

Risk Factors for Recurrences of Cervical Cancer After Radical Hysterectomy and Pelvic Lymphadenectomy at Srinagarind Hospital

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Abstract: *The study of risk factors for recurrence of carcinoma of cervix after radical hysterectomy and pelvic lymphadenectomy for stage I and IIA was carried out among patients operated upon at Srinagarind Hospital from 1976 to June 30, 1988. There was no recurrence among patients with stage IA. The recurrent rates were 8.40 and 19.40% for stage IB and IIA respectively. The recurrent rates among patients with pelvic nodes involvement and without nodes involvement were 15.20 and 8.10% respectively. Again, with endometrial involvement the recurrent rate among these patients was 40.40% while only 7.70% recurrent rate encountered in those without endometrial involvement. The difference was significant statistically. The age of the patients and extent of lesions were the important risk factors. Microscopic findings, type of lesions, surgeons and surgical techniques played no important role in recurrence of the cancer. (Thai J Obstet Gynaecol 1989;1:47-55)*

Keywords: cervical cancer, surgery, recurrence, risk factors

Recurrence of cancer is defined as a tumor found after 3 to 6 months following therapy, while disease found within that time period is often termed persistent disease.⁽¹⁾ It also includes those that later become evident after a period of complete clinical remission. Disease discovered after primary surgical approach should be termed persistent if margins or nodes were involved. Some authors define recurrence within any time period as tumor regrowth in cases in

which no tumor was knowingly left behind.⁽²⁾ Recurrences after radical hysterectomy with pelvic lymphadenectomy for stage IB and IIA vary from 10% to 20% in most institutes, for patients with negative nodes at the time of radical hysterectomy, about 10% recurrent rate.⁽²⁾ Despite postoperative whole pelvis radiation therapy for 88% of all patients, 34.2% developed recurrence in Burke's series.⁽³⁾ Also Burke and coworkers⁽⁴⁾ reviewed 31 cases with FIGO

stage IB cervical carcinoma who developed recurrent disease after radical hysterectomy and pelvic lymphadenectomy. The over all incidence of recurrence was 11.3%. Sites of recurrence were central pelvis in 35%, pelvic side wall, 39%, and distant 26%. Patients treated with postoperative pelvic radiotherapy for positive pelvic nodes or surgical margin involvement were more likely to develop distant recurrence. High-risk factors are apparent in these patients. If tumor is present in vascular spaces, the endometrial cavity, the deep endocervical stroma or the paracervical (cardinal ligament) tissue are invaded, or if a tumor is undifferentiated or 3 cm or larger in size, one may predict a high recurrent rate.⁽³⁾ The disease-free interval depends on different factors including the adequacy of initial treatment, host resistance, the original stage, volume of tumor and adequacy of follow-up.⁽¹⁾

This study was to review risk factors for recurrence after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital during 12 year period and to explore suitable treatment for the future and selection of patients.

Materials and Methods

During 1976 to June 30, 1988, 218 cases of cervical cancer stage IA, IB and IIA were operated on. The data from 1976 to 1983 were retrospectively collected from records of the operative room, the Department of Pathology and the medical record unit. Since 1984, all records were collected prospectively and kept by the Division of Gynaecologic

Oncology, Department of Obstetrics and Gynaecology. The follow-up data were obtained from the Gynaecologic Oncology tumor clinic and the hospital-based cancer registration of the cancer unit, Faculty of Medicine. The operative technique performed in this hospital was class III extended hysterectomy due to Piver's classification⁽⁵⁾ and the modified Okabayashi technique as mentioned by Sekiba.⁽⁶⁾ Postoperative care was closely observed for any complications and prophylactic antibiotics were routinely given.

Follow-up for patients began at the tumor clinic with the first examination 4 weeks postoperatively, then every 3 months for the first year and every 6 months for the rest of their lives. Complete physical and pelvic examinations with Pap smear were done every time.

All recurrence cases were given radiotherapy with or without chemotherapy. Questionnaires would be sent to those who did not attend the tumor follow-up clinic.

The analysis of data was performed using descriptive statistics and contingency tables with chi-square test, and analysis of disease-free interval, using Cutler-Ederer life table analysis with log-rank tests. The censor date was June 30, 1988. Those who missed two appointments were labelled as lost in the analysis.

Results

Incidence of Recurrence and FIGO Stages

From 1976 to June 30, 1988, 218 cases of cervical cancer stage IA, IB and

IIA were operated upon at Srinagarind Hospital. Twenty recurrences(9.10%) were diagnosed, 16 cases of stage IB (8.40%), 4 cases of IIA(19.40%) and there were no cases of stage IA which recurred at the time of censoring with no statistical significant. Fig.1 shows the disease-free curve in different stages with statistical significance.

Nodal Status

Fifteen out of 185 cases of those who had negative lymph nodes had recurrence, while five out of 33 cases of positive lymph nodes recurred without statistical significance(Table 1). The disease-free curve is shown in Fig.2 and no statistical significance is observed.

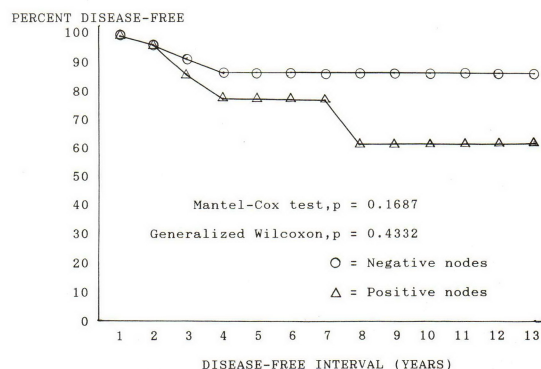
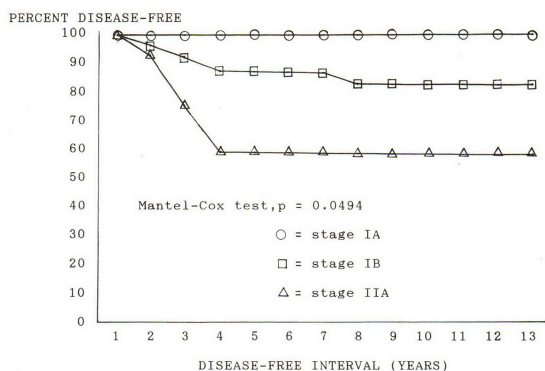


Fig. 1 Disease - free curve after radical hysterectomy at Srinagarind Hospital 1976-1988

Fig. 2 Disease - free curve after radical hysterectomy at Srinagarind Hospital 1976-1988

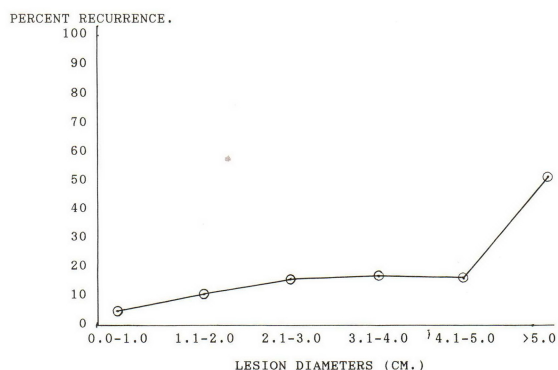


Fig. 3 Radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital : Stratified by lesion sizes

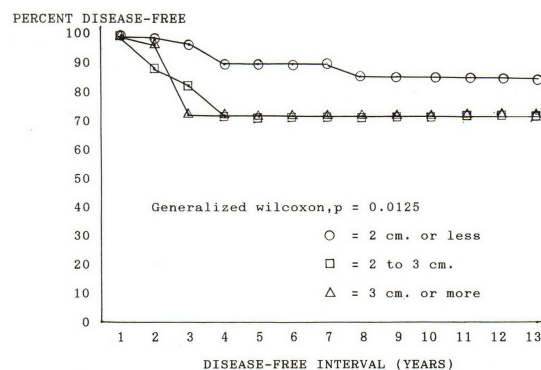


Fig. 4 Disease free - curve after radical hysterectomy at Srinagarind Hospital 1976-1988 : Lesion diameters

Lesion Sizes

Table 1 and Fig.3 show the increased percentage of recurrence with the increase in size of tumors with statistical significance. The percentage increased mostly after the tumor diameter became greater than 4 cm. Fig.4 shows the disease-free curve of those who had 2 cm or less, 2 to 3 cm and 3 cm or more. The curve significantly changed when size became greater than 2 cm.

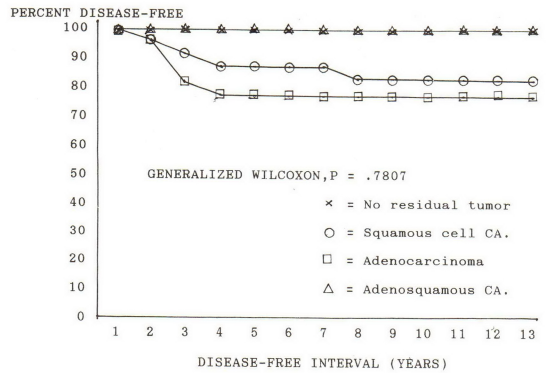


Fig. 5 Disease free curve after radical hysterectomy at Srinagarind Hospital 1976-1988 : Cell types

Table 1 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital

FIGO Stages	Total cases	Recurrence	Percent	p-value
IA	6	0	0.00	
IB	191	16	8.40	
IIA	21	4	19.40	0.201
Nodal Status				
Negative nodes	185	15	8.10	
Positive nodes	33	5	15.20	0.3351
Lesion Diameters (cm)				
0.0-1.0	93	4	4.30	
1.1-2.0	64	6	9.40	
2.1-3.0	33	5	15.20	
3.1-4.0	19	3	15.80	
4.1-5.0	7	1	14.30	
5.1 or more	2	1	50.00	0.0035
Histology				
Squamous cell	180	15	9.09	
Adenocarcinoma	36	5	16.13	
Adenosquamous	2	0	0.00	0.072
Lesion Types				
No lesion*	18	1	5.56	
Ulcerative	75	5	6.70	
Polypoid	35	1	2.90	
Cauliflower	7	11	14.10	
Infiltrative	12	2	16.17	0.3264

* Including postconization and occult IB.

Histology

No statistical significance was observed by histology in recurrent patterns in Table 1 and Fig.5.

Surgical Factors

There was no relationship between surgeons, surgical techniques and recurrence (Table 2).

Lesion Types

There was no different recurrent rates by lesion types (Table 1).

Extent of Tumor

Table 3 shows the correlation of tumor extent and involved different

Table 2 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital : Surgical factors

Surgeons	Total cases	Recurrence	Percent	p-value
Surgeon 1	135	12	8.89	0.2614
Surgeon 2	33	6	18.20	
Surgeon 3	23	1	4.30	
Surgeon 4	21	0	0.00	
Surgeon 5	6	1	16.70	
<i>Surgical techniques</i>				
Wertheim-Meigs	113	12	10.60	0.5947
Okabayashi	105	8	7.60	

Table 3 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital : Tumor extent

Tumor extents	Total cases	Recurrence	Percent	p-value
<i>Vagina</i>				
Involved	9	2	22.20	0.426
Not involved	209	18	8.60	
<i>Left cardinal ligament</i>				
Involved	7	1	14.30	1.0000
Not involved	211	19	9.00	
<i>Right cardinal ligament</i>				
Involved	7	1	14.30	1.0000
Not involved	211	19	9.00	
<i>Endometrium</i>				
Involved	9	4	44.40	0.0016
Not involved	209	16	7.70	

structures with the rate of recurrence. Only endometrial involvement is observed to be a great risk factor for recurrence in this study.

Age

Table 4 shows the percentage of recurrence for different age intervals. When ages were grouped into 35 years or less and above 35, there was statistical

significance in recurrent rates. Fig.6 shows the disease-free curve for those aged below and above 35 years with statistical significance.

Discussion

Radical hysterectomy and pelvic lymphadenectomy is considered to be the treatment of choice for cervical cancer

Table 4 Risk factors for recurrence of cervical cancer after radical hysterectomy and pelvic lymphadenectomy at Srinagarind Hospital : Age factor

Age	Total cases	Recurrence	Percent	p-value
30 or less	12	3	25.00	
31-35	30	5	16.70	
36-40	45	4	8.90	
41-45	46	3	6.50	
46-50	36	2	5.60	
51-55	28	1	3.60	
56-60	16	2	12.50	
60 or more	5	0	0.00	
<i>Cutpoint at age 35</i>				
35 or less	42	8	19.00	
Above 35	176	12	6.80	0.0300

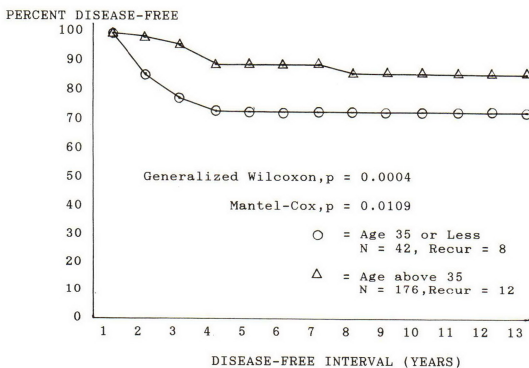


Fig. 6 Disease-free curve after radical hysterectomy at Srinagarind Hospital 1976-1988 : By ages 35 and cutpoint

stage IB and IIA in this hospital. Failure rate of treatment of cervical cancer stage IB and IIA has varied from 10 to 20% in most series with primary surgery or radiation therapy.^(1,2) At Srinagarind Hospital, the recurrence of stage IA,IB and IIA altogether is 9.10%, 8.40% for stage IB and 19.40% for stage IIA, which are in the acceptable range. FIGO stage was found to be one of significant risk factor for recurrence. From this study, the significance was found from the disease-free curve. With increasing stages, the rate of nodal involvement increased, 15.5% for stage IB and 50.0% for stage

IIA in O'Brien's report.⁽⁷⁾ Increase in rate of lymphatic involvement should increase the rate of recurrence.^(2,4,8-17) In this study, the recurrent rate for negative nodes group was 8.10% and for positive nodes group 15.20%, without statistical significance. This is because of the administration of radiotherapy to all cases of positive nodes, vaginal cuffs and parametrium but not endometrial involvement.

It is clearly seen from Table 1, Fig.3 and Fig.4 that lesion size is the important risk factor for recurrence with statistical significance, which corresponds to previous reports.^(2,4,7,9,12,18) Many authors^(2,4,18-20) have mentioned about histology as risk factor for recurrence. Patients with adenocarcinoma or adenosquamous carcinoma had higher risk of recurrence than those who had squamous cell carcinoma. From this study, patients with adenocarcinoma had higher rate of recurrence than patients with squamous cell carcinoma but without statistical significance. Lesion types had no significant relationship to recurrent rate in this study, but in advanced stages, the endocervical infiltrative types had higher recurrent rate than other types.⁽²¹⁾ It was also seen from Table 2 that surgeons and surgical techniques had no influence on recurrence as far as the standard procedure practiced.

Parametrial extension and vaginal involvement was mentioned to be a risk factor for recurrence.^(14,22-23) Due to radiotherapy given to all of those patients with parametrial and vaginal edge involvement, there was no difference in recurrent rate. It was clearly seen from

this study that endometrial involvement was a significant risk factor for recurrence. This finding does agree with previous reports.⁽²⁴⁻²⁹⁾ Those with endometrial invasion should administer adjuvant chemotherapy in combination with routine radiotherapy.

There have been some reports about younger ages, especially those 35 years or less, having higher risk of recurrence than older people⁽³⁰⁻³⁶⁾. Table 4 and Fig.6, show total agreement with previous reports.

The above mentioned risk factors, should be used as guidelines for selecting patients for the surgery in order to decrease recurrence and increase survival rates in treatment of cervical cancer in this hospital.

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