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Lymphatic metastasis in epithelial ovarian carcinoma with respect to clinicopathological variables

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Abstract

Objective. The purpose of this study was to evaluate the prognostic factors, and the patterns of lymphatic metastasis in EOC patients who were treated with systematic pelvic and paraaortic lymphatic dissection.

Methods. A total of 420 EOC patients was retrospectively evaluated. Clinical factors available were evaluated for a possible significance in terms of lymphatic metastasis and paraaortic involvement.

Results. Two-hundred and three patients were found to have lymphatic metastasis. In multivariable analysis, stage ($P < 0.001$), histology ($P < 0.01$ for serous; $P = 0.02$ for mixed, and $P = 0.04$, for Brenner), and Ca-125 level higher than 500 U/ml ($P = 0.04$) were found to be significantly related with the lymphatic involvement. Age and grade were significant factors for paraaortic metastasis both in univariable and multivariable analysis ($P = 0.003$ and $P = 0.02$, respectively). Most of the patients with unilateral tumors had contralateral pelvic and/or paraaortic metastasis. There were eleven patients with lymphatic metastasis in stage I–II disease, and five had paraaortic metastasis while an additional five patients had contralateral pelvic nodal metastasis. However, there was no lymphatic involvement in Stage IA, Grade I–II disease (0/63). Survival analysis revealed no significant difference by the number of metastatic lymph nodes.

Conclusion. In multivariable analysis, lymphatic involvement was predicted independently by stage, histology, and Ca-125 level. In apparently stage I–II disease, a considerable part of patients were upstaged due to lymphatic involvement. Although routine systematic lymphadenectomy is suggested for patients with early stage disease, further series are needed for a definite regimen in patients with stage IA G1–2 disease since we did not detect any lymphatic involvement in this unique group.

Keywords: Lymphatic metastasis; Ovarian cancer; Lymph node; Survival; Upstage; Systematic lymphadenectomy

Introduction

Epithelial ovarian cancers (EOC) are the most lethal tumors among gynecological malignancies [1]. In addition to the well-known intraperitoneal spread, they have the highest propensity to spread via the lymphatic system compared to the other genital malignancies [2,3]. Although therapeutic efficacy of lymphadenectomy is not still clarified, the knowledge of the lymphatic status is valuable in determining both the exact stage and the prognosis of the patients. Proper evaluation of the lymphatic metastasis can only be performed by systematic pelvic and paraaortic lymph node dissection. Therefore, the information gathered by lymph node sampling or selective biopsies is questionable [2,4,6–8].

The pattern of lymphatic spread and its relation with the clinicopathological variables were not evaluated extensively in the literature. Some series contained insufficient

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number of patients, while some others included the patients with lymph node sampling. This lack of data prompted us to evaluate the prognostic factors, and the patterns of lymphatic metastasis in EOC patients who were treated with systematic pelvic and paraaortic lymph node dissection.

Patients and methods

Four hundred and twenty patients with EOC treated at Hacettepe University between January 1982 and June 2001 were retrospectively evaluated. Data were retrieved from the hospital records and special gynecologic oncology files. Exclusion criteria were as follows: borderline malignancies, tumors other than the primary EOCs, patients who did not undergo a systematic lymphadenectomy or who had received preoperative chemotherapy. All the patients were subjected to the primary cytoreductive surgery including systematic pelvic and paraaortic lymphadenectomy. Pelvic lymphadenectomy was accomplished by completely skeletonizing the external iliac vessels and removing all the nodes around the vessels. The common iliac and obturator nodes were dissected using blunt and sharp dissection, and all tissues above the obturator nerve were removed. The paraaortic area was exposed just above the bifurcation. The retroperitoneal space and the lymph nodes at the bifurcation of the aorta anterior to the vena cava and below the renal vessels on the right and left sides were dissected. Patients with residual disease <1 cm were defined as optimally cytoreduced. Surgeries were undertaken by the same surgical team in all patients.

The patients were evaluated with respect to the age at diagnosis, the resected number of lymph nodes, clinical stage, histology, and grade, quantity of ascites, peritoneal cytology findings, Ca-125 levels, maximal tumor diameter, tumor laterality, and cytoreductive effort to observe a possible relation with lymphatic metastasis. Additionally, patients with isolated pelvic lymph node metastasis were compared with the patients having paraaortic involvement. Chi-square, Student's t, and Mann–Whitney U tests were used to estimate the differences between patients in terms of evaluated variables by lymph node status. Survival rates were estimated by the Kaplan–Meier method, and tested for significance by log-rank test. Multivariable analysis was undertaken by logistic regression analysis in a stepwise forward fashion. A P value of <0.05 was considered to be significant.

Results

Mean age at the time of diagnosis was 52.01 ± 13.9 (range, 19–88) years. One hundred sixty-nine patients (40.2%) had stage I–II disease where the tumor was apparently confined to one or both ovaries or limited to the pelvis. The remaining 251 (59.8%) patients had stage III–IV disease (59.8%).

Overall, 203 (48.4%) patients had lymph node metastasis [LN(+)]. Of these patients, 76 (37.5%) had isolated pelvic metastasis, 36 (17.7%) had isolated paraaortic metastasis, and 91 (44.8%) had both pelvic and paraaortic metastases. The mean resected lymph node number was 24.7 ± 12.6 (range, 2–108) without a significant difference between LN(+) and LN(−) groups ($P > 0.1$). The mean number of metastatic lymph nodes was 5.76 (range, 1–54). The clinicopathological variables of the patients were listed in Table 1.

Table 1
Clinicopathological variables of the patients based on lymphatic metastasis

	Total (%)	Lymph node (LN) status		P value
		LN Negative (%)	LN positive (%)	
Number of patients	420	217 (51.6)	203 (48.4)	
Mean age (range)	52.01 (19–88)	50.17 (19–81)	53.97 (23–88)	0.005
Mean LN number removed (range)	24.77 (2–108)	24.88 (2–69)	24.65 (4–108)	0.85
Stage				
I–II	169 (40.2)	145 (85.8)	24 (14.2)	<0.001
III–IV	251 (59.8)	72 (28.7)	179 (71.3)	
Histology				
Serous	219 (52.1)	90 (41.1)	129 (58.9)	<0.001
Mucinous	74 (17.6)	62 (83.8)	12 (16.2)	
Endometrioid	43 (10.2)	27 (62.8)	16 (37.2)	
Mixed	39 (9.3)	16 (41.0)	23 (59.0)	
Anaplastic	21 (5.0)	8 (38.1)	13 (61.9)	
Brenner	12 (2.9)	5 (41.7)	7 (58.3)	
Clear	12 (2.9)	9 (75.0)	3 (25.0)	
Grade				
Grade I	110 (26.2)	90 (81.8)	20 (18.2)	<0.001
Grade II	112 (26.7)	59 (52.7)	53 (47.3)	
Grade III	198 (47.1)	68 (34.3)	130 (65.7)	
Cytology				
Negative	235 (56.0)	141 (60.0)	94 (40.0)	<0.001
Positive	136 (32.4)	55 (40.4)	81 (59.6)	
Not reported	49 (11.6)			
Ascites				
Absent	280 (66.6)	162 (57.9)	118 (42.1)	<0.001
<1000 cc	23 (5.5)	13 (56.5)	10 (43.5)	
≥1000 cc	117 (27.9)	42 (35.9)	75 (64.1)	
Ca-125				
<35	96 (22.9)	81 (84.4)	15 (15.6)	< 0.001
35–500	148 (35.2)	71 (48.0)	77 (52.0)	
≥500	145 (34.5)	44 (30.3)	101 (69.7)	
Not reported	31 (7.4)			
Tumor diameter				
<10 cm	227 (54.0)	100 (44.1)	127 (55.9)	0.001
≥10 cm	193 (46.0)	117 (60.6)	76 (39.4)	
Cytoreduction				
Optimal	321 (76.4)	186 (57.9)	135 (42.1)	< 0.001
Suboptimal	99 (23.6)	31 (31.3)	68 (68.7)	