Associations between tumor diameter and prognostic variables of epithelial ovarian cancer

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Summary

Purpose: Associations of tumor diameter in epithelial ovarian cancer with clinical and pathological prognostic variables were investigated.

Methods: The clinical and pathological records of 233 patients diagnosed with epithelial ovarian cancer and treated at Aichi Cancer Center were studied.

Results: Tumor diameters of 44 patients (18.9%) were < 5 cm, 90 (38.6%) were 5-10 cm, and 99 (42.5%) were > 10 cm. While 90.9% (40/44) of < 5 cm tumors presented with FIGO stage III-IV, 40.4% (40/99) of > 10 cm tumors were advanced. Intra-abdominal disease was also significantly associated with tumor diameter, although differences among lymph-node status were not significant. The incidence of serous and endometrioid adenocarcinoma in < 5 cm tumors were 75.0% (33/44) and 11.4% (5/44), respectively, while those of > 10 cm tumor were 32.3% (32/99) and 17.2% (17/99). Multivariate analysis revealed that tumor diameter was not an independent prognostic variable.

Conclusion: Tumor diameter of ovarian cancer is associated closely with histological subtypes and stage of disease, especially intra-abdominal disease.

Key words: Ovarian cancer; Tumor diameter.

Introduction

Though the size of the residual tumor after surgical treatment has been identified as a prognostic factor of ovarian cancer [1, 2], the diameter of the primary tumor has not been considered to be associated with prognosis, and has been viewed with little interest [3]. Tumor diameter has contributed less than tumor components of tumor or tumor markers in screening of ovarian cancer and distinguishing ovarian tumors whether benign or malignant [4]. Only when a giant tumor [5] or normal-sized ovary carcinoma syndrome [6] was found, did the diameter and/or weight of the primary tumor attract attention. However, the diameter of the primary tumor is a rare variable which could be confirmed before treatment.

The current study focused on the diameter of the primary tumor in epithelial ovarian cancer. We hoped to determine whether tumor diameter is associated with stage of disease, histology, or other clinicopathological variables.

Patients and Methods

The clinical and pathological records of all patients diagnosed with epithelial ovarian cancer at Aichi Cancer Center between 1990 and 2000 were reviewed. All patients had primary lesions diagnosed as epithelial ovarian cancer. A total of 233 patients formed the basis of the study. Informed consent was obtained from each patient regarding the use of clinicopathological variables.

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The age of patients at the initial evaluation, their menopausal state, presence or absence of obesity, and year of treatment were obtained from clinical records. Obesity was defined according to the criteria of the Japan Society of Obesity, i.e., a body mass index of more than 26.4. Primary disease was staged at the initial evaluation according to the staging system of the International Federation of Gynecology and Obstetrics (FIGO) and TNM. Tumor diameter was determined from MRI, CT, or echogram. The maximum diameter was noted for patients with gross tumors. All available pathological slides were reviewed for the diagnosis of histological subtypes.

Student's *t*-test analysis was used in comparing the age of patients. Pearson's chi-square test was used to examine the significance of variables in relation to the tumor diameter. Survival of patients was calculated by the method of Kaplan and Meier. The relationship between each of the variables and survival was assessed by the log-rank test. Multivariate results were confirmed using Cox proportional hazards regression. The stability of the model was certified by a likelihood ratio step-forward and step-backward fitting procedure. The level of significance was taken from the last step of the regression analysis. All variables were assessed for analyses according to the categories listed in Table 1. All tests were two-tailed; a p value of < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS software version 11.0.

Results

Associations between tumor diameter and other clinicopathological variables are summarized in Table 1. All patients in this study were Japanese with a mean age at presentation of 54.3 years (age range, 18.4 to

Table 1. — *Associations between tumor diameter and clinicopatholigical variables of epithelial ovarian cancer.*

		Tumor diameter (cm)				
		total	< 5	5 = 10	> 10	p
total		233	44	90	99	
age	mean	54.3	57.4	52.9	54.2	
	range	18-83	35-70	34-81	18-83	
	-40	76	10	33	33	0.073
	41-60	94	16	39	39	
	61-	63	18	18	27	
menopause	no	79	9	37	33	0.083
	yes	154	35	53	66	
obesity	no	211	38	85	88	0.162
	yes	22	6	5	11	
FIGO stage	I	72	2	24	46	< 0.001
	II	30	2	15	13	
	III-IV	131	40	51	40	
pTNM stage	pT1	78	3	26	49	< 0.001
	pT2	42	3	20	19	
	pT3	113	38	44	31	
	pN0	75	11	33	31	0.779
	pN1	53	10	22	21	
	pNX	105	23	35	47	
	pM0	206	35	79	92	0.037
	pM1	27	9	11	7	
histology	serous	101	33	36	32	< 0.001
	mucinous	35	1	6	28	
	endometrioid	57	5	35	17	
	clear cell	29	1	9	19	
	other	11	4	4	3	
overall	5 years	57.4%	27.6%	57.4%	70.7%	0.009
survival	10 years	48.2%	20.7%	54.5%	54.4%	
disease-free	5 years	45.6%	10.3%	45.6%	58.7%	< 0.001
survival	10 years	45.6%	10.3%	45.6%	58.7%	

83.7 years). Tumor diameters of 44 patients (18.9%) were < 5 cm, while 90 (38.6%) were 5-10 cm, and 99 (42.5%) were > 10 cm. While the mean age of patients with < 5 cm tumors was significantly older than that of those with 5-10 cm tumor ($p = 0.035$), there was no significant difference between < 5 cm and > 10 cm, or between 5-10 cm and > 10 cm. Although 90.9% of patients with < 5 cm tumors presented with advanced cancer more than FIGO Stage III, only 40.4% of > 10 cm tumors were advanced, and 46.5% of > 10 cm tumors were FIGO Stage I. In analyses using the pTNM staging system, intra-abdominal disease (pT classification) was also significantly associated with tumor diameter, although differences among lymph node status (pN classification) were not significant. Although 75.0% of < 5 cm tumors were serous adenocarcinoma, the incidences of 5-10 cm and > 10 cm were 40.0% and 32.3%, respectively. While mucinous and clear cell adenocarcinomas were rare in < 5 cm tumors, the incidences of these histological subtypes increased in > 10 cm tumors to 28.3% and 19.2%, respectively. While the prognosis of < 5 cm tumors was significantly poorer than those of 5-10 cm and > 10 cm tumor (Table 1), multivariate analysis revealed that the FIGO Stage was the only independent prognostic variable (analysis of overall survival; Stage II: odds ratio 8.93, 95% confidence interval 0.93-85.90, Stage III-IV: odds ratio 23.21, 95% confidence interval 3.11-173.34, $p < 0.001$, analysis of disease free survival; stage II: odds ratio 11.86, 95% confidence interval 1.33-106.08, Stage III-IV: odds ratio 35.34, 95% confidence interval 4.80-260.33, $p < 0.001$).

Discussion

Most patients with ovarian cancer present with advanced disease in which the tumor has spread to the peritoneal surface of the upper abdomen [7]. Extensive intra-abdominal disease is difficult to eradicate completely by surgery, and many patients have only a partial response to postoperative chemotherapy [7]. For these reasons, the stage of disease has been considered as the most important prognostic variable of ovarian cancer [1-3, 7, 8], as the multivariate analysis of this study indicated. Another important variable of ovarian cancer is histological subtype [8]. In particular, it has been reported that clear cell adenocarcinoma and mucinous adenocarcinoma have a poor response to conventional platinum-based chemotherapy and the overall prognosis is poor [8]. Unfortunately, the stage of disease and the histological subtype cannot be confirmed without surgical investigation.

Our study revealed that tumor diameter of ovarian cancer was associated with these two important variables. While 90.9% of patients with < 5 cm tumors were diagnosed as having advanced disease, only 40.4% of those with > 10 cm tumors were advanced. Although 9.1% of < 5 cm tumors were diagnosed pathologically as mucinous or clear cell adenocarcinoma, 47.5% of > 10 cm tumors were diagnosed as such. These results suggest that tumor diameter of ovarian cancer is closely associated with the stage of disease and histological subtypes. Moreover, these variables could be estimated more accurately using the tumor diameter together with other variables such as tumor markers, volume of ascites, and solid components of tumors.

In conclusion, the diameter of the primary tumor was associated closely with histological subtype and the stage of ovarian cancer, especially with intra-abdominal disease. Our study suggested that tumor diameter would be a valuable clinical variable of ovarian cancer.

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