.0	0.6	0.2-1.5
60-69	188 (19.7)	94 (16.7)	1.5	1.0-2.3	0.8	0.3-2.6
70-79	195 (20.4)	86 (15.2)	1.7	1.1-2.6	0.7	0.2-2.1
≥80	56 (5.9)	36 (6.4)	1.2	0.7-2.0	0.8	0.2-3.6
Missing	1	2				
Place of residence						
Metropolis	477 (50.1)	338 (60.5)	1.0		1.0	
Urban	288 (30.3)	162 (29.0)	1.3	1.0-1.6	1.0	0.6-1.7
Semi-urban	106 (11.1)	41 (7.3)	1.8	1.3-2.7	1.7	0.8-3.8
Overseas	81 (8.5)	18 (3.2)	3.2	1.9-5.4		
Missing	3	8				
Marital status						
Single	123 (13.1)	76 (15.6)	1.0	0.7-1.3	0.9	0.4-1.9
Married	462 (49.3)	272 (55.9)	1.0		1.0	
WDS	353 (37.6)	139(28.5)	1.5	1.2-1.9	1.3	0.7-2.4
Missing	17	80				
Formal education						
NFE	235 (45.4)	109 (48.6)	0.6	0.3-1.3	0.5	0.1-2.0
Primary	81 (15.7)	34 (15.2)	0.7	0.3-1.5	0.9	0.2-3.7
High school	166 (32.1)	71 (31.7)	0.7	0.3-1.4	0.8	0.2-3.1
Tertiary	35 (6.8)	10 (4.5)	1.0		1.0	
Missing	438	343				
Employment status						
Yes	734	78.8	421	79.1	1.0	
No	197	21.2	111	20.9	1.0	0.8-1.3
Missing	24		35			
Comorbidity count						
No comorbidity	562 (58.9)	320 (56.4)	1.0			
1 count	318 (33.3)	178 (31.4)	1.0	0.8-1.3		
2 counts	70 (7.3)	51 (9.0)	0.8	0.5-1.2		
3 or more counts	5 (0.5)	18 (3.2)	0.2	0.1-0.4		
Missing	0	0				
Basis of diagnosis						
Histology	951 (99.6)	381 (67.2)	1.0		1.0	
Clinical	4 (0.4)	186 (32.8)	0.01	0.003-0.023	0.2	0.01-2.0
Missing	0	0				
Unit of recruitment						
Oncology	948 (99.3)	305 (53.8)	1.0	1.0	1.0	
Gynaecology	7(0.7)	262 (46.2)	0.01	0.004-0.02	0.1	0.014-0.3
Missing	0	0				

Interval; FIGO: International Federation of gynaecology and Obstetrics; **KATH**: Komfo Anokye Teaching Hospital; Korle Bu Teaching Hospital; **OR**: Odd ratio. **WDS**: Widowed/Divorced/Separated; **NFE**: No formal education. **BT**: Businesswomen/Teachers; **HS**: Headdresses/Seamstresses.

Adjusted for all variables in the analysis except ethnicity, employment status, and commodity count. The numbers of these variables were too small to be included in multivariate analyses.

The following variables were not included in the regression output table: No formal education (relative to tertiary education, adjusted OR: 0.5; 95% CI: 0.1- 2.0), hospital of recruitment (KATH relative to KBTH, Adjusted OR: 1.1; 95% CI: 0.6-2.0), positive history of comorbidity (presence of other chronic condition(s) relative to its absence, adjusted OR: 1.1; 95% CI: 0.4-2.4), parity (Para 5+ relative to para 0-2, adjusted OR: 0.8; 95% CI: 0.4-1.8) and FIGO Stage (Stage II relative to Stage I, unadjusted OR: 0.004; 95% CI: 0.002-0.01).

Discussion

Cervical cancer patients from the gynaecologic departments had reduced access to radiation treatment. Differences in demographic and clinical features were observed among women with cervical cancer at the two largest public cancer treatment centres. Overall, women seen at KBTH were younger and single, less likely to have had formal education, and resided in the metropolis or the urban area.

Capacity exists for surgical oncology at gynaecology departments. About 105 (6.1%) had primary surgical treatment and would not be captured by the radiation treatment records. The reduced access to radiation treatment for cervical cancer patients recruited from the gynaecology unit may be attributable to the proportion of women with operable diseases. The association persisted after adjusting for all variables in the analysis. Secondly, referrals of these patients to the oncology departments are effected after receipt of histology reports. A few die before the cancer confirmation due to the late stage of the disease and its associated commodities. Good record-keeping, patient care coordination, as part of a dedicated patient navigation unit, have been shown to bridge gaps and address diverse needs in cancer care system.[14]

Cancer patients in HICs who resided in urban populations had a better chance of receiving radiation.[13,15] This is contrary to the observation made among our subjects who lived in urban areas. The finding that women with semi-urban residence were more likely to receive radiotherapy than those in the metropolis or urban areas suggested that access to cancer treatment in Ghana may be influenced more by financial rather than geographical barriers. Infrastructural developments and emerging business enterprises offer enhanced opportunities for high-income, non-traditional, commercial, and service ventures for many semi-urban households in Ghana.[16] Although the women with urban or metropolitan residences were younger, they were less likely to have had formal education or employment. They migrate from more impoverished communities searching for non-existent jobs in the metropolis. Ghana's capital, Accra, has many urban poor people.[17]

Medical tourism also provides opportunities for cancer treatment abroad.[18] Cross-border arrangements at destination countries often cover medical bills and bursaries. Consistently, women who resided in other

African countries had a better chance at receiving radiation treatment than indigenous urban or metropolitan dwellers. However, this was not statistically significant after adjusting for confounders, as this could be attributed to the small sample size of the women who resided in other African countries.

Although the government has subsidized the cost of radiotherapy for Ghanaians, the out-of-pocket cost for procedures, investigations, and treatment is still a significant part of the cost of cancer care. Thus, lack of financial resources may hinder some Ghanaian women from receiving radiotherapy. Opportunities to improve access to radiation treatment in cervical cancer should reduce the financial barriers in cancer care. All aspects of the patient journey, from diagnosis through treatment and post-treatment, should be covered by the National Health Insurance Scheme (NHIS). The care of human epidermal growth factor receptor-2 (HER 2) positive breast cancer is covered by the NHIS. Similar advocacy is needed in the care of cervical cancer patients. The total cost of pre-treatment assessment and definitive treatment of cervical cancer patients pales in comparison to that accrued from the use of trastuzumab (Herceptin, range from US$ 1,525 to US$ 2,129) in the care of woman with HER-2 positive breast cancer.

Effective cervical cancer management often requires a multidisciplinary team of radiologists, radiation and gynaecologic oncologists, pathologists, nurses, and other professionals.[19] The Ghana College of Physicians and Surgeons has adequate capacity to train essential clinical staff for cancer care. The establishment of a few more cancer treatment centres in other parts of the country may also reduce treatment default by reducing travel costs and improve oncologic outcomes (overall survival and quality of life). Efforts to improve access to gynaecologic oncologic treatment (radical surgery and radiotherapy) and other ancillary treatment interventions are needed in these parts of the country, especially in the northern regions of Ghana.

The main strength of our study was the rigorous review of medical records. The study provides a representative profile of the cervical cancer population in Ghana. A major limitation of our study was the high proportion of women with missing data for key variables such as education, occupation and FIGO stage, which affected the precision of the results obtained. Another potential limitation was the bias that may result from designating women with unknown information on treatment as not having received radiotherapy. However, the separate restricted analysis showed that the direction of the associations did not change for any of the variables included. We also did not know whether some women were offered radiotherapy but declined. Finally, data on tumour board reviews and decisions were not collected, which might have influenced the receipt of radiation therapy.

Conclusion

The current study revealed that women diagnosed with cervical cancer at the gynaecologic departments were less likely to access radiation treatment. Further studies should look at barriers to radiation treatment following initiation assessment at these units.

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