

Prognostic Factors for Survival after Surgery for Early Stages Cervical Cancer

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Abstract : *Two hundred and forty-nine consecutive patients with clinical stage I and IIA carcinoma of the uterine cervix who underwent primary radical hysterectomy and pelvic lymphadenectomy between January 1976 and December 1988 were evaluated for prognostic factors for survival. Univariate analysis, history of smoking, weight of the patients, FIGO staging, surgeons and surgical techniques, histology, lymph nodes status, lesion diameter and recurrent status were the significant factors in death rate. When survival analysis was performed, recurrent status, FIGO staging and lesion diameters remained significant for both corrected and overall survival rates. For preoperative selection of the patients, those with FIGO stage II and tumour diameter 2-4 cm were associated with a less favourable prognosis. (Thai J Obstet Gynaecol 1990; 2: 29-36.)*

Key words : prognostic factors for survival, early stage cervical cancer

Carcinoma of the uterine cervix is the most common gynaecological malignancy in Thailand and is the second most common cancer for the Khon Kaen female population^(1,2). Improvement in early diagnosis and treatment has been achieved over the last two decades. Survival rates in patients whose tumours are confined in the cervix (Stage IB, IIA) treated by both radiotherapy and surgery have remained constant between 82-90% in the past few years. It has been recog-

nized for some time that prognostic factors for survival after surgery are recurrent status⁽³⁾, lymph node metastasis^(4,5-14), tumour size^(9,12-13), stages of the disease^(9,12-13), depth of stromal invasion^(3,19), extracervical extension^(3,19-22), histological types^(3,5,6,13,19-22), lympho-vascular spreading^(9,21,23,24), age and weight of the patients^(12,13,15,17) and the use of adjuvant therapy⁽²⁾. In order to improve survival rates in patients with early cervical cancer, prognostic factors must be identified.

Materials and Methods

Between January 1, 1976 and December 31, 1988, 249 consecutive patients with FIGO stages IA, IB and IIA cervical carcinoma were operated on by radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University. Clinical staging was done according to the International Federation of Gynaecology and Obstetrics (FIGO) for all patients by gynaecological oncologists and radiotherapists. The operative procedures were done according to Piver's type III extended hysterectomy⁽⁵⁾. Patients with tumour involvement of pelvic lymph nodes, surgical margins and parametria were sent for additional radiotherapy.

Table 1 Prognostic factors for survival after radical hysterectomy in cervical cancer

1. Recurrence
2. Lymph nodes status
3. Tumour size
4. Stage of the disease
5. Depth of stromal invasion
6. Extracervical extension
7. Histological type and grading
8. Lympho-vascular spreading
9. Status of the surgical margin
10. Thickness of uninvolved fibromuscular stroma
11. Age of the patients
12. Interval from the previous follow-up examinations
13. Location of the lesion within the cervix
14. The use of adjuvant therapy
15. Lesion type
16. Weight

Epidemiological data, tumour description, parametria involvement, pelvic lymph nodes status, morphometric data, histological diagnosis and follow-up data were recorded by the staffs of the Division of Gynaecological Oncology and the hospital-based cancer registry of the Cancer Unit, Faculty of Medicine, Khon Kaen University. The follow-up period ranged from 2 to 12 years. All variables were first analyzed for significant relationship to death rate by *chi-square* and Mann-Whitney tests. All significant variables were then analyzed for survival by Kaplan-Meier product limit estimation with log-rank test⁽²⁶⁾. Cox's proportional hazard model⁽²⁷⁾ was used for the most significant variables for survival. Algorithm for preoperative prediction were then established.

Table 2 Univariate analysis of prognostic factors for survival after radical hysterectomy for cervical cancer

1. Recurrence
2. Stage of the disease
3. Tumour size
4. Lesion type
5. Histological type
6. Uterine size
7. Persistence of left ovary
8. Smoking
9. Weight
10. Surgeon

Results

Univariate analysis

All variables from previous reports were analyzed by using death

rate as the dependent variable (Table 1) and only 10 variables were still significant (Table 2). From the Kaplan-Meier product limit estimation

only recurrence status, FIGO stages and lesion diameter were still significant for both corrected and absolute survivals (Table 3).

Table 3 Survival analysis of patients after radical hysterectomy for cervical cancer

Prognostic factors	Categories	Absolute survival	Corrected survival
1. Recurrence	No	86.54	100.00
	Yes	15.64 P=0.0000	15.64 P=0.0000
2. Stages	1A	100.00	100.00
	1B	82.53 P=0.0020	91.04 P=0.0400
	IIA	0.00	50.51
3. Lesion size	< 2 cm	79.00	91.91
	2-4 cm	77.59 P=0.0185	81.84 P=0.0006
	> 4cm	75.00	75.00
4. Lesion type	No gross lesion	100.00	
	Polypoid	87.66	
	Ulcer	77.01 P=0.36	
	Cauliflower	71.13	
	Infiltrative	47.41	
5. Histology	No residual	83.33	83.33
	Squamous	74.32	86.63
	Adeno.	90.61 P=0.38	96.97 P=0.36
	Adenosquamous	100.00	100.00
6. Uterine size	≤ 8 cm	91.51	97.67
	> 8 cm	92.10 P=0.81	93.15 P=0.38
7. Persistence left ovary	Yes	86.27	86.27
	No	94.08 P=0.42	97.66 P=0.32
8. Smoking	Yes	74.33	86.42
	No	100.00 P=0.226	100.00 P=0.051
9. Weight	< 50 Kg	100.00	100.00
	> 50 Kg	92.94	93.94 P=0.021
10. Surgeons	S1	78.00	83.20
	S2	86.06	90.30
	S3	100.00	100.00
	S4	100.00 P=0.180	100.00 P=0.80
	S5	37.50	100.00
	S6	60.00	100.00

Figure 1 shows the overall survival rates of the patients with 76.58% absolute survival and 88.08% corrected survival rates. Figure 2 shows the overall absolute survival rates according to recurrent status. Those who had no recurrence had 86.54% survival rate while those who had recurrence had only 15.64% survival rate. Figure 3 shows the 100% overall corrected survival rate for those who had no recurrence and 15.64% corrected survival rate for those who had recurrence. Figure 4 and Figure 5 show the overall absolute survival rates according to FIGO stages with 100% and 0% for stages IA, IB and IIA respectively. Figure 6 and Figure 7 show the overall absolute survival rates of 79%, 77.59% and 75% for those who had a lesion diameter of less than 2 cm, between 2-4 cm and more than 4 cm respectively. For corrected survival, the survival was 91.91%, 81.84% and 75% for those who had a lesion diameter of less than 2 cm, between 2-4 cm and more than 4 cm respectively.

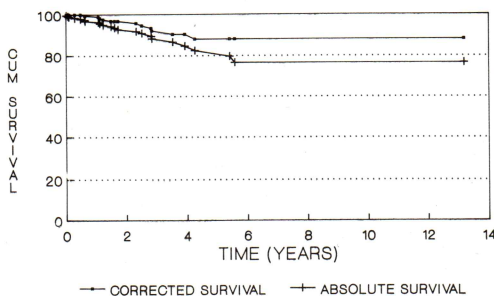


Fig. 1 Survival analysis of patients after radical hysterectomy

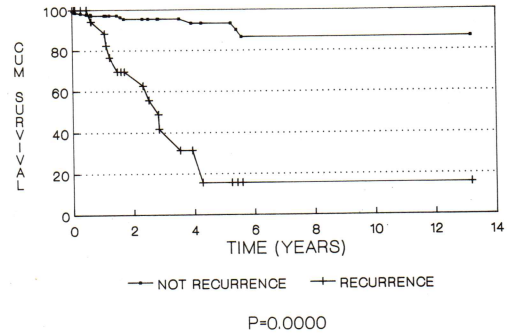


Fig. 2 Absolute survival according to recurrence status

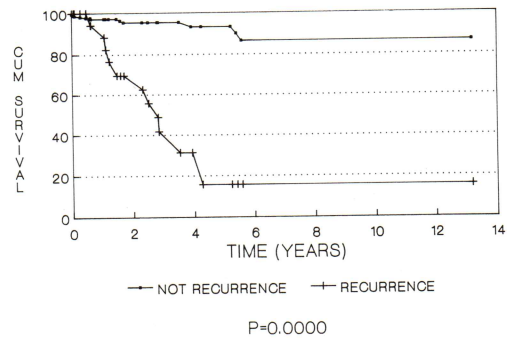


Fig. 3 Corrected survival according to recurrence status

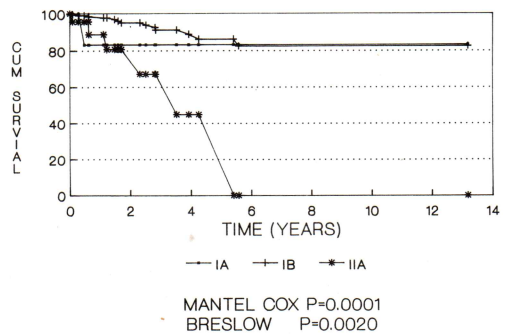


Fig. 4 Absolute survival rates according to FIGO stages

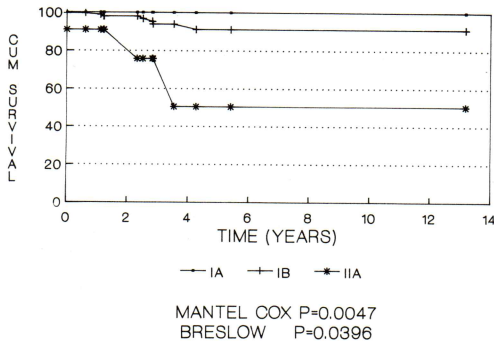


Fig. 5 Corrected survival according to FIGO stages

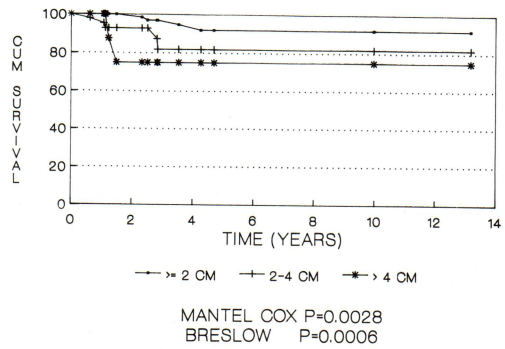


Fig. 7 Corrected survival according to lesion's diameter

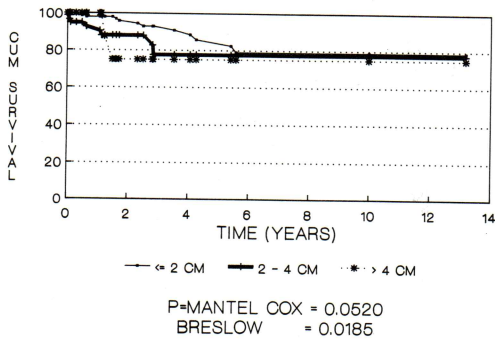


Fig. 6 Absolute survival rates according to lesion's diameter

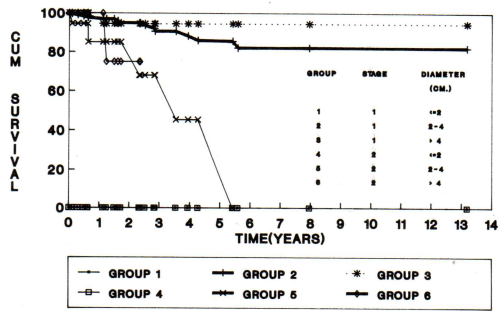


Fig. 8 Grouping of prognostic factors for survival after radical hysterectomy

With Cox's proportional hazard model, only recurrence status and FIGO stages were the most significant prognostic factors for survival. Preoperative grouping of patients was done for FIGO stages in combination with tumour diameters (Figure 8). It was shown that when the patients were grouped into 6 groups the most favourable outcome was those who had stage I without lesion diameter distinction.

Discussion

After radical hysterectomy and pelvic lymphadenectomy, recurrent rate from 10% to 20% is generally expected. The proposed mode of recurrence is the regrowth of the viable cancer cells which were left behind at the time of surgery. Once recurrence occurs, the prognosis of the patients is poor even though several modes of therapy were given. Only 15.64% of

patients survived 5 years, compared to 86.54% for those without recurrence. The risk factors for recurrence in this series was reported⁽²⁴⁾.

FIGO staging has been routinely used as the classification of the disease for planning of treatment and prediction of the outcome. Lee et al⁽¹³⁾ found the absolute 5-year survival rates for stage IB, IIA and IIB to be 86.5%, 71.7% and 60.1% respectively. This series obtained a very poor rate for stage IIA, the patients survived only 2 years.

Tumour size has been observed to be one of the important factor for recurrence and survival in patients who underwent radical hysterectomy and pelvic lymphadenectomy. It was also reported to be the important prognostic factor in radiated patients as confirmed by Patanaphan et al⁽¹⁵⁾. Burghardt⁽⁵⁾ showed the 5-year survival rate decreased correspondingly with the tumour size which he expressed in term of so-called quotient. The 5-year survival rate of 88.9% was observed in the quotient of 0% to 20% while the rate dropped to 58.9% in the quotient of 80% or more. He also confirmed the tumour size to be the most important prognostic criteria and best suited for patient classification. In multivariate analysis of risk factors in stage I adenocarcinoma, Kilgore et al⁽¹⁷⁾ found that clinical stage and lesion size were the most important prognostic factors for recurrence and survival. In this study it was significant by univariate analysis both for absolute and corrected survival.

The rest of the variables were taken into account for follow-up and further study for prognostic factors for survival and recurrence. For high risk patients who had involvement of cancer at lymph nodes, surgical margins and parametria were given radiotherapy and appeared to be nonsignificant variables after analysis. Noguchi et al⁽⁶⁾ reviewed 627 cases of early stage cervical cancer who underwent Okabayashi radical hysterectomy from 1950 to 1984 and found that lymph nodes metastasis correlated with clinical stage, depth of stromal invasion and involvement of the cancer to parametria, vagina and uterine body. Fuller et al⁽⁹⁾ also found the incidence of nodal metastasis increased with the increase of tumour size, tumour grade, and depth of invasion into the cervix.

The two preoperative variables, FIGO stages and lesion size were grouped together and the worse prognosis was found in those who had stage II and lesion diameter 2 to 4 cm. Those who had stage I disease had a better prognosis than stage II and it was not related to lesion size.

From this analysis, it is confirmed that clinical staging as described by FIGO is still useful for preoperative planning in early stage cervical cancer.

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