^{60}Cobalt vs. linear accelerator in the treatment of locally advanced cervix carcinoma: a comparison of survival and recurrence patterns

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Summary

Objective: To compare the survival and recurrence patterns of patients with locally advanced cervical carcinoma treated with ^{60}cobalt radiotherapy units and linear accelerators.

Methods: Two hundred and forty-eight patients with cervical carcinoma stages IIB-IVA who were treated with primary irradiation between the years 1985 and 1988 comprised the study group. The median survival of patients treated with ^{60}cobalt units and linear accelerators was calculated using the method of Kaplan and Meier and compared using the log-rank test. Recurrence patterns were compared using chi-square analysis; $p < .05$ was considered significant for all tests.

Results: One hundred and ninety-five patients were treated with ^{60}cobalt units (Group 1) and 53 patients were treated with a linear accelerator (Group 2). Group 1 and 2 were similar with regard to mean age and weight, stage distribution, and mean dose to point A. The rate of recurrence was comparable between Group 1 and 2 (65.6% vs. 64.2%) and no significant difference was found in overall survival between the groups (20 months vs. 21 months, $p = 81$). There was a trend toward increasing pelvic recurrence in Group 1 (50.8%) compared to Group 2 (35.8%, $p = .08$).

Conclusions: ^{60}Cobalt units and linear accelerators offer comparable rates of overall survival in patients with locally advanced cervix carcinoma.

Key words: Cervical carcinoma; ^{60}Cobalt; Linear Accelerator; Survival.

Introduction

Carcinoma of the cervix in the sixth most common solid malignant neoplasm in American women. The American Cancer Society estimates there were 15,800 new cases diagnosed and 4,800 deaths attributed to the disease in 1995 [1]. Pelvic radiotherapy is the standard treatment for patients with locally advanced cervical cancer (stages IIB-IVA). This radiation is delivered through a combination of teletherapy (external beam irradiation) and brachytherapy (intracavitary irradiation). The external beam portion of the radiotherapy may be delivered using a variety of radiotherapy units including ^{60}cobalt units, betatron accelerators, and medical linear accelerators.

There has been a progressive decrease in the use of ^{60}cobalt radiotherapy units in the United States since the introduction of the medical linear accelerator (Linac) in the 1950's. Linac now accounts for more than 60% of the operational radiotherapy units in the United States and nearly 90% of newly installed units [2, 3]. This change toward more complex and expensive technology has been fueled by expectations of decreased morbidity and improved survival associated with the higher energy linear accelerators. Linac has the capability to deliver radiation at a greater depth with less spread to normal surrounding tissues while providing a more homogenous dose distribution in the central pelvis [4]. Few studies, however, have addressed the impact of increased beam energy on survival in locally advanced cervix cancer. In 1969, Allt [5] compared survival in patients treated with ^{60}cobalt and a 22 MeV betatron unit. A statistically significant improvement in survival was demonstrated for patients with stage III disease treated with the betatron unit. Similarly, Hanks *et al.* [6] reviewed the Patterns of Care Study data between 1972 and 1979 and found that centers using a Linac or betatron unit had a significantly lower recurrence rate compared to centers using ^{60}cobalt only (14% vs. 21%). The purpose of the current study was to compare the median survival and recurrence patterns of patients with locally advanced cervical cancer treated with ^{60}cobalt and a Linac at our institutions.

Materials and Methods

Two hundred and forty-eight patients with cervical carcinoma, stages IIB-IVA who were treated with primary irradiation between the years 1985 and 1998 comprised the study group. Pertinent data was abstracted from the tumor registry, tumor board notes, and radiation oncology discharge summaries. This included demographic information as well as information regarding radiation treatment time, type of radiotherapy unit used, total dosage to point A, use of chemosensitization, recurrence pattern and survival. The median survival of patients treated with ^{60}cobalt units and Linac were calculated using the method

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of Kaplan-Meier [7] and compared using the log-rank test. The frequency and type of recurrence were also compared between the two groups using a chi-square analysis; $p < .05$ was considered significant for all tests.

Radiation Therapy Technique

A standard pelvic radiation technique was used which combined external beam radiation delivered through four fields followed by intracavitary radiotherapy utilizing cesium and a Fletcher-Suit applicator. The borders of the anterior-posterior pelvic portal for external beam radiotherapy were the L4-L5 interspace, a 2 cm margin lateral to the medial aspect of the bony pelvis, and the lower border of the obturator foramen. This standard field was adjusted in selected cases to cover sites of known or suspected disease. In cases of extended field radiation the superior border of the pelvic portal was extended to the L1-L2 interspace with a width of approximately 10 cm. All patients underwent pretreatment simulation. A daily dose of 180 cGy was delivered 5 days per week using a source to skin distance of 80 cm. Concomitant chemotherapy was administered during the external beam portion of the radiotherapy in 58% of patients. Single agent cisplatinum was the most commonly used agent (27%) while cisplatinum/5 flourouracil (9.7%), hydroxyurea (5.9%), and other regimens (11.7%) were used in the remainder of patients.

Table 1. — *Stage distribution of patients treated with Cobalt vs. Linac.*

	Cobalt	LINAC	Total
Stage II	79	20	99
	40.5%	37.7%	39.9%
III	102	26	128
	52.3%	49.1%	51.6%
IV	14	7	21
	7.2%	13.2	8.5%
Total	195	53	248
	100.0%	100.0%	100.0%

Chi-square (2) = 1.95, p = .38.

Table 2. — *Comparison of radiation dose, treatment time, and chemosensitization use in patients treated with ^{60}Cobalt and LINAC.*

	^{60}Cobalt	LINAC	p value
Dose to Point A	4480 cGy	4782 cGy	*.22
Treatment Time (weeks)	11	8	*.002
Chemosensitization	54.8%	73.4%	**.01

* Independent Sample T-test; ** Chi-Square test.

Results

One hundred and sevently-eight (71.8%) of the patients were African American or of Caribbean descent. Thirty-five patients (14.1%) were Hispanic and the remainder were either Caucasian (11.3%) or of other ethnicities (2.8%). Of the 248 patients in the study group, 195 patients were treated with ^{60}cobalt (Group 1) and 53 patients were treated with Linac (Group 2). All patients in Group 1 were treated at Kings County Hospital and received 1.25 MeV γ irradiation. All patients in Group 2 were treated at SUNY-Health Science Center at Brooklyn. Twenty-six patients in Group 2 (49%) received high-energy megavoltage (25 MeV irradiation) while the remainder received low-energy megavoltage (4-6 MeV). There was no significant difference in the mean age (54.3 vs. 53.9 years) or weight (149.9 vs. 156.3 lbs.) of patients in Groups 1 and 2, respectively. Table 1 illustrates the similar stage distribution within each group. Overall, 51% of patients were stage III, 40% were stage II, and 9% were stage IV. Table 2 outlines the mean dose to point A, overall treatment time in weeks, and frequency of chemosensitiziation for Group 1 and 2. Patients in Group 1 had significantly longer overall treatment time (11 weeks vs. 8 weeks, p = .002) and received significantly less chemosensitization (54.8% vs. 73.4%, p = .01) when compared to patients in Group 2. The mean follow-up of patients in Group 1 was 56 months compared to 35 months for patients in Group 2 (p = .04).

The rate of overall recurrence was similar for patients in Group 1 and 2 (65.6% vs. 64.2%, respectively). Linac appeared to offer superior pelvic control compared to ^{60}cobalt (Table 3), however the difference was not statistically significant. There was a trend toward increasing pelvic recurrence in Group 1 (50.8%) compared to Group 2 (35.8%). Conservely, distant recurrence was seen more frequently in Group 2 (22.6% vs. 12.8%, respectively).

Figure 1 shows the cumulative survival for patients in Group 1 and Group 2. The median survival of patients treated with ^{60}cobalt was 22 months compared to 20 months for patients treated with Linac (p = .54). Stratification by stage revealed no significant difference in median survival between Group 1 and 2 for patients with stage II (Figure 2) or stage III disease (Figure 3). There was no significant difference in median survival between patients treated with 25 MeV Linac and cobalt units (25 months vs. 20 months, p = .32).

Discussion

Prior to the 1940's radiotherapy for carcinoma of the cervix was delivered mainly through X-rays in the 200-400 KV range. Treatment with these units was often complicated by desquamation over the treatment area as well as late complications in bone because of increased bone absorption. The development of nuclear reactors in the 1940's, which offered the ability to produce ^{60}cobalt in a cost-effective manner, and the development of linear accelerators in the 1950's caused major changes in the delivery of radiotherapy for cervix cancer in the United States. Montana and co-workers [8] reviewed the Patterns of Care Process Survey data from 1978 to 1989 and found that the number of treatment centers utilizing ^{60}cobalt units decreased from 35% to 2% while those utilizing linear accelerators increased (52% to 95%) over the same period. Clinicians and researchers reasoned that the improvement in dose distribution would allow a higher dose to be delivered to the tumor than surrounding normal structures and that this change would translate into improvements in survival and toxicity. The findings

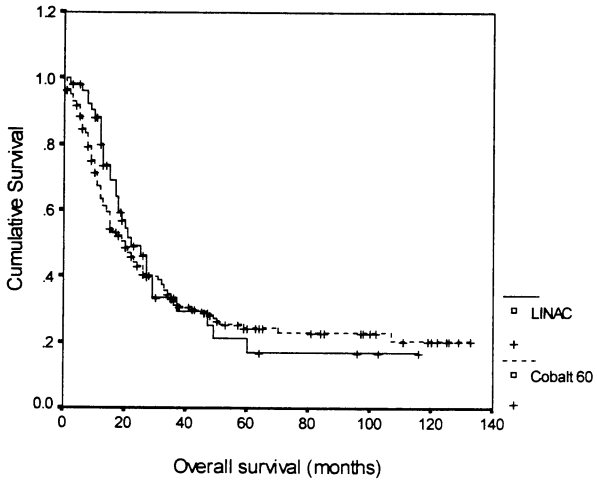

Figure 1. — Overall survival of patients with locally advanced cervical cancer treated with Linac vs. ^{60}Cobalt

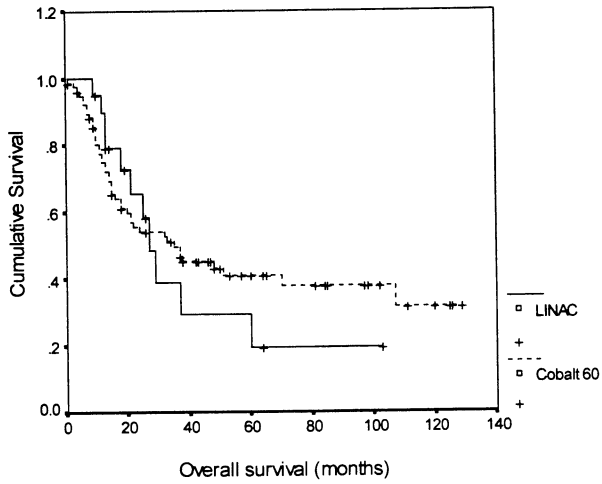

Figure 2. — Overall survival of patients with stage II cervical cancer treated with Linac vs. ^{60}Cobalt.

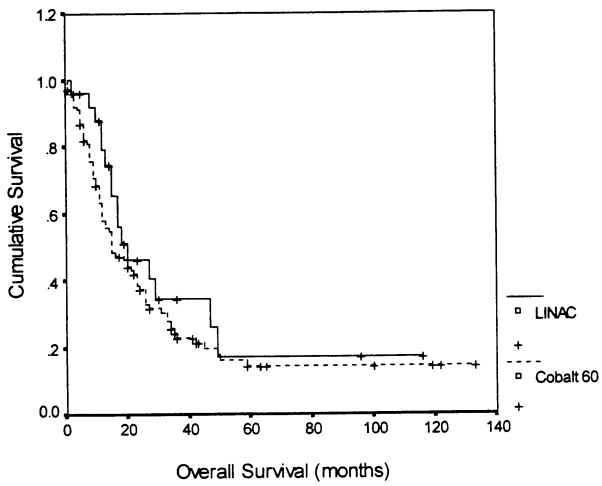

Figure 3. — Overall survival of patients with stage III cervical cancer treated with Linac vs. ^{60}Cobalt.

of Allt [4], Bush [9], and Jons [10] supported this reasoning. These authors demonstrated a significant improvement in survival for cases of locally advanced cervix carcinoma treated with megavoltage energy as compared to orthovoltage energy.

The findings of the current study, however, failed to demonstrate a significant survival advantage for patients with locally advanced cervical cancer treated with linear accelerators ranging from 4 to 25 MeV in energy compared to those treated with ^{60}cobalt. The study groups were similar in age, weight, stage distribution, and dose of external beam radiation delivered. Stratification by stage failed to identify a survival advantage for stage II or III disease associated with the use of Linac. These findings may be explained by the fact that both groups received similar doses of external beam irradiation and had similar radiation field sizes. In the study by Allt [4], the patients treated with the betatron unit received radiation to slightly larger fields than that used in the ^{60}cobalt treatment plan. It was suggested by the author that the higher dose of radiation to the region adjacent to the tumor in the case of the betatron patients probably contributed more to the difference in cure rate observed than differences in the relative biologic effectiveness of the two radiation beams.

It is also possible that the small number of patients treated with high-energy megavoltage in the current study limited the ability to detect a survival advantage associated with the increase in radiation beam energy (only 49% of patients in Group 2 were treated with a 25 MeV Linac). However, when the survival of patients in Group 2 who were treated with a 25 MeV Linac was compared to that of patients in Group 1 no significant difference was found (25 months vs. 20 months, $p = .32$).

Hanks *et al.* [5] reviewed the Patterns of Care Study data and noted that facilities which utilize a Linac or betatron unit have significantly lower recurrence rates when compared to facilities utilizing ^{60}cobalt units only. These authors, however, also noted that facilities utilizing < 80 cm source to skin distance (SSD) ^{60}cobalt units were less likely to have a full-time radiation oncologist, less likely to use pretreatment simulation and had poorer patient follow-up compared to facilities using a betatron or Linac. They concluded "... the linear accelerator itself is not responsible for the relatively better outcome observed, but acts as a surrogate for the medical skill and technical and physics support for treatment that tends to be present in facilities with more sophisticated equipment". The radiation oncology services of Kings County Hospital and SUNY-Health Science Center at Brooklyn are both staffed by full-time radiation oncologists, utilize pretreatment simulation, and provide adequate patient follow-up. These factors may explain the similar clinical outcome of patients treated with ^{60}cobalt and Linac at these institutions.

The use of a Linac was associated with a lower rate of pelvic recurrence when compared to ^{60}cobalt, although the difference did not reach statistical significance. The less frequent use of chemosensitization in patients treated with ^{60}cobalt may account for this difference. Hreshchyshyn *et al.* [11], in a randomized comparison of hydroxyurea or placebo combined with radiation in the treatment of stage IIIB and IV cervical cancer documented improved pelvic control in the patients receiving chemosensitization.

In conclusion, our data indicate that Linac and ^{60}cobalt offer similar survival rates in the treatment of patients with locally advanced cervical carcinoma. The previously demonstrated improvement in survival associated with the use of megavoltage therapy may be explained by differences other than the biologic effectiveness of the radiation beam. In institutions which are staffed with full-time radiation oncologists, utilize pretreatment simulation, and provide adequate patient follow-up, there appears to be no survival benefit associated with Linac over ^{60}cobalt in the treatment of locally advanced cervical carcinoma.

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