Thai Journal of Obstetrics and Gynaecology
December 2001, Vol. 13, pp. 221-229

GYNAECOLOGY

Recurrent rate and prognostic factors in early stage common epithelial ovarian cancer at King Chulalongkorn Memorial Hospital between 1995-1999

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ABSTRACT

Objective The aims of this study were to evaluate possible prognostic factors that related to disease-free survival in patients with apparent early stage epithelial ovarian carcinoma.

Study design Retrospective analytical study.

Setting Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital.

Methods A retrospective analysis was conducted including 110 patients who were diagnosed to have apparent early stage epithelial ovarian carcinoma, and treated at King Chulalongkorn Memorial Hospital between 1995-1999. Epidemiological data was obtained from each patient chart. Prognostic variables were evaluated by univariate and multivariate analysis.

Findings The recurrent rate in patients with apparent early stage epithelial ovarian carcinoma was 12.7% (14 out of 110 cases); median follow up time was 27 months (range 5-62). Adjuvant chemotherapy was given to 88 (80%) patients. All cases with tumor recurrence were patients who received adjuvant chemotherapy. Among these, 3 out of 52 (5.7 %) patients who received cisplatin and 10 out of 31 (32.2%) patients who received carboplatin relapsed. A univariate model revealed that FIGO staging ($p<0.001$) and type of adjuvant treatment ($p<0.001$) were associated with poor disease-free survival. Multivariate analysis disclosed that adjuvant chemotherapy was the single reliable prognostic indicator of disease-free survival ($p < 0.05$) in which the finding show that carboplatin contribute to lower disease-free survival rate. None of the following was shown to have prognostic value: age, parity, tumor volume, ascites, tumor adhesion, associated endometriosis, histological type and rupture of the tumor during operation.

Interpretation Type of adjuvant chemotherapy was the most reliable prognostic indicator in early stage epithelial ovarian carcinoma.

Key words: prognostic factors, common epithelial ovarian cancer

table 2. The characteristics found to associated with disease-free survival in univariate analysis were type of adjuvant chemotherapy and FIGO staging (log rank test, $p < 0.05$). Age, body weight, parity, volume of tumor, site, amount of ascites, adhesion, rupture of capsule and histological type did not seem to be significant for overall survival. Life table plots of disease-free survival according to age, events of ascites, rupture of capsule, staging, histological type, adjuvant chemotherapy were shown in figure 1.

Staging and adjuvant chemotherapy were entered in the multivariate model. The only factor that was significant and independent predictors of disease-free survival was type of adjuvant chemotherapy, according to figure I, we could see that carboplatin contribute to lower disease free survival rate when compared to other chemotherapy. (hazard ratio = 2.3, 95% CI = 1.2, 4.4)

Table 1. Patient characteristic and recurrence

Characteristics	Number	Number	
		recurrence	no recurrence
Age			
<45	55	6	49
>45	55	8	47
Status			
Single	42	5	37
married	68	9	59
Menopause			
Premenopause	38	10	28
postmenopause	72	4	68
Parity			
0	77	9	68
1-2	19	3	16
>2	4	2	2
Body weight			
<56	69	8	61
>56	41	6	35
Tumor volume			
<10	41	5	36
10-20	57	8	49
>20	12	1	11
CA 125			
Not record	87	12	75
>35	5	2	3
<35	18	-	18
Site			
Right	40	4	36
Left	48	4	44
Both	22	6	16

Characteristics	Number	Number	
		recurrence	no recurrence
Ascites			
No	63	6	57
<100	20	4	16
100-1000	19	2	17
>1000	8	2	6
Rupture			
No	50	5	45
Spontaneous	12	1	11
During	48	8	40
Adhesion			
No	52	8	44
Yes	58	6	52
Endometriosis			
No	89	13	76
Yes	21	1	20
Stage			
Ia	36	1	35
Ib	6	2	4
Ic	57	8	49
II a	2	2	-
II b	2	-	-
II c	7	1	8
Histological type			
Clear cell	33	5	28
Serous	16	2	14
Mucinous	21	1	20
Endometrioid	35	6	29
Mixed	5	-	5
Surgery			
Complete stage	40	6	34
TAH c BSO	58	7	51
Unilateral SO	12	1	11
Treatment			
Surgery	21	0	21
Surgery + chemo	89	14	75
Adjuvant chemoRx			
No	22	1	21
Cisplatin	52	3	49
Carboplatin	31	10	21
Melphalan	5	-	5

Table 2. Patient Outcome

Characteristics	5-year disease- free survival (%)	P value	
		Univariate	Multivariate
Age			
<45	86.0		
>45	56.4	0.98	NA
Rupture of tumor capsule			
No	91.0		
Previous	90.0		
During	81.1	0.59	NA
Ascites			
No	89.9		
<100	70.9		
100-1000	93.3		
>1000	-	0.20	NA
Histological type			
Clear cell	84.3		
Serous	-		
Mucinous	95.1		
Endometrioid	81.3		
Mixed	100.0	0.59	NA
FIGO staging			
Ia	91.3		
Ib	-		
Ic	85.0		
II a	-		
II b	-		
II c	-	< 0.001	0.186
Adjuvant chemotherapy			
No	100.0		
Cisplatin	94.2		
Carboplatin	53.8		
Melphalan	83.3	< 0.001	0.006

Note. NA, not applicable

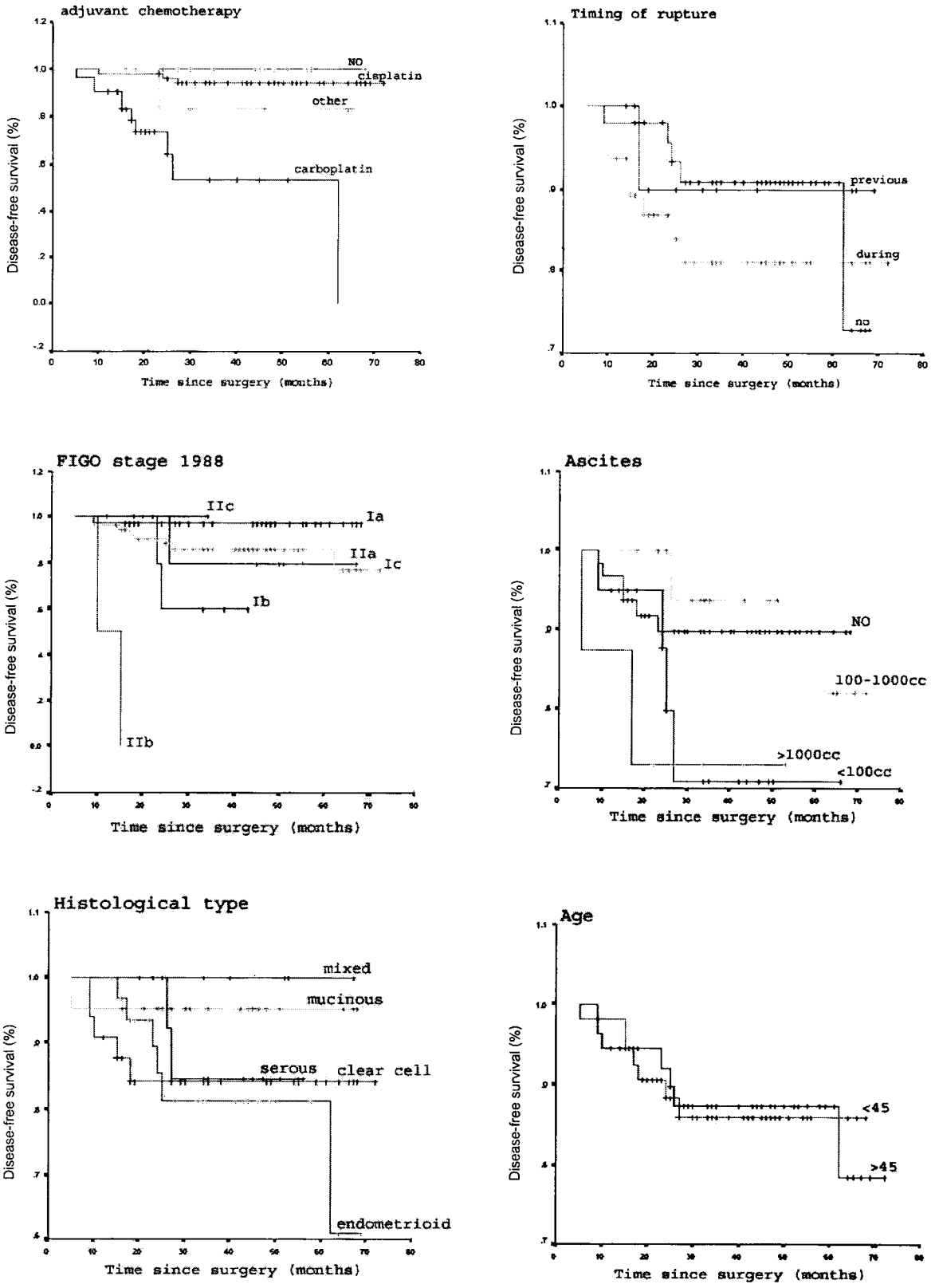

Fig. 1. Disease-free survival according to prognostic variables.

Discussion

FIGO staging and type of adjuvant chemotherapy were adverse prognostic factors found in our study while other variables such as rupture tumor's capsule or extension of the tumor to the surface of the ovaries had no prognostic significance. These results were different from the findings reported by Webb, Einhorn and Vergote.[6,7,15,16]

Since 70 out of 110 patients (63.6%) were not adequately staged, this rendered a particular problem when analyzing the impact of FIGO staging on disease outcome. To compensate this weakness, it should be noted that there was no patients who dropped out of her follow-up one-year and was the only strength of this study.

Though our study did not prove that disease staging was significant in multivariate analyses, but the importance of surgical staging should not be overlooked. To explain this, the importance of surgical staging might be undermined by effect of adjuvant treatment and the lack of standardized surgical staging during the years encompassed in this report. Since universal surgical staging was not performed, there was no risk classification to widely accepted low risk or high risk as suggested by Young et al[17] and Piver.[18] Decision on prescribing adjuvant chemotherapy was made by clinical findings which was inaccurate for determining extent of disease. If patients were properly staged, adjuvant chemotherapy might be unnecessary especially in the low-risk group, many of these patients who received postoperative chemotherapy would be considered overtreated and might influence recurrence, disease free survival and most of those variables that lost significant in univariate analysis. Emphasize had been made by Young et al[17] and Piver[18] who showed that 20% to 30% of stage I ovarian cancer were upstaged after restaging by laparotomy which included total abdominal hysterectomy, omentectomy, peritoneal washing, paraaortic and pelvic lymphadenectomy.

It is interesting to find that carboplatin as an adjuvant treatment employed in our study was shown to be single independent prognostic factor in both univariate and multivariate analysis. Carboplatin was obviously observed to correlate with higher recurrence and poor survival when compared with cisplatin in our study. This may be explained by a rather low dose of carboplatin being used in our patients ranging from 300-330 mg/m^2. An increment to AUC of 7 may be considered comparable to cisplatin dose of 70 mg/m^2. Though carboplatin was considered to be equally effective to cisplatin, all reported citations were made originally from a comparative trial conducted in advanced disease. There was no such a single trial to compare cisplatin and carboplatin in an early stage disease setting. Few randomized trials in early disease setting[19,20] have been reported, but each of them was too small to establish the role of adjuvant platin therapy in early ovarian cancer.

Type of chemotherapy and extent of disease exerted influence on disease recurrence and disease-free survival in our study. Proper staging is generally recommended to verify cases with high risk and necessitate adjuvant chemotherapy. Further study on optimal carboplatin dose and the others prognostic factor example oncogenes should be explored in early ovarian carcinoma.

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