Cervical carcinoma remains the leading cause to death among gynecological cancers in developing countries. With the progression of the screen and early diagnostic techniques, more and more cervical carcino-

Mitomycin(MMC) for adenocarcinoma with 2~6 cycles at 3~4-weeks intervals. 22 patients (12.0%) were performed adjuvant radiotherapy and chemotherapy as listed above.

All the patients were followed up after the treatment. The follow-up rate was 79.6% (183/230). The median follow-up time was 39 months (1~79months).

Disease-free survival (DFS) was defined as the time from the surgery date to recurrence or metastasis. Overall survival (OS) was defined as the time from the surgery date to death. Data analysis was performed with SPSS10.0 statistical package. The survival curve were constructed by Kaplan-Meier method. The differences in survival were compared with Log-rank test. Multivariate analyses were performed with the Cox proportional hazard model. A probability value of $P<0.05$ was considered significant.

## RESULTS

**Survival rate**

The 2-year and 5-year DFS were 75.12% and 69.91%. the 2-year and 5-year OS were 77.02% and 69.53%, respectively.

**Prognosis analysis**

Among the 12 variables, patients age (≥ 40 years), clinical stage(IIB), tumor size(≥ 4 cm), histological type (non-squamous carcinoma), pelvic lymph node metastasis, parametrial extension, vaginal margin involved, deep stromal invasion and lymphvascular permeation were the poor prognostic factors in univariate survival analysis ($P<0.05$). Cox proportional hazard model analysis showed that two or more pelvic lymph nodes metastasis, vaginal margin involved and lymphvascular permeation were independent survival predictors ($P<0.05$) (Table 2).

**Comparison of survival between high –risk and low–risk group**

According to the three significant facors, the patients were classified into two groups. One was high-risk group with positive vaginal margin and lymphvascular permeation and two or more than two lymph nodes metastasis. The other one was low-risk group with negative vaginal margin or no lymphvascular permeation or 0~1 lymph node metastasis. The DFS and OS of the high risk group were significantly lower than those of the low-risk group respectively ($P<0.01$). According to recurrence rate=1-DFS, the 2-year recurrent rates of the high-risk and low-risk group were 51.47% and 12.54%, respectively; the 5-year recurrent rates of the high-risk and low-risk group were 61.61% and 15.84%, respectively ($P<0.01$) (Table 3 and Figure 1).

## *DISCUSSION*

The reported risk factors of cervical carcinoma included clinical stage, bulky tumor, histological types, cellular differentiation, deep stromal invasion, parametrial extension, vaginal margin involved, lymphvascular permeation, lymph node metastasis, race, age[1-6]. Univariate survival analysis showed that patients with age older than 40, clinical stage IIB, bulky tumor (≥ 4 cm), non-squamous carcinoma, pelvic lymph node metastasis, parametrial extension, vaginal margin involved, deep stromal invasion and lymphvasvular permeation had much poorer prognosis ($P<0.05$). Multivariate analysis showed that two or more pelvic lymph nodes metastasis, vaginal margin involved and lymphvascular permeation were independent survival predictors ($P<0.05$). According to the three survival determinant factors, the patients were classified into high-risk and low-risk groups. The former's 5-year survival dropped from 84.60% of the low-risk group to 39.22% ($P<0.01$). However, the former's 5-year recurrent rate increased from 15.48% of the low-risk group to 61.61%. So intensive attention should be paid to these high-risk patients in order to decrease the local recurrence and distant metastasis and improve the survival. Now many large scale prospective clinical trial had shown that concomitant chemotherapy and radiotherapy after radical hysterectomy and lymphadenectomy could improve overall and progression-free survival and reduce local and distant recurrence in high-risk cervical carcinoma, which was informative in clinical practice[7,8]. In our paper, the patients with adjuvant therapy had poorer prognosis than

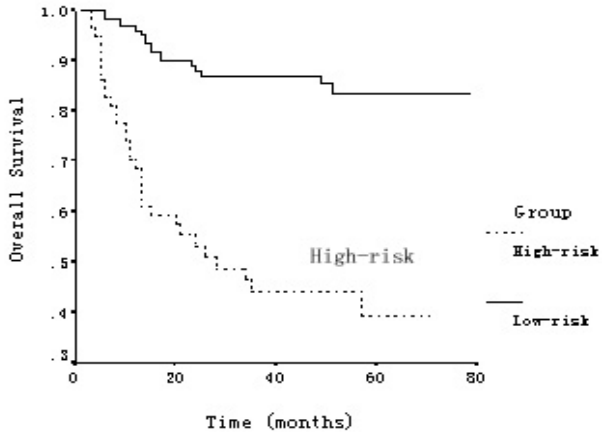


**Figure 1**. The survival curve of patients with cervical carcinoma in high-risk and low-risk groups

**Table 1**. Univariate Analysis of Clinicopathologic Variables

| Factors | n | RFS (%) | | *P* value | OS (%) | | *P* value |
|---|---|---|---|---|---|---|---|
| | | 2-year | 5-year | | 2-year | 5-year | |
| Age(yrs) | | | | | | | |
| <40 | 42 | 85.38 | 85.38 | <0.05 | 84.98 | 84.98 | <0.05 |
| ≥ 40 | 141 | 72.04 | 65.07 | | 75.15 | 59.62 | |
| Stage | | | | | | | |
| IB~IIA | 140 | 83.05 | 78.13 | <0.01 | 81.72 | 73.13 | <0.01 |
| IIB | 43 | 49.79 | 43.56 | | 58.41 | 47.81 | |
| Tumor size(cm) | | | | | | | |
| <4 | 100 | 88.60 | 83.22 | <0.01 | 86.78 | 76.22 | <0.01 |
| ≥ 4 | 83 | 58.77 | 54.04 | | 63.25 | 55.83 | |
| Histology | | | | | | | |
| Squmous | 135 | 80.05 | 75.79 | <0.01 | 80.99 | 72.66 | <0.05 |
| Non-Squamous | 48 | 61.42 | 52.90 | | 63.01 | 50.41 | |
| Grade | | | | | | | |
| Poor | 54 | 68.07 | 62.72 | >0.05 | 66.70 | 58.98 | >0.05 |
| Moderate-Well | 129 | 78.08 | 72.87 | | 79.96 | 69.81 | |
| Lymph node metastasis | | | | | | | |
| 0 | 139 | 82.20 | 78.79 | <0.01 | 82.73 | 79.33 | <0.01 |
| 1 | 11 | 83.33 | 55.56 | | 75.00 | 37.50 | |
| ≥ 2 | 33 | 36.64 | 32.57 | | 44.64 | 31.96 | |
| Parametrial extension | | | | | | | |
| Negative | 171 | 78.12 | 73.30 | <0.01 | 80.56 | 69.89 | <0.01 |
| Positive | 12 | 33.33 | 22.22 | | 37.50 | 18.75 | |
| Vaginal margin involved | | | | | | | |
| Negative | 177 | 75.98 | 72.04 | <0.01 | 76.78 | 68.13 | <0.01 |
| Positive | 6 | 50.00 | 0.00 | | 50.00 | 25.00 | |
| Depth of stromal invasion | | | | | | | |
| <2/3 | 96 | 86.89 | 83.36 | <0.01 | 84.56 | 76.90 | <0.01 |
| ≥ 2/3 | 87 | 62.31 | 54.93 | | 66.77 | 55.74 | |
| Lymphvascular permeation | | | | | | | |
| Negative | 154 | 77.31 | 74.15 | <0.05 | 77.70 | 72.82 | <0.01 |
| Positive | 29 | 63.81 | 46.88 | | 65.16 | 34.21 | |
| Nerve invasion | | | | | | | |
| Negative | 180 | 74.77 | 70.22 | >0.05 | 75.22 | 66.59 | >0.05 |
| Positive | 3 | 50.00 | 50.00 | | 50.00 | 50.00 | |
| Adjuvant therapy | | | | | | | |
| Negative | 126 | 83.64 | 78.25 | <0.01 | 82.64 | 72.88 | <0.01 |
| Positive | 57 | 56.04 | 51.37 | | 61.67 | 53.06 | |

**Table 2**. Multivariate Analysis of variables in predicting overall survival

| Factor | Coefficient | Relative risk | 95%CI | P value |
|---|---|---|---|---|
| Age | 0.007 | 1.007 | 0.979-1.036 | >0.05 |
| Stage | 0.948 | 2.581 | 0.851-7.828 | >0.05 |
| Tumor size | 0.067 | 1.069 | 0.870-1.314 | >0.05 |
| Histology | 0.310 | 1.364 | 0.921-2.020 | >0.05 |
| Grade | -0.272 | 0.762 | 0.465-1.247 | >0.05 |
| Lymph node metastasis | 0.944 | 2.571 | 1.016-6.507 | <0.05* |
| Parametrial extension | 0.790 | 2.203 | 0.844-5.752 | >0.05 |
| Vaginal margin involved | 1.744 | 5.723 | 1.361-24.058 | <0.05* |
| Stromal invasion | 0.163 | 1.177 | 0.814-1.702 | >0.05 |
| lymphvascular permeation | 0.783 | 2.187 | 1.072-4.464 | <0.05* |
| Nerve invasion | -2.562 | 0.077 | 0.006-1.007 | >0.05 |
| Adjuvant therapy | -0.049 | 0.952 | 0.409-2.217 | >0.05 |

**Table 3**. Comparison of Prognosis Between High-risk and Low-risk Group

| Groups | n | RFS (%) | | *P* value | OS (%) | | *P* value |
|---|---|---|---|---|---|---|---|
| | | 2-year | 5-year | | 2-year | 5-year | |
| Low-risk | 125 | 88.01 | 83.60 | <0.01 | 12.54 | 15.48 | <0.01 |
| High-risk | 58 | 53.10 | 39.22 | | 51.47 | 61.61 | |

those without adjuvant therapy. The reason lied there were more high-risk patients (61.40%) in the adjuvant therapeutic group than 16.67 percent in no adjuvant therapeutic group ($P$<0.01). That meant we could not drew a certain conclusion about the role of adjuvant therapy. It should be adressed in a prospective clinical trials.

It had been proven that pelvic lymph node metastasis was the independent prognostic factors in many clinical studies. However, the relationship between the number of positive nodes and prognosis was still in discussion. Tsai et al [9] stated that the 5-year survival of patients with two or more positive nodes was lower than that of patients with no or just one positive node. Pillerson reported that no patients with more than 30 percent positive nodes could have long term survival, even given adjuvant radiotherapy. However, it was reported that five of nine cervical carcinoma patients with six or more lymph nodes metastasis had long progression free survival. In our study the 5-year survival of patients with none, one and two or more positive nodes were 79.33%, 37.50% and 31.96%, respectively ($P$<0.01). The 2-year survival (75.0%) of patients with one positive node dropped to 37.5% at the fifth year. The result support that pelvic lymph node metastasis is the very important prognostic factor, and the more the namber of positive nodes is, the poorer the prognosis is. Although there was no significant difference in the prognosis of the patients between none and one positive node in Tsai's paper, our study showed that the patients even with one positive node should also be taken seriously. As a matter of fact, it was the quantity difference between the number of positive nodes. However, it was the quality difference between the none and one positive node. We need more data to draw a conclusion and act as a guideline.

## *REFERENCES*

1. Soisson AP, Soper JT, Clarke-Pearson DL, et al. Adjuvant radiotherapy following radical hysterectomy for patients with stage IB and IIA cervical cancer. Gynecol Oncol, 1990, 37:390-395.
2. Curtin JP, Hoskins WJ, Venkatraman ES, et al. Adju vant chemotherapy versus chemotherapy plus pelvic irradiation for high-risk cervical cancer patients after radical hysterectomy and pelvic lymphadenectomy (RH-PLND): A randomized phase III trial. Gynecol Oncol, 1996, 61:3-10.
3. Aoki Y, Sasaki M, watanabe M, et al. High-risk group in node-positive patients with stage IB, IIA, and IIB cervical carcinoma after radical hysterectomy and postoperative pelvic irradiation. Gynecol Oncol, 2000,77:305-309.
4. Monk BJ, Cha DS, Walker J, et al. Extent of disease as an indication for pelvic radiation following radical hysterectomy and bilateral pelvic lymph mode dissection in the treatment of stage IB and IIA cervical carcinoma. Gynecol Oncol, 1994, 54:4-9.
5. Iwasaka T, Kamura T, Yokoyama M, et al. Adjuvant chemotherapy after radical hysterectomy for cervical carcinoma: A comparison with effects of adjuvant radiotherapy. Obstet Gynecol, 1998, 91:977-981.
6. Tattersall MHN, Ramirez C, Coppleson M, et al. A randomized trial of adjuvant chemotherapy after radical hysterectomy in stage IB-IIA cervical cancer patients with pelvic lymph node Metastases. Gynecol Oncol,1992, 46:176-181.
7. Peters III WA, Liu R, Barrett II RJ, et al. Concurrent chemotherapy 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, 2000, 18:1606-1613.
8. Green JA, Kirwan JM, Tierney JF, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and Meta-analysis. Lancet, 2001, 358:781-786.
9. Tsai CS, Lai CH, Wang CC, et al. The prognostic factors for patients with early cervical cancer treated by radical hysterrec-