original reports abstract

Radical External-Beam Radiotherapy in Combination With Intracavitary Brachytherapy for Localized Carcinoma of the Cervix in Sri Lanka: Is Treatment Delayed Treatment Denied?

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PURPOSE Radical external-beam radiotherapy (EBRT) followed by intracavitary brachytherapy is standard of care for patients with localized carcinoma of the cervix unsuitable for radical surgery. However, outcome data are scarce in resource-limited settings. We conducted a retrospective analysis of survival in a cohort of patients treated with this strategy in Sri Lanka.

PATIENTS AND METHODS All patients with localized cervical cancer treated with primary EBRT and intracavitary brachytherapy from 2014 to 2015 were included in the study. Primary end point was disease-free survival (DFS), defined as time to local or systemic recurrence or death. Univariable analysis was performed to determine the prognostic significance of the following variables: age, stage, use of concurrent chemotherapy, EBRT dose, brachytherapy dose, and time to completion of treatment (dichotomized at 60 days). Factors significant on univariable analysis were included in a multivariable model.

RESULTS A total of 113 patients with available data were included in the analysis. Mean age was 58 years (range, 35-85 years), and most patients (n = 103 of 113) presented with stage ≥ IIB disease. Median time to delivery of brachytherapy from commencement of EBRT was 110 days (range, 34-215 days), with only 12 (11%) of 113 patients completing treatment within 60 days. Median follow-up was 28 months (range, 5-60 months), and 2-year DFS was 63.7% (95% CI, 55.4% to 73.2%). Treatment delay was the only significant factor associated with inferior DFS on univariable analysis (log-rank $P = .03$), and therefore, multivariable analysis was not performed.

CONCLUSION There are significant delays in receiving intracavitary brachytherapy after completing EBRT for cervical cancer in Sri Lanka, which is associated with inferior DFS. Increasing brachytherapy resources is an urgent priority to improve outcomes of patients with cervical cancer.

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INTRODUCTION

Carcinoma of the cervix is the third leading cancer among women in Sri Lanka, with > 800 new cases diagnosed each year, according to a hospital-based data registry from the National Cancer Control Program.[1] However, the actual incidence is likely to be much higher because of underreporting of cases in the cancer registry. Globally, as well as locally, cervical cancer accounts for one tenth of all cancers among women.[1,2] There is a wide disparity in the distribution of cases, with almost 80% occurring in less affluent developing countries with poor access to screening services and limited uptake or availability of human papilloma virus (HPV) immunization.[2]

Case-control studies performed in Sri Lanka have shown that in keeping with global data, the prevalence of HPV infection among patients with histologic confirmation of carcinoma of the cervix is approximately 80%, with HPV types 16 and 18 being the commonest subtypes.[3,4] The incidence of cervical cancer is expected to decrease with the introduction of HPV vaccination.[5] In Sri Lanka, this vaccine was introduced to the expanded program of immunization in 2014, and currently, all girls age 12 years receive the vaccine. However, because it will take nearly 20 years for a tangible reduction in incidence to occur, the burden of cervical cancer is likely to remain high during the next decades.

In Sri Lanka, screening for cervical cancer is available through well-women clinics and conducted by public health teams across the country.[6,7] However, the uptake of screening remains low as a result of both social stigma and lack of awareness.[6,7] Although some centers have achieved reasonable success in getting women to opt for the initial test, few women comply with subsequent testing.[6,7] As a consequence, many patients present with locally advanced disease.

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CONTEXT

Key Objective

We sought to analyze disease-free survival and impact of treatment delay in patients with cervical cancer treated with radical external-beam radiotherapy and intracavitary brachytherapy in Sri Lanka.

Knowledge Generated

Nearly 90% of patients had a significant delay in receiving brachytherapy. Survival was inferior in patients with treatment delays.

Relevance

Ensuring timely completion of treatment is of pivotal importance for patients with cervical cancer treated with radical radiotherapy. Improving brachytherapy resources and optimizing workflows along the referral and treatment pathways are key priorities to improve outcomes.

In its earliest stages (International Federation of Gynecology and Obstetrics [FIGO] stage IA1), cervical cancer is cured by cone biopsy or extrafascial hysterectomy, but more advanced cases that are still confined to the cervix (FIGO stages IA2 and IB1) require radical hysterectomy and pelvic lymph node dissection.[8,9] Spread to the parametrium or pelvic lymph nodes and large tumor size (FIGO stages IB2, II, and III) render the disease inoperable, and these patients are treated by radical external-beam radiotherapy (EBRT) in combination with cisplatin-based radiosensitizing chemotherapy followed by intracavitary brachytherapy.[8,9]

There are no published studies on the survival of patients with cervical cancer in Sri Lanka to our knowledge. In this report, we describe survival outcomes of a cohort of patients treated with radical EBRT and intracavitary brachytherapy.

PATIENTS AND METHODS

Patients

All patients with localized cervical cancer treated with primary EBRT and intracavitatary brachytherapy at the National Cancer Institute, Maharagama, Sri Lanka, from 2013 to 2015 were included in the study. Patients treated with adjuvant RT after radical surgery and those with a history of malignancy were excluded from the study, as were patients who did not receive the full course of prescribed EBRT and brachytherapy.

Data Collection

Clinic records were reviewed and data collected on the following variables: age, histology type, disease stage (FIGO 2009 classification), date of commencement of EBRT, EBRT dose, date of completion of intracavitary brachytherapy, brachytherapy dose and fractionation, date of recurrence, site of recurrence, and treatment toxicities.

Diagnosis and Staging

Patients underwent biopsy and clinical staging by examination under anesthesia. Chest radiography and ultrasound scan were performed in all patients to complement clinical staging. Computed tomography (CT) scans and magnetic resonance imaging were not performed routinely because of resource limitations.

EBRT

EBRT to a dose ranging from 45 to 50.4 Gy in 23 to 28 fractions was delivered over 4.5 to 5.5 weeks using either a two-dimensionally planned four-field box plan or an anatomy-based anterior-posterior parallel-pair field arrangement in cobalt-60 teletherapy units.

Patients with good performance status and normal renal function were treated with concurrent weekly intravenous cisplatin to a radiosensitizing dose of 40 mg/m^2 (capped at 70 mg). Patients ineligible for cisplatin were treated with RT alone or with concurrent weekly carboplatin at a dose of area under the curve ×2.

Brachytherapy

Brachytherapy was delivered based on the traditional anatomy-based Manchester technique. The patient was catheterized, and contrast was injected to the catheter bulb while a radio-opaque marker was inserted into the rectum. Under light sedation, the tandem and ovoids were inserted, followed by packing of the vagina. Dose was prescribed to point A, defined as 2 cm superior and lateral to the cervical os, and point doses to the bladder and rectum were noted, which were kept at $<$ 60% of the dose prescribed to point A.

Patients received one of three brachytherapy fractionation regimens, as decided by the treating oncologist: 16 Gy in two fractions, 21 Gy in three fractions, or 24 Gy in three fractions.

Survival Outcomes

Primary end point was disease-free survival (DFS), defined as the time to development of local, regional, or distant recurrence or death from commencement of EBRT. Loss to follow-up was considered an event, and patients were censored at the date of last follow-up. Patients were reviewed clinically (including per vaginal examination)

every 2 months for the first 2 years and every 3 months thereafter. CT scans were performed only if clinical features were suggestive of local or distant disease recurrence.

Statistical Analysis

Univariable analysis was performed to determine the prognostic significance of the following variables: age, stage, use of concurrent chemotherapy, EBRT dose, brachytherapy dose, total biologic effective dose, and time to completion of treatment (dichotomized at 60 days). The American Brachytherapy Society recommendation is to complete treatment 56 days from commencement of EBRT. We chose a pragmatic cutoff of 60 days (2 months) to account for the variation of a few days that could have occurred because brachytherapy was delivered in weekly fractions. In the univariable analysis, the log-rank test was used to determine statistical significance of categorical variables, whereas for continuous variables, the univariable Cox proportional hazards model was used. The hazard ratios of variables achieving significance were determined using the Cox proportional hazards model. Factors significant on univariable analysis were included in multivariable analysis using the multivariable Cox proportional hazards model. Associations between age, dose of EBRT, and dose of intracavitary brachytherapy and treatment toxicity were determined.

Ethical Approval

The study was approved by the Ethical Review Committee of the Postgraduate Institute of Medicine of the University of Colombo, Colombo, Sri Lanka.

RESULTS

Clinical and brachytherapy treatment records of 242 patients were reviewed. Complete data were available for 113 patients who had completed the prescribed course of EBRT and brachytherapy. Clinicopathologic and treatment characteristics of the study population are listed in Table 1. Mean age at diagnosis was 58 years (range, 35-85 years). Most patients presented with stage IIB (46%) or IIIB (35%) disease, and 91% (n = 103 of 113) received concurrent chemoradiotherapy. Most patients received concurrent weekly cisplatin, with five of 103 patients treated with weekly carboplatin. Median time to completion of brachytherapy from commencement of EBRT was 110 days (range, 34-187 days), with only 12 patients (11%) completing within 60 days. There were no significant delays in completing EBRT, with 105 (93%) of 113 patients finishing treatment within 3 days of the scheduled date.

TABLE 1. Clinical and Pathologic Characteristics of Study Cohort

Characteristic	No. (%)
Age, years	
Mean	58
Range	35-85
Disease stage at presentation	
IB	7 (6)
IIA	3 (3)
IIB	52 (46)
IIIA	9 (8)
IIIB	40 (35)
IVA	2 (2)
Histopathologic type	
Squamous cell carcinoma	73 (64)
Adenocarcinoma	11 (10)
Not available	29 (26)
Brachytherapy regimen, Gy in No. of fractions	
16 in two	62 (55)
21 in three	31 (27)
24 in three	20 (18)
EBRT regimen, Gy in No. of fractions	
45 in 25	6 (5)
46 in 23	30 (26)
50 in 25	42 (38)
50.4 in 28	31 (27)
Other	4 (4)
Total equivalent dose delivered in 2-Gy fractions, Gy_{10}[a]	
68-72.9	21 (19)
73-77.5	55 (49)
77.6-82	18 (16)
82.1-86.5	19 (16)
Concurrent chemotherapy	
Yes	103 (91)
No	10 (9)
Treatment duration, days[b]	
< 60	12 (11)
60-90	21 (19)
90-120	49 (43)
> 120	31 (27)

Abbreviation: EBRT, external-beam radiotherapy.
[a]α/β = 10 Gy.
[b]From start of EBRT to completion of brachytherapy.

Median duration of follow-up was 27 months (range, 5-60 months). DFS for the whole population is depicted in Figure 1, and DFS with the population dichotomized by time to completion of treatment at 60 days is shown in Figure 2. The 2-year DFS for the whole cohort was 63.7% (95% CI, 55.4% to 73.2%). Among patients completing treatment within 60 days, 2-year DFS was 91.7% (95% CI, 77.3% to 100%), in comparison with 60.4% (95% CI, 51.6% to 70.7%) in patients requiring > 60 days to complete treatment. Although it did not reach statistical significance, numerically inferior DFS was seen in

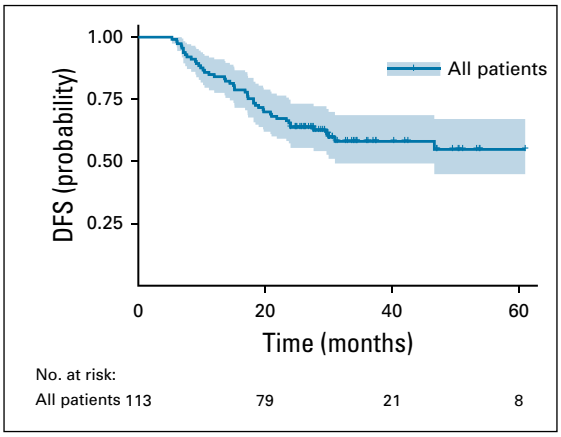

FIG 1. Disease-free survival (DFS) of the whole cohort.

patients with stage ≥ IIIB disease, as shown in Figure 3 (60.9% *v* 68.9%; log-rank *P* = .19).

Results of the univariable analysis of DFS are summarized in Table 2. Treatment delay (dichotomized at 60 days to completion of treatment) was the only significant factor, and therefore, multivariable analysis was not performed. We performed an exploratory analysis of treatment delay as a continuous prognostic variable, but it was not significant (*P* = .11). Because the *P* value for stage on univariable analysis was .12, another exploratory analysis was performed with a survival model fitting stage and treatment delay, but neither stage (*P* = .19) nor treatment delay (*P* = .08) was significant.

Patients who completed treatment within 60 days had superior survival, and we proceeded to compare the distribution of clinical and prognostic variables between the two groups, which did not reveal any significant differences, as shown in Table 3.

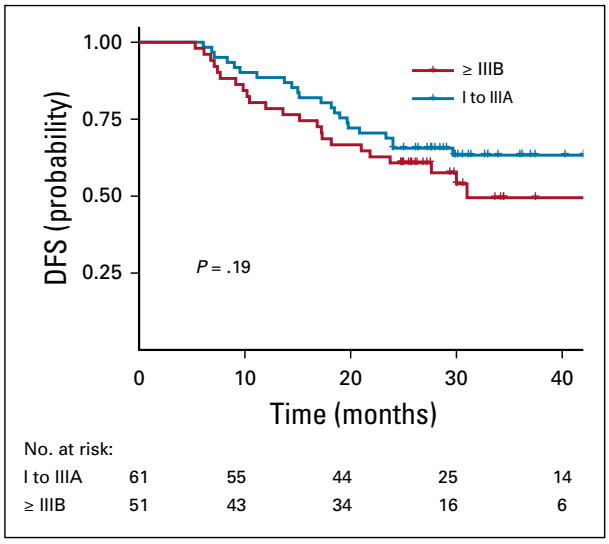

FIG 3. Disease-free survival (DFS) by disease stage.

Because an overwhelming proportion of patients (n = 103 of 113) received concurrent chemotherapy along with EBRT, we performed an exploratory analysis of survival after excluding patients treated with RT alone. The results of this analysis are summarized in Table 4, and they are in broad conformity with the results of the whole cohort.

Eight patients were lost to follow-up, and site of relapse could be determined in 31 patients. As shown in Figure 4, most patients experienced local or regional relapse.

Overall, only nine (8%) of 113 patients had documented evidence of grade ≥ 3 toxicity, as defined by the Common Toxicity Criteria. Two patients (2%) developed grade 3

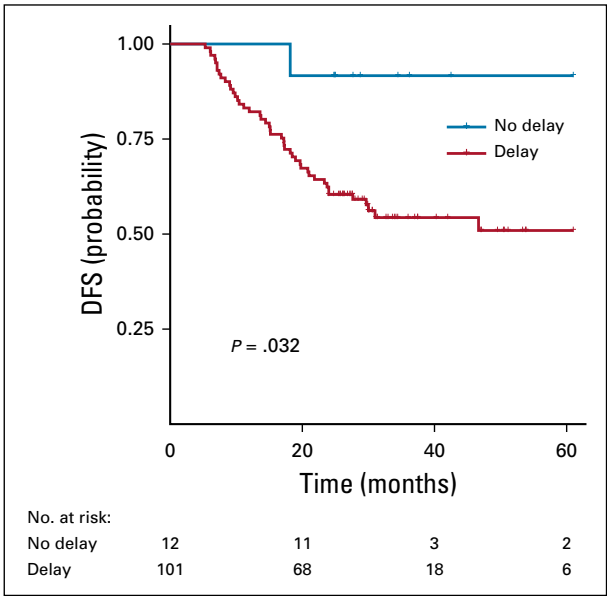

FIG 2. Disease-free survival (DFS) dichotomized by treatment delay.

TABLE 2. Univariable Analysis of Prognostic Variables Associated With DFS

Prognostic Variable	HR	*P*
Age	—	.52
Stage	—	.12
Concurrent chemotherapy	—	.55
Brachytherapy dose	—	.18
EBRT dose	—	.33
Total equivalent dose delivered in 2-Gy fractions[a]	—	.41
Treatment duration (continuous variable)[b]	—	.11
Treatment duration (dichotomized at 60 days)[b]	6.5	.03
	95% CI 2.7 to 15.6	

Abbreviations: EBRT, external-beam radiotherapy; DFS, disease-free survival; HR, hazard ratio.

[a]α/β = 10 Gy.

[b]Time from start of EBRT to completion of brachytherapy.

TABLE 3. Comparison of Known Prognostic Variables in Patients With and Without Treatment Delay

Variable	No. (%) Treatment Duration (days)[b] < 60	> 60	P[a]
Age, years			.61
Median	57	58	
Range	48-65	35-85	
Disease stage at presentation			.9
IB, IIA, or IIB	5 (42)	57 (58)	
IIIA, IIIB, or IVA	7 (58)	42 (42)	
Histopathologic type			.1
Squamous cell carcinoma	6 (50)	67 (66)	
Adenocarcinoma	3 (25)	8 (8)	
Not available	3 (25)	26 (26)	
Brachytherapy regimen, Gy in No. of fractions			.77
16 in two	6 (50)	56 (55)	
21 in three	—	31 (31)	
24 in three	6 (50)	14 (14)	
EBRT regimen, Gy in No. of fractions			.67
45 in 25	—	6 (6)	
46 in 23	2 (17)	28 (28)	
50 in 25	7 (58)	35 (35)	
50.4 in 28	3 (25)	28 (28)	
Other	—	4 (4)	
Concurrent chemotherapy			.99
Yes	11 (92)	92 (91)	
No	1 (8)	9 (9)	

Abbreviation: EBRT, external-beam radiotherapy.

[a]*t* test was performed for continuous variables; χ^2 and Fisher's exact tests were used for categorical variables.

[b]From start of EBRT to completion of intracavitary brachytherapy.

TABLE 4. Univariable Analysis of Prognostic Variables Associated With DFS in Patients Receiving Concurrent Chemotherapy

Prognostic Variable	HR	P
Age	—	.39
Stage	—	.3
Brachytherapy dose	—	.6
EBRT dose	—	.6
Total equivalent dose delivered in 2-Gy fractions[a]	—	.6
Treatment duration (continuous variable)[b]	—	.07
Treatment duration (dichotomized at 60 days)[b]	5.7	.05
	95% CI 1 to 41.6	

Abbreviations: EBRT, external-beam radiotherapy; DFS, disease-free survival; HR, hazard ratio.

[a]α/β = 10 Gy.

[b]Time from start of EBRT to completion of brachytherapy.

bladder toxicity, and seven patients (6%) developed grade 3 rectal toxicity. Bladder toxicity numbers were insufficient to make any determination on association with treatment regimen, and Fisher's exact test did not reveal a significant association between rectal toxicity and brachytherapy dose (P = .6) or EBRT dose (P = .9).

DISCUSSION

In this study, we report for the first time to our knowledge survival outcomes of a cohort of patients with localized cervical cancer treated with radical EBRT and intracavitary brachytherapy in Sri Lanka. An important finding in our study was the negative prognostic impact of treatment delay. This is further confirmed by the fact that there was no substantial difference in the distribution of prognostic variables in those experiencing treatment delay in comparison with those completing treatment on time, as summarized in Table 3.

In cervical cancer, the phenomenon of accelerated repopulation, where surviving clonogenic tumor cells begin to repopulate faster during treatment than at disease outset, is known to occur.[10] This process is widely held to begin approximately 3 to 4 weeks after commencement of therapy, when tumor shrinkage creates a permissive environment for rapid tumor cell proliferation.[10,11] Median time to completion of treatment was 108 days, with some treatments extending beyond 6 months. Indeed, just one in six patients was able to complete the brachytherapy course within 60 days of commencement of EBRT, and patients whose treatment was delayed were six times more likely to develop recurrence.

In relative terms, Sri Lanka possesses an adequate RT workforce of radiation oncologists, physicists, and therapeutic radiographers. However, securing government funding for expanding RT resources, including brachytherapy equipment, remains challenging. Our results indicate that expanding resources to deliver brachytherapy in Sri Lanka is an urgent need, because presently, only two centers in the country have the facilities to ensure its delivery.[12] In addition, improving workflows along the referral, registration, and treatment pathways as well as optimizing human resources could reduce treatment delays by ensuring better use of existing facilities.

More than half of all patients in our study received two brachytherapy fractions of 8 Gy each, which is radiobiologically suboptimal to some of the more standard regimens; this is a major limitation of our analysis. Because of the scarcity of resources, a two-fraction regimen is preferred by many clinicians, and because EBRT was delivered in the cobalt unit, there was a reluctance to increase the fractional dose to 9 Gy, arising from concerns about increased toxicity. However, some clinicians opted to

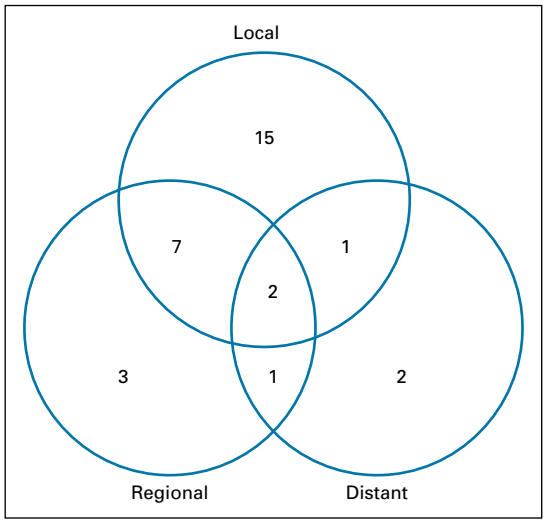

FIG 4. Patterns of disease recurrence.

deliver three fractions of 7 to 8 Gy each, and there was no difference in either outcome or toxicity between these regimens, further highlighting the significant impact of treatment delay.

In light of our findings, it would seem prudent to adopt the two-fraction brachytherapy regimen of 9 Gy each (9 Gy × 2) rather than regimens involving ≥ three fractions, because this would ensure more patients could be treated with existing resources. Another approach to ensure resource optimization is the delivery of multiple fractions (7-8.5 Gy × 3) using a single application, which would improve treatment compliance versus the current practice of weekly applications. More studies are needed to determine the optimal brachytherapy fractionation regimen in resource-limited settings.

Although in our study there was no significant difference in outcome between brachytherapy fractionation regimens, a recently concluded randomized controlled trial sponsored by the International Atomic Energy Agency (IAEA) and conducted in low- to middle-income countries revealed that four fractions (7 Gy × 4) of brachytherapy were superior to two fractions (9 Gy × 2) in terms of locoregional control and DFS.[13] In this study, which has been reported only in abstract form, there was 10% improvement in locoregional control (88% *v* 78%) in favor of the four-fraction regimen. However, there was no difference in overall survival between treatment arms.[13]

There could be a number of reasons as to why the results of our study are at variance with those of the IAEA trial. First, in our study, few patients completed treatment within the recommended timeframe. The significant delays in delivery of brachytherapy would have rendered irrelevant any gains achieved with dose escalation. Second, in terms of biologic dose, the regimens used in the IAEA trial had greater differences than in our study. Third, patients with stage IB, IIA, IIIA, or IVA disease were excluded from the IAEA trial, which was restricted to patients with stage IIB or IIIB disease. In patients with stage IIB or IIIB disease, dose of brachytherapy would play a more pivotal role because of lateral spread of disease, in comparison with patients with stage IIA, IIIA, or IVA disease, where the spread is predominantly in the superior-inferior plane. The IAEA study was a 2 × 2 factorial trial that randomized the use of concurrent chemotherapy in addition to a fractionation regimen, resulting in only half of all patients receiving chemotherapy, as opposed to 90% of patients in our cohort.

It is also pertinent to note that the rates of locoregional control were significantly lower in our study than in the IAEA trial. At 2 years, our study reported locoregional control of 64%; it ranged from 78% to 88% at 5 years in the IAEA trial. These findings reinforce the highly detrimental impact of treatment delay on tumor control, and attempting to focus on dose escalation without ensuring timely treatment is an exercise in futility.

The benefit of concurrent chemotherapy in patients with cervical cancer has been well established by a meta-analysis, which showed a 6% gain in absolute survival, and by a recent clinical trial conducted in India, which revealed an 8% gain in overall survival.[14,15] However, in the IAEA trial, concurrent chemoradiotherapy did not improve either locoregional control or overall survival.[12] In our study, too, the use of concurrent chemoradiotherapy was not associated with any improvement in survival.

Tumor stage was not a significant prognostic factor in our data set, even though patients with stage ≥ IIIB disease had a numerically inferior outcome. Although the small sample size undoubtedly contributed to the failure to reach statistical significance, it is worth noting that patients with stage ≥ IIIB disease whose tumor had progressed to a state when radical treatment was no longer feasible at the time of delivering brachytherapy were excluded from the study.

Regarding treatment toxicity, our data are similar to those of other reported studies in terms of rectal toxicity, despite some patients receiving EBRT with anterior-posterior beam parallel opposed fields in cobalt teletherapy units. However, because our study was a retrospective analysis, toxicity data may have been underreported. As in the case of tumor control, delayed treatment with brachytherapy would have permitted some recovery of normal tissue, which could translate into lower rates of overt clinical toxicity.

Apart from the fact that our study was a retrospective analysis with a small sample size, there were additional limitations. Missing records and data resulted in study exclusion of more than half of the patients, which may have resulted in an overestimation of survival. Long delays made it inevitable that many patients would not have received brachytherapy, and these patients were excluded from the study. Patients are referred to the National Cancer Institute for intracavitary brachytherapy from regional centers throughout the country. Given the retrospective nature of our study and the absence of uniform clinic records, it was

not possible to determine the survival of these patients or the reasons for treatment default. However, given the large number of missing data, a prospective outcome-tracking study is urgently needed to delve deeper into the causes and effects of treatment default.

In summary, our data suggest that treatment delay is the single most important prognostic factor in patients with cervical cancer treated with radical EBRT and intracavitary brachytherapy, making expanding facilities to deliver brachytherapy an imperative need to improve outcome.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

1. National Cancer Control Programme, Ministry of Health, Sri Lanka: Cancer Incidence Data Sri Lanka 2014. http://www.health.gov.lk/moh_final/english/public/elfinder/files/publications/2018/Cancer%20Incidence%20in%20Sri%20Lanka%20-2014.pdf
2. Singh GK, Azuine RE, Siahpush M: Global inequalities in cervical cancer incidence and mortality are linked to deprivation, low socioeconomic status, and human development. Int J MCH AIDS 1:17-30, 2012
3. Burd EM: Human papillomavirus and cervical cancer. Clin Microbiol Rev 16:1-17, 2003
4. Karunaratne K, Ihalagama H, Rohitha S, et al: Human papillomavirus prevalence and type-distribution in women with cervical lesions: A cross-sectional study in Sri Lanka. BMC Cancer 14:116, 2014
5. Partridge EE, Abu-Rustum NR, Campos SM, et al: Cervical cancer screening. J Natl Compr Canc Netw 8:1358-1386, 2010
6. Shivanthan MC, Arunakiri K, Wickramasinghe SI, et al: Low uptake of Pap smear testing among medical clinic attendees in a tertiary care hospital in Sri Lanka. Int Health 6:138-143, 2014
7. Witharana C, Wijesiriwardhana P, Jayasekara K, et al: Awareness of female malignancies among women and their partners in Southern Sri Lanka and implications for screening: A cross sectional study. BMC Public Health 15:1179, 2015
8. Colombo N, Carinelli S, Colombo A, et al: Cervical cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 23:vii27-vii32, 2012 (suppl 7)
9. Nag S, Erickson B, Thomadsen B, et al: The American Brachytherapy Society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys 48:201-211, 2000
10. Fyles A, Keane TJ, Barton M, et al: The effect of treatment duration in the local control of cervix cancer. Radiother Oncol 25:273-279, 1992
11. Fowler JF: 21 years of biologically effective dose. Br J Radiol 83:554-568, 2010
12. Joseph N, Gunasekera S, Ariyaratne Y, et al: Clinical oncology in Sri Lanka: Embracing the promise of the future. Int J Radiat Oncol Biol Phys 105:466-470, 2019
13. Hendry J, Jones GW, Mahantshetty UM, et al: Radiobiological analysis of outcomes using external beam radiotherapy plus high dose-rate brachytherapy (4x7 Gy or 2x9 Gy) for cervical cancer in a multi-institution trial. Int J Radiat Oncol Biol Phys 99:1313-1314, 2017

14. Vale C, Tierney JF, Stewart LA, et al: Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: A systematic review and meta-analysis of individual patient data from 18 randomized trials. J Clin Oncol 26:5802-5812, 2008
15. Shrivastava S, Mahantshetty U, Engineer R, et al: Cisplatin chemoradiotherapy vs radiotherapy in FIGO stage IIIB squamous cell carcinoma of the uterine cervix: A randomized clinical trial. JAMA Oncol 4:506-513, 2018