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Endometrial Carcinoma : Surgical Staging and Survival Analysis.

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ABSTRACT

Objective To determine the five year survival rate according to the FIGO surgical staging system and to analyze the significance of prognostic factors.

Design Prospective descriptive study

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Subjects and methods 84 patients with endometrial carcinoma who underwent surgical exploration between 1 January 1988 and 31 December 1992 were enrolled. The Kaplan – Meier method for estimation of survival time and univariate analysis was used. The Log rank was used for comparing factors. In the multivariate analysis, Cox's proportional Hazard model was also used.

Results Five-year survival rate 93%, 75%, 42% and 0% in surgical I,II,III and IV respectively. Age, histologic grade, depth of invasion, cervical invasion, adnexal metastasis, lymph node metastasis all correlated to survival in the univariate analysis. In the multivariate study, only depth of invasion was statistically significant correlated to survival.

Conclusion Surgical staging correlates to survival. The outcome of early stage compared favourably with the previous published reports.

Key words : endometrial carcinoma, surgical staging, survival

Endometrial carcinoma is one of the most common gynecologic cancers. An estimated 6,300 deaths could be attributed to this cancer during 1998.[1] Inaccuracy of clinical staging has been reported. Boronow et al studied 222 cases with clinical stage I and found 12.6% upstaged when compare to surgical stage,[2] while Cowles et al found error as high as 21.7%.[3] FIGO announced a new surgical staging system in 1988.[4] Subsequent published reports of the results by this staging were favourable. Wolfson found a 90.6% 5 – year survival for stage I and demonstrated surgical staging to be the strongest predictor of survival.[5] Gal found a 98% survival rate for stage I, and commented on the benefit of improving adjuvant treatment.[6] Increasing popularity in the usage of this system was noted.[7] Nulliparity was considered to be adverse to survival.[8] Survival in higher stages were reported.[9–13] Various prognostic factors have been extensively studied.[14–18] We have collected surgicopathological data at our institute since 1 January 1988. The aim of this study was to determine the 5-year survival rate among surgically staged patients and also to define the significance of prognostic factors.

Subjects and methods

Eighty five patients who underwent surgical exploration between 1 January 1988 and 31 December 1992 were enrolled in this study to reveal demographic characteristics. One case of clear cell histologic type was excluded from the survival study due to its distinct behaviour. Eighty four patients were followed for a minimum of 60 months. Survival time was defined from the date of the first diagnosis to death of disease or the last date of contact at the closing date of data collection (30 September 1988). Thirteen cases were lost during follow up. Patients with high recurrent risks, namely, poor grade, invasion more than one-half of myometrium, extrauterine disease, were individually treated with radiation, hormone as adjuvant treatment. Sixteen patients received postoperative radiation, 7 of 20 in stage I (high risk), 2 of 4 in stage II and 7 of 13 in stage III. 3 cases received progesterone each in stage I, III and IV.

Statistics

The 5-year survival rate was estimated by the Kaplan-Meier's method. (program SPSS version 7.5) In the univariate study, prognostic factors were compared by Log rank method, statistical significance defined if p-value < 0.05. We dichotomized factors : age into 60, > 60 years; grade into well and moderate, poorly differentiated; depth of invasion into equal or less than one-half and or more than one-half. In the multivariate study, Cox's proportional hazard model method was used.

Results

The demographic characteristics of 85 patients are shown in Table1. Median age was 53 years (range 30-79 years). 26 patients (30.6%) were nulliparous , 59 (69.4%) were multiparous. Adenocarcinoma was the most common histology found in 66 cases (77.6%) while clear cell was least found with only 1 case (1.2%). Distribution by surgical stage was 63(74.6%) in stage I, 4(4.7%) in stage II, 13(15.3%) in stage III, and 5 (5.9%) in stage IV.

After excluding one case of clear cell (present with stage I) from the survival study. 84 patients were followed, there were 13 cases (15.5 %) lost during follow up period (Table 2) with median of 13 months. Higher rates were in an advanced stage. The surgicopathologic findings are shown in Table 3. Cervical invasion and adnexal metastases were most commonly found in 14.3% and 13 .1% cases respectively. Pelvic and paraaortic lymph node metastases were positive in 6/76 (7.9%), 5/51 (9.8 %). 3 cases with disease confined to the uterine corpus only had retroperitoneal lymph node metastases, all with more than half of myometrial invasion. A low rate of lymphovascular invasion was found just in 2 cases (2.4%), positive peritoneal cytology found in 3/67 cases (4.5%), all with disease penetrating through the uterine serosa. 65.5 % were well differentiated grade, moderate differentiated 19.0%, while poorly differentiated15.5%. 41.7% were found with more than half of myometrial invasion present, while disease limited to endometrium only was found in 20.2%.of cases.

Table 1. Demographic characteristics of 85 patients with endometrial adenocarcinoma

Characteristics		Number of patients	Percent
Ages			
	Median = 53 years Range (30 – 79)	85	100
Parity			
	Nulliparous	26	30.6
	Parous	59	69.4

Histology			
	Adenocarcinoma	66	77.6
	Adenoacanthoma	14	16.5
	Adenosquamous	4	4.7
	Clear cell	1	1.2
Surgical stages			
	Stage I	63	74.1
	Stage II	4	4.7
	Stage III	13	15.3
	Stage IV	5	5.9

Table 2. Distribution of loss among 84 patients in survival study

Stages	Number of patients loss (cases)	Total (cases)	Percent	Median(Range) (months)
Stage I	9	62	12.9	33 (7 – 57)
Stage II	0	4	0	-
Stage III	3	13	23	4 (2 – 13)
Stage IV	2	5	40	3 (1-3)
Total	13	84	15.5	13 (2 – 57)

Table 3. Operative findings among 84 patients

Prognostic factors	Positive cases	Cases performed	Percent
Peritoneal cytology	3	67	4.5
Adnexal metastasis	11	84	13.1
Pelvic node	6	76	7.9
Paraaortic	5	51	9.8
Intraabdominal invasion	5	84	6.0
Cervical invasion	12	84	14.3
Lymphovascular invasion	2	84	2.4
Grade			
G1 (well)	55	84	65.5
G2 (moderate)	16	84	19.0
G3 (poor)	13	84	15.5
Depth of invasion			
None	17	84	20.2
< 50 %	32	84	38.1
> 50 %	35	84	41.7

5-year survival rate is shown in Figure 1 with 93% in stage I, 75% in stage II, 42% in stage III, and 0% in stage IV. Patients who received adjuvant radiation in stage I showed no difference in survival to the non radiation group.(Figure 2) In stage III, although the radiation group appeared to have better survival (Figure 3), it did not reach a statistically significant level. Prognostic factors were compared in univariate analysis (Table 4). Since there was a too low positive number, lymphovascular invasion and positive peritoneal cytology were not studied. Age > 60, histologic grade 3, > 50% depth of invasion, positive cervical invasion, positive adnexal metastasis, positive lymph node metastasis were statistically worse in survival while nulliparity was not.

When these factors proceeded into multivariate analysis, only depth of invasion was a significant independent factor with odd ratio 4.77 and 95% confident interval at 1.33 -17.10 (Table 5).

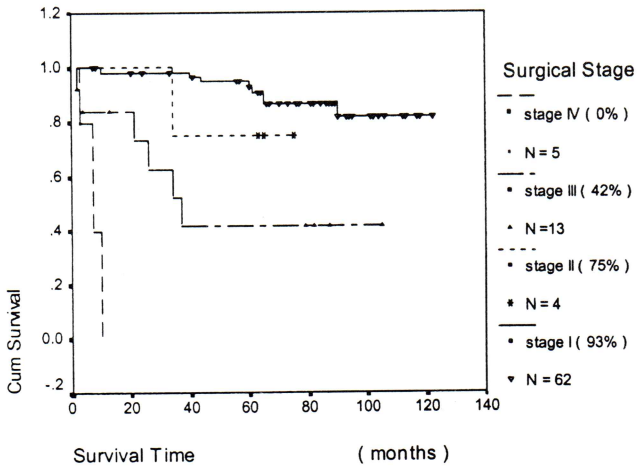


Fig. 1. Survival curves of surgically staging.

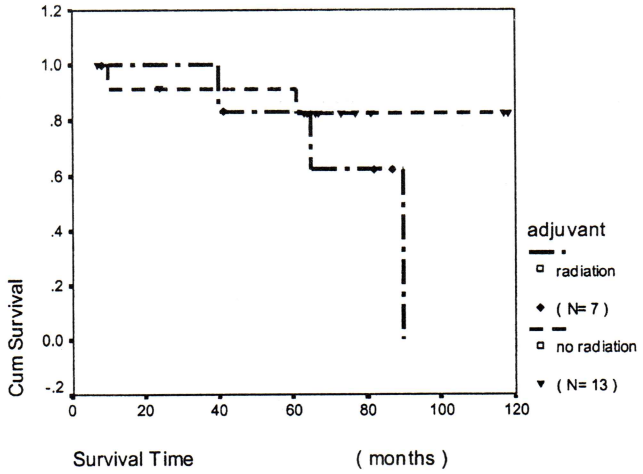


Fig. 2. Survival curve in staging I (high risk).

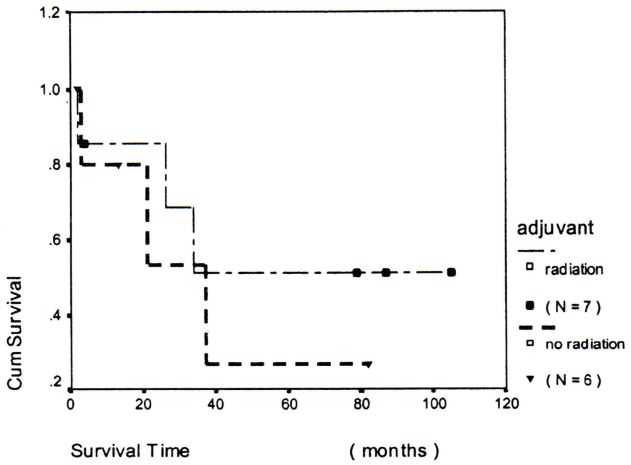


Fig. 3. Survival curve in stage III.

Table 4. Univariate analysis of prognostic factors

Prognostic factors		Total = 84 N (case)	5-year survival	P-value (< 0.05)
Ages				
	< or = 60	65	83 %	0.04
	> 60	19	75 %	
Parity				
	Nulliparous	26	87 %	0.27 NS
	Parous	58	81%	
Grades				
	G 1 – G 2	71	87%	0.001
	G3	13	53%	
Depth of invasion				
	< 50 %	49	93 %	0.001
	> 50 %	35	62 %	
Cervical invasion				
	Negative	72	88 %	0.03
	Positive	12	55 %	
Adnexal metastasis				
	Negative	73	83 %	0.001
	Positive	11	36 %	
Lymph node metastasis *				
	Negative	69	85 %	0.001
	Positive	7	55 %	

* Retroperitoneal lymph node biopsy done in 76 cases.

Table 5. Multivariate analysis among 84 patients

Factors	Exp (B)	Significant	95 % CI
Age	1.16	0.80	0.37 - 3.64
Parity	7.90	0.34	0.50 - 7.90
Grade	3.12	0.60	0.97 - 10.06
Depth of invasion	4.77	0.17	1.33 - 17.10
Cervical invasion	1.43	0.58	0.40 - 5.04
Adnexal metastasis	2.92	0.84	0.86 - 9.88
Lymph node metastasis	0.99	0.87	0.85 - 1.15

Discussion

Endometrial carcinoma is one of the most common gynecologic cancers.[1] Borronow et al,[2] Cowles et al,[3] had reported the inaccuracy of clinical staging system. Surgical staging was introduced by FIGO in 1988.[4] Wolfson et al[5] demonstrated surgical staging to be the strongest prognosticator of survival. Gal et al[6] also stated the benefit of subsequent therapeutic disposition. Increasing popularity in this system had been noted.[7] In this study the median age was 53 years, lower than the 60-65 of other studies.[5,8] 13 cases (15.5%) lost during follow up due to geographic restrictions ,a particular problem for those with advanced disease. The 5-year survival rate by surgical staging was 93% for stage I, 75% for stage II, 42% for stage III, 0% for stage IV, comparable to other published report where the survival rate ranges were 90-98% for stage I,[5,7] 72-76%for stage II,[9,10] 54-70% for stage III,[5,11,12] and 0-10% for stage IV[13] Although nulliparity has been considered as adversely affecting survival, it was not found to be an influence in our study. Increasing age is also considered to have poorer prognosis,[14 - 17] although this is contradicted in the Evans - Metcalf et al study.[18] We arbitrarily dichotomized age into < or = 60 and > 60 year , and a statistically significant result , the same as reproduced by Aziz et al,[15] was obtained , with 42% of latter group being in the higher stages.

In view of the surgicopathologic features, a relatively lower positive peritoneal cytology rate (4.5 %) was shown than 8.4 %-12.6 % by others.[17,19] No positive peritoneal cytology was found where the disease was confined to the uterus. Lymphovascular invasion was found in only 2.4%, Since Inoury et al [20] extensively reviewed pathologic specimen and reported as high as 34.5 %, more investigation of this aspect is warranted. Cervical invasion was found in 14%, comparable with the 13 % by Kadar et al.[17] Interestingly, 66.7% had extrauterine disease compared to 20 % - 30 % reported by others.[9, 10] In node positive cases, 3 cases had disease confined to uterine corpus only but with more than half of myometrial invasion. To estimate the depth of myometrial invasion may be valuable in deciding whether lymph node dissection should be done. Goff[21] found the depth of invasion was accurately determined by gross examination in 87.3% in grade 1 and less reliable as the grade of tumor increased. Fanning[22] used intraoperative frozen section to assess depth of myometrial invasion with 95% accuracy. However, Takeshima et al [23] found incidence of pelvic lymph node metastasis was 4% in endometrial carcinoma with no myometrial invasion. More than half of myometrial invasion had a significantly adverse affect upon survival in our study. We believe that the surgical approach plays an important role in justification of the adjuvant treatment. Despite the prognosis in advanced stage is poor, Goff et al[13] and Chi et al[24] suggested that surgical cytoreduction in stage IV should be done due to survival improvement. In this preliminary study any conclusion regarding the benefit of adjuvant radiation could not be drawn. A greater number of cases, combined with improvement and refinement the follow up program , would be needed for further study in this area.

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