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Poor Prognosis of Patients with Stage Ib1 Adenosquamous Cell Carcinoma of the Uterine Cervix with Pelvic Lymphnode Metastasis

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From January 1990 to December 2004, the prognosis of 28 patients with stage Ib1 adenosquamous cell carcinoma (ASC) were assessed in comparison with those of matched counterparts of pure adenocarcinoma (ADC) and squamous cell carcinoma (SCC). The mean ages were 46.6, 48.3, and 48.5 years for patients with ASC, ADC, and SCC, respectively. All the patients underwent radical hysterectomy with pelvic lymphadenectomy and postoperative adjuvant therapy was given to the patients with positive pathological risk.

The incidence of lymph node metastasis for ASC at 21.4% was not significantly different from those for ADC (13.6%) and SCC (15.8%). There was also no significant difference in the incidence of lymphatic or vascular space involvement (LVSI) and depth of stromal invasion between three cell types. Since the tumor sizes of all ASC cases examined in this study were less than 4cm, the prognoses were compared among stage Ib1 disease according to the classification system of the International Federation of Gynecology and Obstetrics (FIGO). The overall 5-year survival rates of stage Ib1 ASC, ADC, and SCC were 82.4%, 92.4%, and 94.0%, respectively, suggesting poor prognosis of ASC, but there was no significant difference.

Patients with stage Ib1 ASC were retrospectively assigned to a low- or high-risk group based on the surgical-pathologic factors including positive lymph node metastasis, 2-4cm of tumor size, positive LVSI, and/or deep stromal invasion. While all 9 patients in the low-risk group are alive without disease, 7 of the 19 patients in the high-risk group developed recurrence. The overall 5-year survival rates were 100% for a low risk group and 74.8% for a high-risk group, respectively, but this difference did not reach statistical significance. However, the prognosis of high-risk patients with lymph node metastasis was significantly (p=0.01) worse than low-risk group. The present study suggests that ASC histology appears to carry a poor prognosis than SCC, but low-risk group of stage Ib1 ASC has a good prognosis without postoperative adjuvant therapy.

Adenosquamous cell carcinoma (ASC) is composed of a malignant glandular component and a malignant squamous component and accounts for 5 to 10% of all cervical carcinomas. Recently, pure adenocarcinoma (ADC) of the cervix is increasing in incidence, with a higher

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tendency in the young as compared with squamous cell carcinoma (SCC) (1) and ADC histology is known to carry a poorer prognosis than SCC (2). However, since ASC has been usually treated as one of the histological subtype of ADC, the independent prognosis of ASC has not been well investigated. In this study, the independent prognosis of ASC compared to that of pure ADC and SCC is analyzed by the recent experience of one institution.

MATERIALS AND METHODS

From January 1990 to December 2004, we experienced 39 patients with ASC from stage Ia to IVb. In this study, the prognosis of 28 ASC patients with stage Ib disease was assessed in comparison with those of patients with ADC and SCC of the same stage. All the patients underwent radical hysterectomy with pelvic lymphadenectomy and postoperative adjuvant therapy was given to the patients with one of the combinations of risk factors such as lymph node metastasis, lymphatic or vascular space involvement (LVSI), or 10mm or more deep stromal invasion. Since the tumor sizes of all 28 ASC cases examined in this study were less than 4cm, the prognoses were compared among the stage Ib1 disease (81 patients with pure ADC and 266 with SCC) according to the classification system of FIGO. Of 28 patients with ASC, 4 patients received neoadjuvant chemotherapy consisted of irinotecan (60 mg/m^2) + cisplatin (60 mg/m^2) or irinotecan (100 mg/m^2) + mitomycin C (10 mg/m^2) prior to surgery. Postoperatively, 19 patients with one of the combinations of risk factors received adjuvant therapy; 4 patients received postoperative chemotherapy consisted of cisplatin+adriamycin+cyclophosphamide or etposide+cisplatin and 12 patients received radiation therapy (45-50.4Gy) using external beam of linear accelerator, in which 4 patients received concurrent chemoradiation with weekly nedaplatin.

Furthermore, patients with stage Ib1 ASC were retrospectively assigned to a low- or high-risk group based on the surgical-pathologic factors as defined in Table 3 and prognosis of both groups were compared.

Survival was calculated from the date of surgery to the date of last contact or death. Life tables were computed using the method of Kaplan and Meier. The difference in surgical-pathologic factors and survival was evaluated using log-rank test. P value of 0.05 was used to determine statistical significance.

Table 3. Comparison of low-risk group and high-risk group of ASC stage Ib1 cases

		Adjuvant therapy		Recurrence
Low-Risk group (n=9)	Negative Lymph node metastasis Negative LVSI Tumor size ＜20 mm Stromal invasion ＜ 10 mm (All of the above are required)	+(n=1)		−
		−(n=8)		−
High-Risk group (n=19)	Positive Lymph node metastasis Positive LVSI Tumor size ≧ 20 mm Stromal invasion ≧ 10 mm (Either of the above is required)	+(n=18)	┬	+(n=7) −(n=11)
		−(n=1)		−

LVSI: lymphatic or vascular space involvement

RESULTS

Incidences of the surgical-pathologic risk factors were compared among three histological types (Table 1). The incidence of lymph node metastasis was 21.4% (6/28) for ASC, 13.6% (11/81) for ADC, and 15.8% (42/266) for SCC, suggesting higher incidence in ASC, but there was no significant difference. Positive LVSI was found in 50.0% for ASC, 43.2% for ADC, and 56.8% for SCC, indicating no significant differences among histological types. Tumor size and depth of stromal invasion are listed in Table 2. Since the tumor sizes of all ASC cases examined in this study were less than 4cm, the prognoses were compared among stage Ib1 disease of ADC and SCC.

The overall 5-year survival rates of stage Ib1 patients with ASC, ADC, and SCC were 82.4%, 92.4%, and 94.0%, respectively, suggesting poor prognosis of ASC, but there was no significant difference (Fig 1).

In comparison between high- and low-risk groups of stage Ib1 ASC as defined in Table 3, while all 9 patients in the low-risk group are alive without disease, 7 of the 19 patients in the high-risk group developed recurrence. The overall 5-year survival rates were 100% for the low risk group and 74.8% for the high-risk group, respectively, but this difference did not reach statistical significance(Fig 2). However, the prognosis of high-risk patients with lymph node metastasis was significantly (p=0.01) worse than low-risk group (Table 4, Fig 3).

Table 1. Incidences of the surgical-pathologic risk factors in three histological types of ASC, ADC, and SCC stage Ib1 cases

Histology	Number	Age (Average)	Lymph node metastasis	LVSI
ASC	28	30-61(46.5)	21.4%(6)	50.0%(14)
ADC	81	26-75(48.3)	13.6%(11)	43.2%(35)
SCC	266	22-79(48.7)	15.8%(42)	56.8%(151)

ASC: adenosquamous cell carcinoma
ADC: adenocarcinoma
SCC: squamous cell carcinoma
LVSI: lymphatic or vascular space involvement

Table 2. Tumor size and depth of stromal invasion in stage Ib1 ASC

Tumor size	(n)	stromal invasion	(n)
9 mm ≧	3	5 mm ≧	10
10～19 mm	9	6～ 9 mm	3
20～29 mm	7	10 mm ≦	15
30～39 mm	9		

FIG 1. Five-year overall survival of patients with stage Ib1 cervical carcinoma (ASC, ADC, and SCC)

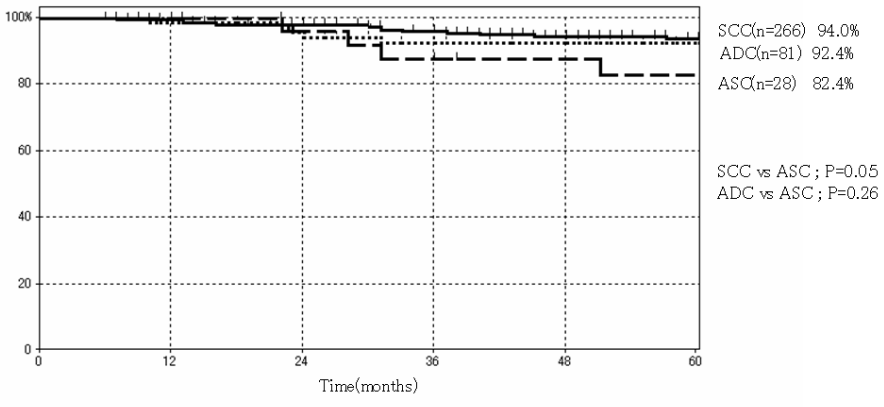


FIG 1

ASC: adenosquamous cell carcinoma
ADC: adenocarcinoma
SCC: squamous cell carcinoma

FIG 2. Five-year overall survival of patients with stage Ib1 ASC by low-risk versus high-risk groups

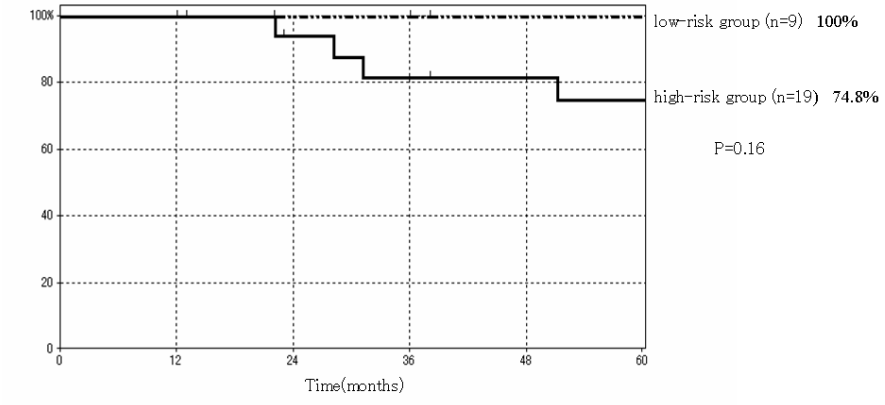


FIG 3. Five-year overall survival of patients with stage Ib1 ASC by positive versus negative lymph node metastasis

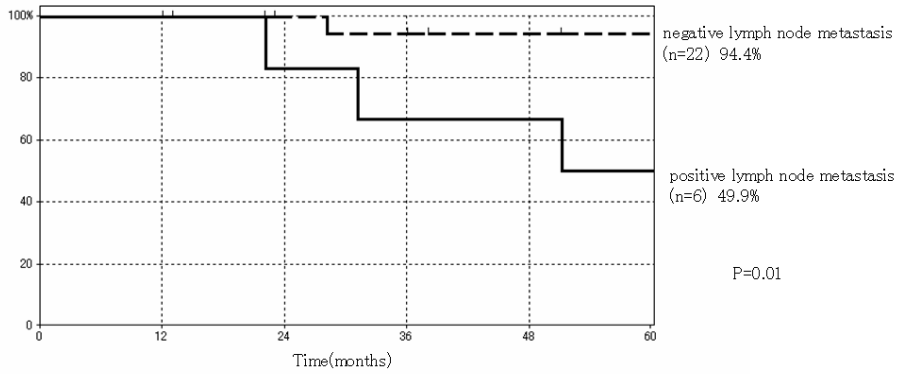


Table 4. Comparison of surgical-pathologic factors and 5-year survival rate of ASC stage Ib1 cases

	5-year survival rate (%)	P value
Positive Lymph node metastasis (n=22)	49.9	0.01
Negative Lymph node metastasis (n=6)	94.4	
Positive LVSI (n=19)	78.7	0.06
Negative LVSI (n=9)	88.9	
Tumor size ≧ 20 mm (n=15)	69.6	0.07
Tumor size <20 mm (n=13)	100.0	
Stromal invasion ≧ 10 mm (n=15)	68.4	0.06
Stromal invasion < 10 mm (n=13)	100.0	

LVSI: lymphatic or vascular space involvement

DISCUSSION

Although the reported prognosis of ASC ranged from better to worse than pure ADC or SCC (6-12), the recent reports emphasized that ASC cell type is more aggressive with a poorer survival rate and atypical presentation than ADC or SCC cell types (13-14).

Gallup et al. found a marked decrease in survival in patients with ASC. The survival for patients with ASC was 20% compared with 83% and 80% respectively, for patients with SCC and with ADC. This decreased survival was significant at all stages of ASC. (9)

Saigo et al. confirmed the hypothesis that lesion size and stage are the significant clinical factors in decreased prognosis for patients with ASC. (10)

Farley et al. (13) compared survival between 88 patients with ASC and 185 patients with ADC. They described that when patients with early-stage (stage I) were examined separately, there was no statistically significant difference in the 5-year survival (ASC, 85%; ADC, 89%). However, when patients with advanced-stage disease (stage II-IV) were analyzed, ASC was associated with a significant decrease in median and overall survival as demonstrated in previous reports. (9-12) They concluded that ASC histology appears to be an independent predictor of poor outcome in patients with advanced cervical carcinoma and this decreased survival may be related mainly to the histological grade of ASC.

Lea et al. (14) investigated poor prognostic factors of 230 patients with stage Ib1 cervical adenocarcinoma including 65 patients with ASC histology. Patients were retrospectively assigned to a low- or intermediate/high-risk cohort based on the surgical-pathologic criteria of Gynecologic Oncology Group protocols 92 (15) and 109 (16). They showed the significantly lower 5-year disease-free survival of 79% for low-risk ASC patients compared to 96 % for other histologic subtypes and that ASC cell type was the only independent risk factor of disease recurrence in the low-risk group.

In this study, the overall 5-year survival rates of stage Ib1 patients with ADC and SCC were 92.4% and 94.0%, respectively. These are almost consistent with the 5-year survival rates of 88.7% for ADC and 89.1% for SCC as described by FIGO Annual Report, 2003.

Our patients with stage Ib1 ASC showed 82.4% of the overall 5-year survival rate, suggesting poorer prognosis of ASC than ADC and SCC, but there was no significant difference. In comparison between a low- and high-risk group of stage Ib1 ASC patients assigned by one of the combinations of the surgical-pathological risk factors including positive lymph node metastasis, 2-4cm of tumor size, positive LVSI, and/or deep stromal invasion, the overall 5-year survival rates were 100% for a low risk group and 74.8% for a high-risk group, respectively, but this difference did not reach statistical significance. However, the 5-year survival rate of high-risk patients with lymph node metastasis was 49.9%, which was significantly ($p=0.01$) worse than low-risk group (Table 4, Fig 3). In addition, 7 of the 19 patients in the high-risk group developed recurrence even after postoperative adjuvant therapy. Five of the 7 patients who died of disease had distant metastases with or without local recurrence, suggesting high incidence of distant metastasis in ASC. This high incidence of distant metastasis may be related mainly to the histological grade of ASC as emphasized in previous reports. (13, 14) In contrast, all 9 patients with stage Ib1 ASC in the low-risk group are alive without disease, even though none received adjuvant therapy.

We conclude that ASC histology appears to carry a poor prognosis than SCC even in early stage and in particular the prognosis of patients with lymph node metastasis is significantly poor. However, low-risk group of stage Ib1 ASC has a good prognosis without postoperative adjuvant therapy.

REFERENCES

1. **Peter Sasieni, Joanna Adams.** 2001. Changing rates of adenocarcinoma and adenosquamous carcinoma of the cervix in England. Lancet **357**:1490-1493.
2. **S Liu, R Semenciw, A Probert, Y Mao.** 2001. Cervical cancer in Canada: Changing patterns in increasing and mortality. Int J Gynecol Cancer **11**:24-31.
3. **Kjorstad KE, Bond B.** 1984.Stage IB adenocarcinoma of the cervix: metastatic potential and patterns of dissemination. Am Jobstet Gynecol **150**:297-299.
4. **Kleine W, Rau K, Achwoeorer A.** 1989.Prognosis of the adenocarcinoma of the cervix :uteri: a comparative study. Gynecol Oncol **35**:145-149.
5. **Eifel PJ, Burke TW, Morris M, Smith TL.** 1995.Adenocarcinoma is an independent risk factor for disease recurrence in patients with stage IB cervical carcinoma. Gynecol Oncol **59**:38-44.
6. **Harrison TA, Sevin B-U, Koechili O, Nguyen HN, Averette HE, Penalver M, Donato DM, Nadji M.** 1993. Adenosquamous carcinoma of the cervix: Prognosis in early stage disease treated by radical hysterectomy. Gynecol Oncol **50**:310-315
7. **Yazigi R, Sandstad J, Munnoz AK, Choi, DJ, Nguyen PD, Risser R.** 1990. Adenosuamous carcinoma of the cervix: prognosis in stage IB. Obstet Gynecol **75**:1012-1015
8. **Alfsen GC, Kristensen GB, Skovlund E, Abeler VM.** 2001. Histologic subtype has minor importance for overall survival in patients with adenocarcinoma of the uterine cervix. Cancer **92**:2471-2483.
9. **Gallup DG, Harper RH, Stock RJ.** 1985. Poor prognosis in patients with adenosquamous cell carcinoma of the cervix. Obstet Gynecol **65**:416-422.
10. **Saigo PE, Cain JM, Kim WS, Gaynor JJ, Johenson K, Lewis JL Jr.** 1986. Prognosis factors in adenocarcinoma of the uterine cervix. Cancer **57**:1584-1593.
11. **Look KY, Brunetto VL, Clarke-Pearson DL, Averette HE, Major FJ, Alvarez RD, Homesley HD, Zaino RJ.** 1996. An analysis of cell type in patients with surgically

staged stage IB carcinoma of the cervix.Gynecol Oncol **63**:304-311.

12. **Schorge JO, Lee KR, Lee SJ, Flynn CE, Goodman A, Sheets EE.** 1999. Early cervical adenocarcinoma:Selection criteria for radical surgery. Obstet Gynecol **94**:386-390.
13. **Farley JH, Hickey KW, Carlson JW, Rose GS, Kost ER and Harrison TA.** 2003. Adenosquamous histology predicts a poor outcome for patients with advanced-stage, but not early-stage, cervical carcinoma. Cancer **97**:2196-2202.
14. **Lea JS, Coleman RL, Garner EO, Duska LR, Miller DS, Scorge JO.** 2003. Adenosquamous histology predicts poor outcome in low-risk stage IB1 cervical adenocarcinoma. Gynecol Oncol **91**:558-562.
15. **Sedis A, Bundy BN, Rotman MZ, Lentz SS, Muderspach LI, Zaino RJ.** 1999. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphoadenectomy: A gynecologic Oncology Group Study. Gynecol Oncol **73**:177-183.
16. **Peters WA, Liu RJ, Stock RJ, Monk BJ, Berek JS, Souhami L, Grigsby P, Gordon W, Alberts DS.** 2000. Concurrent chemoradiation and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early stage cancer of the cervix. J Clin Oncol **18**:1606-1613.
17. **Iwasaka T.** 2000. Chemotherapy for Cervical Adenocarcinoma. Obstetrics and Gynecology **67**:1181-1188.