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Comparison of The Survival Rate between Squamous Cell Carcinoma and Adenocarcinoma of the Uterine Cervix

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ABSTRACT

Objective To compare the survival rate between squamous cell carcinoma (SCC) and adenocarcinoma (ACA) of the uterine cervix.

Design Retrospective cohort study.

Settings Gynecologic Oncology Division, Radiation Oncology Division. Bangkok Metropolitan Administration (BMA) Medical College and Vajira Hospital, Bangkok,Thailand.

Subjects All patients with cervical carcinoma who were diagnosed and treated in our institute from January 1, 1994 to December 31, 1998.

Methods All medical records and pathological reports were reviewed. The patients who lost to follow up were contacted by telephone, mail, or computerized death data from local registration sector at BMA.

Results Five hundred and seventy three patients were studied. SCC, the most common histologic type, was found in 79.23%. ACA including adenosquamous cell carcinoma and other subtypes consisted of 20.77%. The mean age in ACA group was 47.85 $\pm$ 10.99 years which was significantly lower than 51.15 $\pm$ 11.87 years of SCC group (p=0.006). Most patients (65.9%) with SCC had tumor grade II but patients with ACA were commonly found in grade III(42.0%). Regarding clinical presentation, ACA was found at earlier stages than SCC (p<0.0001). About half of these patients with ACA had tumor characteristics as exophytic mass(56.7%) whereas tumor of patients with SCC were mainly ulceroinfiltrative lesion(56.2%). With the median follow up time of 51 months(range 0 – 110 months), the overall survival of SCC was 61.34% and ACA was 62.27%(p =0.7467). Comparing the survival of SCC and ACA, stage by stage, ACA had poorer survival rate in every stage, with no statistically significant difference.

Conclusion SCC was the most common cell type in cervical carcinoma. The patients with SCC were older, and presented at more advanced stage than patients with ACA. The overall survival of patients with both cell types were not significantly different.

Key words: cervical carcinoma, survival, squamous cell carcinoma, adenocarcinoma

Cervical cancer is the most common cancer found in Thai women. The National Cancer Institute annual report in 1997 revealed about 5,462 new cases of cervical carcinoma per year.[1]

Although the incidence of cervical carcinoma is higher in developing countries including Thailand, most studies regarding natural history, course of disease, treatment and survival rate were brought about in other developed areas. So far, we cannot presume that these data would be the same in our place since many factors such as race, age, stage at diagnosis and treatment modalities might contribute to the difference in nature of disease and treatment outcome.

Squamous cell carcinoma (SCC) is the most common histologic type of cervical carcinoma. It accounts for 67-91% of all cervical carcinoma while adenocarcinoma (ACA) accounts for 8-22%.[2-6] Many authors have found that the survival rate of ACA was significantly lower than SCC, even comparing stage by stage.[2,3] Conversely, Kilgore et al in their matched study of patients with median follow up 7 years, found no statistical difference in survival rate between SCC and ACA ($P > 0.05$).[7]

In this study, we aim to determine the survival rate of ACA of the uterine cervix in comparison with SCC in our institute.

Materials and Methods

All medical records and pathological reports of newly diagnosed cervical cancer patients who were treated in BMA Medical College and Vajira Hospital between 1994 - 1999 were reviewed. All patients were clinically staged according to the International Federation of Gynecology and Obstetrics (FIGO) staging[8] and treated with the same modalities for SCC and ACA. In stage IB – IIA, treatment was mainly surgery or surgery with adjuvant radiation. In stage IIB or more advanced disease, most patients received radiation alone and few recieved concurrent chemoradiation. After treatment, all patients were scheduled for a revisit every three months for two years, every six months for three years, and every year afterward.

Before the end of our study (March 31, 2002), patients who lost to follow up were contacted by telephone or by mail at least twice. We also tried to find whether these patients were dead from the computerized data at the registry section of local administration with permission of the district registrar.

The data was analysed by using SPSS program version 9.0. Descriptive statistics were used for demographic baseline data and summarized as mean with standard deviation (SD) or median with range. Continuous variables were examined for normal distribution (Kolmogorov-Smirnov test) before using parametric statistics. Differences between continuous variables were evaluated with unpaired t-test for variables that were normally distributed and the Mann-Whitney U test for variables that were not normally distributed. Categorical variables were evaluated with Chi-squared test or Fisher's exact test as appropriate. Survival curves were obtained by the Kaplan- Meier method. Differences in survival rates between groups were compared using the Mantel-Haenszel log rank test. The p-value of 0.05 and less were considered as statistical significance.

Results

During the study period (January 1, 1994 to December 31, 1999), there were 573 new cases of cervical cancer who had not received any kind of treatment before coming to our institute. Four hundred and fifty four cases were SCC (79.23%) while 109 cases (19.02%) were ACA, 9cases (1.57%) were adenosquamous cell carcinoma and 1 case (0.18%) was clear cell carcinoma. In this study, we

compared SCC with ACA (including adenosquamouscell carcinoma and clear cell). The characteristics of these patients are listed in Table 1

Table 1. Characteristics of cervical cancer patients

Characteristics	Squamous cell carcinoma (total n = 454)	Adenocarcinoma (total n = 119)	p
Age (years)	n = 454	n = 119	
(mean ± S.D.)	51.15 ± 11.87	47.85 ± 10.99	0.006*
Parity**	n = 319	n = 78	
- nulliparity	12 (3.8%)	6 (7.7%)	0.137†
- 1-3	157 (49.2%)	42 (53.8%)	
- ≥ 4	150 (47.0%)	30 (38.5%)	
Stage	n = 454	n = 119	
- stage I	69 (15.2%)	26 (21.9%)	<0.001 ‡
- stage II	142 (31.3%)	55 (46.2%)	
- stage III	196 (43.2%)	32 (26.9%)	
- stage IV	47 (10.3%)	6 (5.0%)	
Tumor characteristic***	n = 409	n = 104	
- exophytic	179 (43.8%)	59 (56.7%)	0.021§
- ulceroinfiltrative	230 (56.2%)	45 (43.3%)	
Tumor size (mm.)****	n = 454	n = 119	
(mean ± S.D.)	40.98 ± 17.68	37.92 ± 17.01	0.130*
Tumor grade	n = 454	n = 119	
- grade I	111 (24.4%)	22 (18.5%)	<0.001‖
- grade II	299 (65.9%)	47 (39.5%)	
- grade III	13 (2.9%)	50 (42.0%)	
- unspecified	1 (0.2%)	-	
- small cell	30 (6.6%)	-	

*Unpaired t-test .

† Fisher's exact test compare nulliparity with multiparity.

‡ Chi-square test compare stage I+II with III + IV.

§ Chi-square test.

‖ Chi-square test compare gr I + II with gr III

** the data about parity was not available in 176 cases

*** the data about tumor characteristics was not available in 60 cases

****the data regarding tumor size was not available in 128 cases

The mean age of patients with ACA was significantly lower than SCC. Most patients with ACA presented at earlier stages (I + II) than patients with SCC (68.1% compared to 46.5%). The common tumor characteristic type in ACA was exophytic whereas in SCC was ulceroinfiltrative type.

The comparison of the mean age of SCC and ACA stage by stage were demonstrated in table 2. ACA patients in stage III were significantly younger than those with SCC (52.86 ± 12.35 versus 47.22 ± 9.33

years, P = 0.004). In stage II, patients with ACA were also younger than patients with SCC (51.23 ± 10.97 and 48.24 ± 11.22 years, P = 0.089) but with only borderline statistical significance. However, in stage I, there was no difference in the mean age between the two groups(46.39 ± 9.99 and 46.23 ± 11.43 years, P = 0.947). In stage IV, the mean age cannot be compared due to small number of patients with ACA.

Table 2. Distribution of FIGO stage and mean age by histologic type

FIGO stage	Squamous cell carcinoma			Adenocarcinoma			P*
	N	Mean age ± S.D.	95%CI	N	Mean age ± S.D.	95%CI	
Stage I	69	46.39 ± 9.99	43.99-45.79	26	46.23 ±11.43	41.75-50.71	0.947
Stage II	142	51.23 ± 10.97	46.75-55.71	55	48.24 ± 11.22	45.22-51.26	0.089
Stage III	196	52.86 ± 12.35	51.02-54.70	32	47.22 ± 9.33	43.92-50.52	0.004
Stage IV	47	50.79 ± 13.36	46.89-54.69	6	54.67 ± 14.95	42.47-66.87	0.511
Total	454	51.15 ± 11.87	50.03-52.27	119	47.85 ± 10.99	45.83-49.87	0.006

* unpaired t-test

Fourteen cases (2.5%) refused to receive any kind of treatment after staging procedures because they wanted to seek for alternative herbal medicine. Five hundred and ten cases (89%) received complete treatment, while 34 cases (6 %) were lost to follow up before complete treatment was achieved. Twelve cases (2 %) could not tolerate complications and denied to receive further treatment. Three cases (0.5%) continued their treatment at other hospitals.

At the end of the study, 192 cases (33.5%) were dead. There are 288 cases (50.3%) who are still followed up and 93 cases (16.2%) were lost to follow up. With the median follow up time of 51 months (range 0 –110 months), the overall survival rates of SCC (61.3%) and ACA (62.3%) were not different (Fig. 1). When we compared the survival rate, stage by stage, there was a trend that patients with ACA had poorer survival rate than patients with SCC, but these differences were not statistically significant. (Fig. 2 – 5)

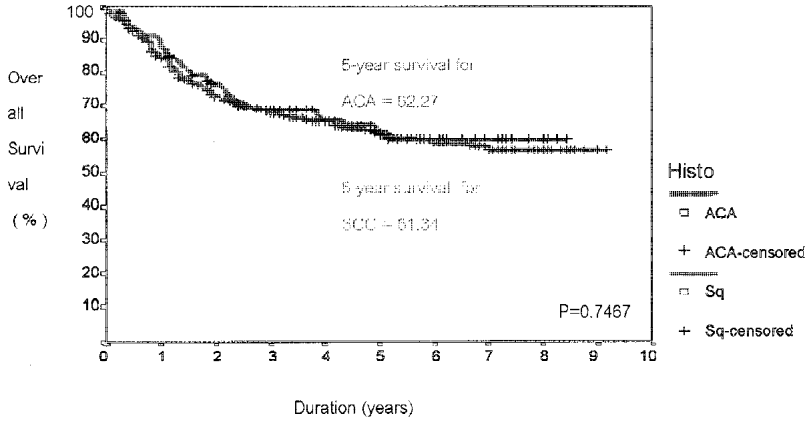

Fig. 1. Overall survival of SCC compared to ACA.

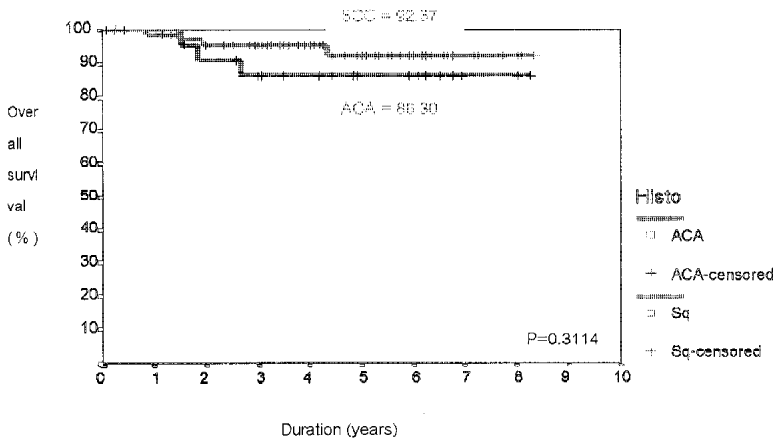

Fig. 2. 5-year survival in stage I of SCC compared to ACA.

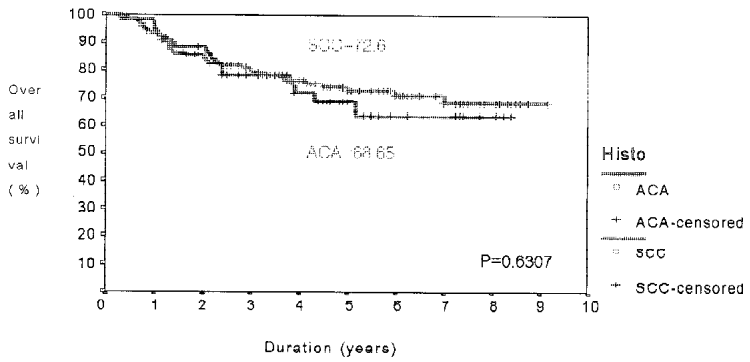

Fig. 3. 5-year survival in stage II of SCC compared to ACA.

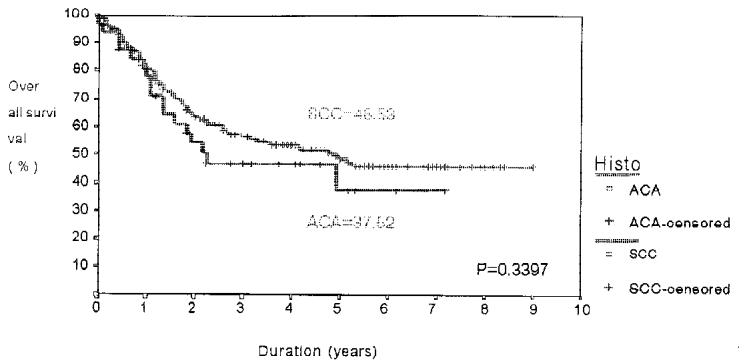

Fig. 4. 5-year survival in stage III of SCC compared to ACA.

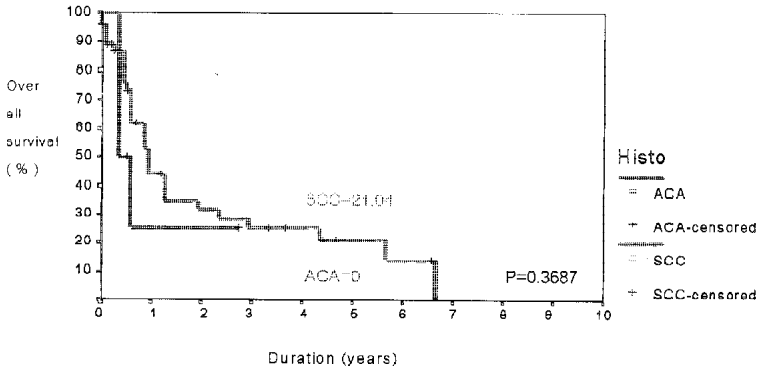

Fig. 5. 5-year survival in stage IV of SCC compared to and ACA.

Discussion

Cervical carcinoma is the most common gynecologic cancer in Thai women. In our institute, cervical cancer accounts for about 80 % of all gynecologic malignancy. SCC is the most common histologic type, accounting for 79.2% of all cervical carcinoma compare to 20.8% of ACA. These incidence are within the range as in other reports.[2-6]

Regarding the age incidence, Herbert et al, in 2001, found that most cases of ACA (59%) aged less than 50.[9] When compared to SCC, there were still conflicting data as Anton-culver et al, in 1992, found mean age of ACA was lower than SCC (47.31 years old versus 50.85 years old)[4] whereas Silcocks et al, in 1987, discovered insignificant difference in mean age of the two groups (58.92 years old of ACA versus 56.21 years old of SCC).[10] From our study, the mean age of patients with ACA was significantly lower than patients with SCC, 47.85$\pm$ 10.99 and 51.15 $\pm$ 11.87 respectively. We also found that patients with ACA presented at earlier stages (stage I and II) than SCC, 68.1% versus 46.5%($p<0.0001$). Other studies, Smales et al, in 1987,[11] Ashby et al, in 1987,[12] and Brewster et al, in 1999[13] found that invasive carcinoma in young women were found in earlier stage than old age group. Ashby found that young women presented in stage IB 64% and 13% in stage II.[11] Kilgore et al in 1988 had reported that patients with ACA were found 80.3% in stage I and 14.2% in stage II.[7] Chen et al also reported in 1997 that 67.2% of patients with ACA were found in stage I and 24.5% in stage II.[14]

About the tumor characteristics, Saigo et al, in 1986, reported that most common characteristics in ACA patients visible abnormality were exophytic mass.[15] From our study, most patients with ACA had exophytic lesion while most patients with SCC had ulceroinfiltrative lesion.

Regarding to tumor differentiation, patients with ACA in our study had higher grade than SCC. Our result was in accordant to that of Hopkin et al[2] and Kilgore et al, in 1988.[7] The latter found that most ACA cases (60.2%) had tumor of either grade II or III. In contrast to Chen et al[14] who reported that more than half of patients with ACA (57.3%) had tumor grade I or II. In relation to parity, Hopkin et al[2] and Silcocks et al[10] found that ACA was associated with nulliparity. Other reports had different findings as Chen et al[14] found multiparity in 85.7% of ACA. From our study, we found no difference concerning the parity of both cell types.

According to the study of Hopkin et al, mean tumor size in our study in both cell types were not different.[2] Shingleton et al found that a large percentage of patients with SCC (63.8%) had tumor size larger than 3 cm.[5]

Regarding the 5–year survival rate, Kjorstad et

al, in 1977, reported a decreased survival of patients with ACA.[16] Silcocks et al,in 1987, also found that the mean survival of SCC was about 2 years greater than that of ACA.[10] Chen et al,in 1999, reported ACA or adenosquamous carcinoma had a lower 5-year survival rate than SCC (66.5%versus 74%, P =0.0009).[3] However there were few authors who found no such different survival in ACA and SCC. Kilgore et al in their matched study of patients with SCC and ACA with median follow up 7 years, found no statistical difference in survival rate (P >0.05).[7] Anton–Culver et al, in 1992, also reported that survival of SCC and ACA was not significantly different (P = 0.76).[4] Generally, patients with earlier stages should have better prognosis than advanced stages. Since there were authors who claimed that ACA were more commonly found at earlier stages,[7,14] so this should have some influence to the survival outcome. Anyway there has been no consensus on this aspect yet. There were studies about survival rate of SCC and ACA at each tumor stage.[2,5] Hopkin et al, in 1991, found that patient with ACA had significantly decrease survival compared to patient with SCC, stage by stage.[2] While Shingleton et al reported no significant difference in 5-year survival among the ACA and SCC in any clinical stage except stage II.[5] From our study, the overall 5–year survival rate were not different between SCC and ACA, despite our patients with ACA were at earlier stages than patients with SCC. However, when we compared the two cell types stage by stage, ACA had poorer 5–year survival rate than SCC but this was not statistically significant.

In conclusion, we cannot confirm any difference in overall survival between these two histologic types of cervical cancer patients due to small number of patients in each group. So, if we want to find out any difference of the survival rate between these two types of cancer, more number of patients are required in each stage before arrival to the conclusion.

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