
ADENOCARCINOMA OF THE CERVICAL CANCER : RADIATION TREATMENT IN SIRIRAJ HOSPITAL 1993 – 1995

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ABSTRACT

Objective : To evaluate the incidence and the results of the radiation treatment in adenocarcinoma and adenosquamous cell carcinoma of the cervical cancer.

Study design : A retrospective review of 125 patients with adenocarcinoma and adenosquamous cell carcinoma of the cervical cancer who had the primary radiation treatment in between 1993 – 1995.

Result : After the completion the radiation treatment, there were 35 patients (28.0 %) who had residual disease. The median follow up time was 43.5 months, 61 patients (48.8 %) still had no evidence of disease, 16 patients (12.8%) had local recurrence and 23 patients (18.4 %) developed distance metastasis.

Conclusion : The radiation treatment is the primary treatment for stage II and stage III adenocarcinoma of the cervical cancer. The total abdominal hysterectomy is recommended after the completion of radiation treatment to improve the local control. For stage I diseases, radiation treatment can be used as the primary treatment especially for bulky lesions. The adjuvant hysterectomy is also recommended to improve local control. The concurrent chemo-radiation is suggested for locally advanced lesions to improve the tumor control. The adjuvant chemotherapy should be benefit for the residual tumor, which is not suitable for surgery and also recommended for improving the survival in lymph nodes positive patients. Any how, a further study should be done.

INTRODUCTION

Cervical cancer is the most common malignancy in Thailand. The histology type of squamous cell carcinoma is the most common, while adenocarcinoma and the subset, adenosquamous cell carcinoma are relatively rare. The incidences of adenocarcinoma and adenosquamous cell carcinoma of all cervical cancer are only 4-12.6 percent and 2-3.6 percent, respectively. ⁽¹⁻⁵⁾

Due to the number of reports has been limited, the management of adenocarcinoma and adenosquamous cell carcinoma is still controversial. The purpose of this study is to evaluate the

response of primary radiation treatment, especially for stage II and III diseases and stage I that is not suitable for surgical treatment.

MATERIALS AND METHODS

This study was the retrospective review of the 131 patients who came for primary radiation treatment at the Division of Radiation Oncology, Department of Radiology, Faculty of Medicine Siriraj Hospital, between January 1993 to December 1995. The mean age was 47.77 years (range 26-74 years). The clinical staging was applied

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according to the International Federation of Gynecology and Obstetrics (FIGO) classification. Seventeen patients (12.97 %) had stage I, 67 patients (51.14 %) had stage II, 44 patients (33.58 %) had stage III, and 3 patients (2.29 %) had stage IV disease.

The primary radiation treatment planning was the combination of the external radiation 50 Gy in 5-6 weeks and a setting of medium dose-rate (Cesium) intracavitary brachytherapy which the *TDF at point A was 81.* The external beam radiation was given by using Cobalt machine or Linear accelerator (10 MV.) machine, anterior-posterior field technique, 1.8-2 Gy conventional fraction.

The criteria of the results to be studied

*TDF = Time-Dose-Fractionation

*Remark : TDF 81 at point A medium dose-rate (Cesium) intracavitary brachy therapy is equivalent to 2800cGy / 3 weeks external radiation.

Table 1. Stages distribution by histology

	Stage I	Stage II	Stage III
Adenocarcinoma (n = 96)	12 (12.50 %)	51 (53.12 %)	33 (34.37 %)
Adenosquamous cell carcinoma (n = 29)	4 (13.79 %)	15 (51.72 %)	10 (34.48 %)
Total (n = 125)	16 (12.8 %)	66 (52.8 %)	43 (34.4 %)

After the completion of radiation treatment, there were 35 patients who had residual disease (stage I; n = 1, stage II; n = 10 and stage III; n = 24). Fourteen patient (stage II; n = 8 and stage III; n = 6) were treated with a second course of intracavitary radiation after the completion of

were the residual disease, the local recurrence and the distance metastasis.

RESULTS

For the 3 – year period from 1993 – 1995, we excluded 7 patients who did not have complete treatment (Stage I; n = 1, Stage II; n = 1, Stage III; n = 1 and Stage IV; n = 3). This study included 125 evaluated patients. There were 96 patients who had pure adenocarcinoma and 29 patients who had the subset adenosquamous cell carcinoma. Most of the patients were stage II (n = 66) and stage III (n = 43) diseases. There were some of stage I disease who was not suitable for surgery (n = 16). The stage distribution by histology is shown in Table 1.

external radiation within 6-8 weeks. Twelfth patients showed well local control. Four patients who had stage III disease still had residual disease and 3 of them developed distance metastasis. The adjuvant chemotherapy had been used in 16 patients and they all still had residual diseases

after completion of the course of treatment, and 6 of them developed distant metastasis.

Most of the patients were planned to have radiation treatment alone. However, there were 16 patients who have further elective total hysterectomy (stage I; n = 5 and stage II; n = 11) after radiation therapy had been completed. Four patho-

logical sections showed positive microscopic residual disease at the cervix, but all lymph node sampling were negative for malignancy. Eleven patients had no evidence of disease, 3 patients had local recurrence and 2 patients had distant metastasis while the primary site was well controlled. The result of treatment comparing radiation alone and combined radiation and surgery is shown in Table 2.

Table 2. The result of treatment : Radiation alone and combined radiation and surgery.

	Radiation alone		Radiation → Surgery	
	No	Disease control	No	Disease control
Stage I	11	9 (81.81 %)	5	4 (80.00 %)
Stage II	55	30 (54.54 %)	11	7 (63.63 %)
Total	66	39 (59.09 %)	16	11 (68.75 %)

The median follow up time was 43.5 months (range from 2 – 72 months). The patients who were alive without evidence of disease were 61 patients (48.8 %). Thirty-five patients (28.0 %) had residual disease. Sixteen patients (12.8 %) had local recurrence. The median time to recurrence was 21.5 months (ranged from 8 – 42 months). Twenty-three patients (18.4 %) developed distant metastasis. The median time to have distant metastasis was 14 months (range from 2 – 53 months). There were 10 patients who had residual disease and then developed distant

metastasis. The median time to have distant metastasis was 11 months (range from 2 – 30 months). Compared to 13 patients who had distant metastasis with the primary cancer well controlled, the median time to have distant metastasis was 14 months (range from 4 – 53 months). The reported organ metastasis were lung (n = 8), liver (n = 1), bone (n = 1), brain (n = 1), supraclavicular lymph nodes (n = 4) and para-aortic lymph nodes (n = 3). The histology type and the end result of the follow up are shown in Table 3.

Table 3. The histology type and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 96)	28 (29.16 %)	12 (12.50 %)	17 (17.70 %)	48 (50.00 %)
Adenosquamous cell carcinoma (n = 29)	7 (24.13 %)	4 (13.79 %)	6 (20.68 %)	13 (44.82 %)
Total (n = 125)	35 (28.00 %)	16 (12.80 %)	23 (18.40 %)	61 (48.80 %)

For stage I disease, the median follow-up time was 44 months (ranged from 1 – 67 months). The patients who were alive without evidence of disease were 13 patients (81.25 %). One patient had residual disease and 1 patient had local recurrence and 1 patient developed distant metastasis.

For stage II disease, the median follow up time was 43.5 months (range from 2 – 71 months). The patients who were alive without evidence of disease were 37 patients (56.06 %). Ten patients had residual disease and 9 patients had local recurrence and 12 patients developed distant metastasis. One patient had HIV positive and died

at the 24th month after treatment. Two patients had ovarian cancer at the 13th and the 14th month.

For stage III disease, the median follow up time was 43 months (range from 6 – 72 months). The patients who were alive without evidence of disease were 11 patients (25.58 %). Twenty-four patients had residual disease and 6 patients had local recurrence and 10 patients developed distant metastasis. Two patients had febrile sepsis and died at the 2nd and the 6th month during the courses of palliative chemotherapy. One patient had breast cancer at the 25th month. The stage distribution by histology and the end result of the follow up are shown in Table 4, 5 and 6.

Table 4. Stage I and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 12)	1 (8.3 %)	1 (8.3 %)	1 (8.3 %)	9 (75.0 %)
Adenosquamous cell carcinoma (n = 4)	0 (0 %)	0 (0 %)	0 (0 %)	4 (100 %)
Total (n = 16)	1 (6.25 %)	1 (6.25 %)	1 (6.25 %)	13 (81.25 %)

Table 5. Stage II and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 51)	8 (15.68 %)	7 (13.72 %)	7 (13.72 %)	30 (58.82 %)
Adenosquamous cell carcinoma (n = 15)	2 (13.33 %)	2 (13.33 %)	5 (33.33 %)	7 (46.66 %)
Total (n = 66)	10 (15.15 %)	9 (13.63 %)	12 (18.18 %)	37 (56.06 %)

Table 6. Stage III and the end result of the follow up.

	Residual disease	Local recurrence	Distance metastasis	Disease control
Adenocarcinoma (n = 33)	19 (57.57 %)	4 (12.12 %)	9 (27.27 %)	9 (27.27 %)
Adenosquamous cell carcinoma (n = 10)	5 (50.00 %)	2 (20.00 %)	1 (10.00 %)	2 (20.00 %)
Total (n = 43)	24 (55.81 %)	6 (13.59 %)	10 (23.25 %)	11 (25.58 %)

The tumor size is the important prognostic factor for the treatment of cervical carcinoma. There were 101 patients whose tumour sizes of the primary lesion had been recorded. Thirty-eight patients (37.62 %) had a lesion less than or equal to 3 cm and 78 patients (72.27 %) had a lesion

greater than 3 cm. There was higher chance of residual disease and developed distant metastasis in a lesion greater than 3 cm group. The size of lesions and the end result of the follow up are shown in Table 7.

Table 7. The size of lesions and the end result of the follow up.

Lesion (n = 101)	Residual disease	Local recurrence	Distance metastasis	Disease control
≤ 3 cm (n = 38)	7 (18.42 %)	5 (13.15 %)	4 (10.52 %)	23 (60.52 %)
> 3 cm (n = 73)	16 (21.19 %)	7 (9.58 %)	16 (21.91 %)	33 (45.20 %)

DISCUSSION

From the Tumor Registry, Siriraj Hospital, between 1993-1995 the number of cervical cancer patients was 1786 patients. Among these, 259 patients (14.5%) were adenocarcinoma and 43 patients (2.4%) were adenosquamous cell carcinoma.⁶⁻⁸ The incidence of adenocarcinoma and adenosquamous cell carcinoma appears to be increasing.⁹ It was difficult to draw conclusion about the influence of histology on prognosis. The patients with adenocarcinoma did not have worse prognosis than squamous cell carcinoma.^{10,11} The size of the lesions and the lymph node metastasis were the important prognostic factors. Some

studies showed the evidence that the patients with adenocarcinoma have a poorer prognosis than the patients with squamous cell carcinoma of the same stages.^{4,12,13} The rate of lymph node metastasis and distant metastasis were more commonly found for the patients with adenocarcinoma. The combination of radiotherapy and surgery has been controversy. The survival in patients who underwent adjuvant hysterectomy did not significantly improve and the combination of two modalities was also associated with a relatively high risk of treatment complications.^{12,14}

Among the adenocarcinoma groups, adenosquamous cell carcinoma was considered a subtype of adenocarcinoma. There is no statistical significant difference in survival between adenocarcinoma and adenosquamous cell carcinoma.³ In our study, we found no difference in stage distribution, and response of treatment.

For stage I disease, the radical abdominal hysterectomy and pelvic lymph node dissection has been the primary treatment. Adjuvant whole pelvic irradiation might decrease the risk of local recurrence but did not improve survival.⁹ For the bulky lesions, the regression is more slowly or less completely after radiation treatment alone. The addition of a hysterectomy was helpful to improve the local control but did not improve the survival.^{10,14} From this study, there is no difference in disease control between patients who had adjuvant hysterectomy after radiation treatment compared to patients who had radiation treatment alone. The poor prognosis of stage I disease is associated with the lymph node metastasis.^{2,9,12,15} The 5 year survival fell from 81.3% to 42.7% when tumor had lymph node metastasis.³ The CT-scanning or MRI could detect the lymph nodes metastasis as well as measured the lesion size.¹⁶⁻¹⁷ We suggest to use the CT-scanning or MRI to find the evidence of lymph node metastasis which is the poor prognostic factors of the disease. To date it is unclear which treatment modalities are the most efficacious as adjuvant therapy for stage I disease. The cisplatin – base concurrent chemo-radiation therapy and adjuvant chemotherapy was suggested to improve survival.^{15,18}

For stage II disease, we also recommend adjuvant hysterectomy after the completion of radiation treatment as for stage I disease. The disease control of the combined treatment group was better than that receiving radiation treatment alone. Several authors reported the attempts to improve the outcome of radiation treatment with an extrafascial hysterectomy.^{1,10,14}

For stage III disease and the patient with a lesion greater than 3 cm., we found that most of the patients had the residual disease after the completion of radiation treatment and developed distant metastasis. From many studies, for the locally advanced diseases, the cisplatin – base chemotherapy was suggested to use as concurrent chemo-radiation to improve local control and adjuvant chemotherapy to improve the survival.¹⁹⁻²³

CONCLUSION

The radiation treatment is the primary treatment of the cervical cancer in every histologic type and every stage of disease (except stage I that is suitable for surgery). The adjuvant treatments that might improve the local control and survival should be further investigated in randomized control trial to show the results.

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