

Complication of radiotherapy in the management of invasive cancer of the cervix at Kenyatta National Hospital

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Abstract

Background: Cancer of the cervix is not only the second most common cancer affecting women worldwide but is also the most common gynecological cancer in Kenya. An estimated 500,000 cases occur every year of which 80% are from the developing countries. Presentation is usually during late stages requiring radiotherapy as the main form of management. Radiotherapy has its side effects which could be late or early.

Objective: This study sought to evaluate the complications of radiotherapy among patients with advanced carcinoma of the cervix treated at the Kenyatta National Hospital.

Patient and Methods: This was a descriptive retrospective study of the data collected from the radiotherapy unit of Kenyatta National Hospital, which is the only public hospital with radiotherapy facilities in Kenya. The study population was from that of women treated for cervical cancer at Kenyatta National Hospital between 2000 to 2004. The data collected included age, parity, histological type, stage at presentation, comorbidities, duration and dose of radiotherapy and complications. The files were sampled in such a way that only every fifth file was analyzed for the above data.

Results: There were 1545 patients during this period. Of the above 306 files were analyzed. The average age at presentation was 48.6 years. 5.2% were HIV positive. 3.3% were at stage IB, 41.5% stage II, 47.5% stage III and 7.7% stage IV. 86.7% had squamous cell carcinoma. Common early toxicities included skin burn, diarrhea and rectal bleeding. The common late complication included skin fibrosis and proctitis.

Conclusion: Most patients present at late stage of the disease. The commonest complications affect skin and gastrointestinal systems. Duration and dosage of radiotherapy were significantly associated with the number of systems affected.

Introduction

Cervical cancer is the most common gynecological cancer in Kenya (1, 2) while it forms 80% of cancers that occur every year in the developing countries (3,4). In the developed world the incidence rates are generally low with age-standardized rates less than 14 per 100,000 women compared to 37.4 per 100,000 women in East Africa (4, 5). Presentation is usually on late stage requiring palliative radiotherapy as the only management. Radiotherapy has its complications which include burns, rectal bleeding, and vaginal stenosis to mention but a few. Pederson *et al* (6) found early complications of 7.7% while that of Sood *et al* (7) was 4%. Both studies recorded that gastrointestinal complication occur early. Pelvic failure rates have been reported to be 19% in a study by Gichangi *et al* (2) and between 10-74% depending on the stage in two studies by Lanciano *et al* and Perez *et al* (8, 9).

This study sought to evaluate the complications of radiotherapy among patients with advanced carcinoma of the cervix treated at the Kenyatta National Hospital.

Materials and Methods

This was a retrospective study for a period of 5 years (2000-2004). The study population were women being treated with radiotherapy at Kenyatta National Hospital. The sample size was calculated using Fischer's formula with complication rate estimated at 27%, normal standard deviation at 1.96, with significance set at 0.05.

The minimum number of files that were to be analyzed for accuracy in this study was set at 302. The final number was determined by a sampling procedure in which all the file numbers found was put in a sampling frame and every fifth file picked. The data collected included age, parity, histological type of cancer, stage at presentation, duration of radiotherapy, dose and duration of radiotherapy, systems where complications were noted. Inclusion criteria were all patients who had histologically confirmed diagnosis of cancer of cervix who were treated at the radiotherapy department. All patients in this study received external beam radiotherapy using of Cobalt 60 (Siemens or Theratrons T²⁸⁰) machine via parallel-opposed anterior

and posterior fields. The field sizes adopted depending on the clinical stage. Most patients received doses of 40-50 Grays to point A. Point A was a reference location 2 cm lateral and 2 cm superior to the cervical ostium. Fractionation was 1.8-2.0 Gy tumor dose daily, 5 fractions per week within 5 weeks with two days rest from treatment during the week. Once the radiotherapy was initiated, patients were seen after completion unless where toxicity led to discontinuation of therapy. They were then seen after 3-6 months in the radiotherapy department.

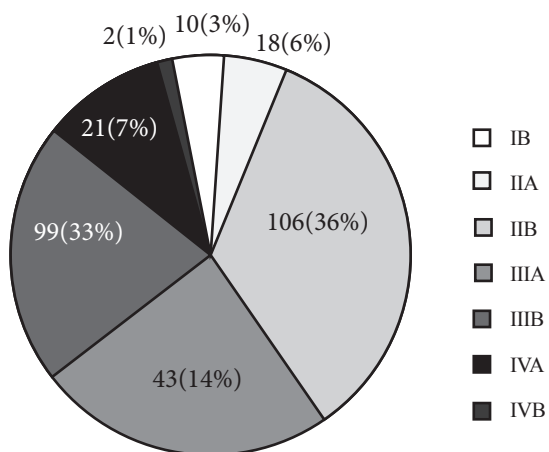
The data was coded and entered into SPSS Version 11.0 for analysis. The results are presented in tables and figures. The statistical significance was deemed if P value was less than 0.05.

Results

The number of files retrieved was 1545 for the stated study period. Using the sample frame, a total of 306 files were picked for analysis. The average age was 48.6 years with a median of 48 years. The age range was from 20-80 years. The mean parity was 5.9.

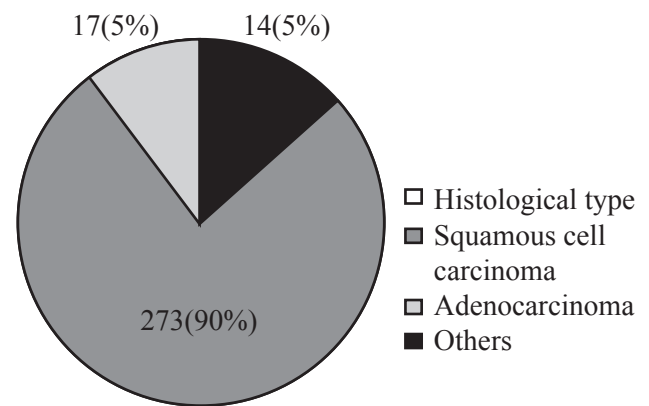
Majority (47%) presented at stage III, in total those presenting at late stage were 91%. There were only 9% in stage IIA and IB as shown in Figure 1.

Figure 1: Presentation by stage



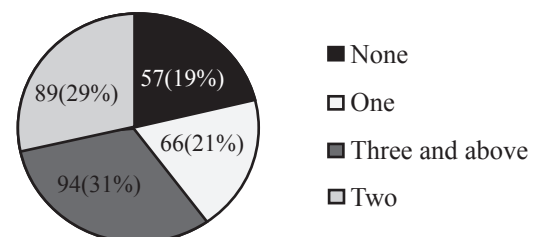
The commonest histological type at presentation was squamous cell carcinoma (90%) as shown in Figure 2. The majority (56.8%) of which were poorly differentiated. Thirty five patients (11.6%) had surgical procedure before radiotherapy. The average hemoglobin level at presentation was 10.8g/dl and of the 56 patients tested for HIV 16(5.2%) were positive. The average dose prescribed was 49.85 Grays while the average received was 45.7 Grays. Of the 306 patients whose files were analyzed only 258(84.3%) completed their radiotherapy treatment.

Figure 2: Presentation by histological type



Thirty one percent of the patients experienced complications in more than three systems with only 19% having no complications after radiotherapy as shown in Figure 3. The percentage cumulative complications by systems are shown in Table 1. The commonest systems affected were skin and gastrointestinal. In the skin the early complication was burns that gave way to fibrosis after one year while for gastrointestinal diarrhea and proctitis respectively. Rectal bleeding present both in acute and chronic phases of the study. Anemia were more prevalent initially but reduced subsequently.

Figure 3: Complications by number of systems



Analysis of the factors that contributed most to the severity of complications denoted by the number of systems affected, it was found that significance factors were the duration of therapy and the radiation dose as shown in Table 2.

Table 1: Percentage complication by systems

Toxicity	Duration (Months)			
	3	6	12	24
Skin (burns/fibrosis)	44	47	45	40
Gastrointestinal (diarrhea, proctitis)	40	59	35	26
Anemia	23	29	30	27
Genitourinary (dysuria, cystitis)	14	13	8	8
Rectal bleeding	28	10	11	9
Vaginal stenosis	6	7	8	8
Recurrence	31	38	41	39

Table 2: Effect of age, Hb, parity, duration and dose on severity of complications

	None of the systems affected	One system	Two systems	Three and above	P value
Mean age (years)	47.79	49.23	47.94	49.21	0.807
Parity	5.8	6.1	5.9	5.7	0.900
Initial HB	10.5	10.5	11.2	10.9	0.241
Duration of radiotherapy (days)	27.7	31.8	34.9	43.1	0.000
Radiation dose on Grays	34.7	43.8	46.2	52.1	0.000

Discussion

From the study, the annual average from the 1545 figure would be 300-350. It is reported that 3600 women die from cancer of the cervix yearly in Kenya (1). This is a paltry figure of the actual number of women requiring care at specialized centers. The average age at presentation was 48.6 years, which is similar to the age found in the American population of 50 years, though the age range in this study was from 20-80 years. A study done 16 years ago reported similar age of presentation; it therefore seems there has been no change in terms of age at presentation over the 2 decades (1).

The majority of patients in this study presented at stage III (46%), this differs from earlier studies (1,2) where about 80% presented at stage III. This improvement in patient presenting relatively early could be attributed to improvement in the health system. This study is similar albeit with slightly higher figures to a study in India (10) where stages II was 33.7% while stage III was 21.8%. In that study stage IB was significantly high (26.6%) signifying the differences in health care systems between the two countries hence better access to services (10).

The histological type is comparable to the known literature that squamous cell carcinoma is the commonest type. The number of patients who received surgical intervention before radiotherapy is low, which may imply that most patients were either under staged or progression after surgery was faster. The staging indicated was that done before being referred for radiotherapy treatment regardless of duration to initiation of radiotherapy.

Occurrence of acute and late morbidities associated with treatment or disease progression was significantly higher than in other studies with only 19% not having complications (6, 7, 10). The most frequent toxicity involved the gastrointestinal tract, having a peak of occurrence at six months (59%). This is similar to world wide data that shows that gastrointestinal system is the most affected system (6 - 8).

Vaginal stenosis averaged 7% for the whole period. This differs with an earlier prospective study done in

the same unit in 2002 (11) which found that almost all women had vaginal stenosis post radiotherapy. This difference could be explained by the study design that allowed the clinician to ask patients concerning their sexual practices, while in a retrospective study it is possible that the lack of records could be due to the fact that most clinicians do not ask those questions.

Rectal bleeding, cystitis, dysuria and vaginal stenosis occurred in less than 20%. Comparable studies have figures less than 5% for most of these morbidities, in a retrospective study in India, rectal bleeding was 1.2%, vaginal stenosis 1.1% (8). This can be explained by the different treatment methods: in this study it was external beam radiotherapy while in the former study, brachytherapy, chemotherapy and external beam radiotherapy were used.

Diarrhea and colitis were an acute morbidity that decreased after the first six months, and the gastrointestinal system complication reduced from 42.8% at 3 months to 27.4% at 24 months. In a study by Pederson *et al* (7) only 7.7% had early complication (6); in another by Sood *et al* (7) they had 4%. The recurrence rate was 32.6% at 3 months, higher than the one in the study by Gichangi *et al* (5) in 2002 where the recurrence rate was 19% at 4-7 months. Lanciano *et al* (8) and Perez *et al* (9) both reported a 5-year pelvic failure of 10-74% depending on the clinical stage. Majority of patients had more than three systems affected by toxicities. This compares well with Gichangi *et al* (2) study at the same site. The number of systems affected had significant association with radiation dose and duration.

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