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Study on Surgical Staging, Type of Histology and Tumor Grade in Patients with Ovarian Cancer in North West of Iran

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Abstract: Ovarian cancer is the second most common malignancy of the female genital tract and the seventh most common cancer in women. Ovarian cancer is 4% of all women cancers. Total 90% of ovarian cancers are epithelial type. The aim of this study was to evaluate FIGO stage, tumor histology and grade in patients with ovarian cancer. We performed a retrospective chart review of all patients with ovarian carcinoma who received their primary treatment at our institution between 2004 and 2006. A total of 42 patients were identified. Of these, 50% was in stage III, 59.6% had grade 2 and 54.8% had parity 5 and more. The most common histologic type was epithelial (85.7%). Significantly correlation was not found between histology and grade of tumor ($p = 0.586$) but histology of tumor had significantly correlation with stage of tumor ($p = 0.017$). Histology of tumor had not significantly correlation with age group of patients ($p = 0.111$). With increasing of tumor grade the stage of tumor was increased. Significantly correlation was found between ascites and presence of malignant cells in ascitis fluid. With increase of grade and stage of disease, frequency of ascites was high and with increase of patients age, stage of tumor significantly increased. With increase of tumor grade, frequency of omentum involvement and ascites were high. With attentive that in present study on 42 patients, stage and grade of disease were high, establishing the programs for improving of women's attitude about ovarian cancer are necessary.

Key words: Ovarian cancer, tumor grade, tumor cell type, tumor stage

INTRODUCTION

Ovarian cancer is the second most common malignancy of the female genital tract and the seventh most common cancer in women. A woman's risk at birth of having ovarian cancer sometime in her life is 1-1.5% and that of dying from ovarian cancer almost 0.5%. It accounts for 4% of all female cancers and 31% of cancers of the female genital organs (Gershenson, 2000; Jonathan, 2004, 2007).

Ovarian cancer is the fourth most frequent cause of cancer death in women and accounts for 5% of all cancer death. The death rate from ovarian cancer exceeds that of cervical and endometrial carcinomas (Robert *et al*., 2005).

Approximately 90% of ovarian cancers are derived from tissues that come from the celomic epithelium or "modified mesothelium". Approximately 75-80% of epithelial cancers are of the serous histology type. Less common types are mucinous (10%), endometrioid (10%), clear cell, Brenner and undifferentiated carcinomas, each of the latter three representing less than 1% of epithelial lesions. Nonepithelial malignancies of the ovary account for approximately 10% of all ovarian cancers. Nonepithelial ovarian cancers include malignancies of germ cell origin, sex cord-stromal cell origin, metastatic carcinomas to the ovary and a variety of extremely rare ovarian cancers (e.g., sarcomas, lipoid cell tumors) (Jonathan, 2004).

The molecular events leading to the development of epithelial ovarian cancer are unknown. Epidemiologic studies, however, have identified endocrine, environmental and genetic factors as being important in the carcinogenesis of ovarian cancer. Epidemiologically established risk factors include nulliparity, family history, early menarche and late menopause, white race, increasing age and residence in North America and Europe. The understanding of the early natural history and patterns of spread of epithelial ovarian cancer form the basis for a rational system for staging the disease and for the surgical management of apparent early ovarian cancer. Surgery accurately stages a patient and allows the evaluation of a series of clinicopathologic variables that are often used to select postoperative therapy. These prognostic factors are; tumor stage, volume of residual disease, histologic subtype and grade. Controversy remains about the prognostic importance of other surgical

observations. Tumor size, bilaterality and ascites without cytologically positive cells are not considered to be of prognostic significance in patients with early-stage disease. However, tumor spillage capsular penetration and cytologically malignant ascites (FIGO stage IC) are generally believed to be associated with a worse prognosis (Robert *et al*., 2005). The aim of this study was to evaluate FIGO stage, tumor histology and grade in patients with ovarian cancer.

MATERIALS AND METHODS

A total of 42 patients who had been operated for ovarian cancer in referral Alzahra Teaching Hospital located in north west of Iran between 2004 and 2006 were retrospectively evaluated. All the patients had undergone an initial staging and debulking surgery including total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, bilateral pelvic and para-aortic lymphadenectomy. Multiple peritoneal biopsies, cytologic washings and sampling of ascites (if present) were gathered from each patient at the beginning of the operation. All pathologic and cytologic specimens were sent to the laboratory for evaluation just after the operation. Depending on the pathologic findings, all the patients were treated with initial cytoreductive surgery and followed up by chemotherapy, if necessary. Operative reports, especial gynecological oncology files and pathologic findings were reviewed for the clinico-pathologic variables analyzed in this study.

Exclusion criteria were as follows: Patients with borderline malignancies, patients with tumors other than the primary ovarian cancer (Krukenberg's tumors, primary serous papillary carcinoma of the peritoneum, etc.), patients who had been given preoperative chemotherapy before admission to the hospital and patients who were not properly staged according to the recommendations of FIGO and patients with recurrent ovarian tumors.

Age, parity, stage, tumor grade, histologic type, tumor spread (lymphatic, omental) and ascites were the variables analyzed.

All statistical calculations were performed by using the SPSS software package version 12. Chi-square, ANOVA one way, Mann Whitney U and t-test, statistics were used to compare of the study variables. p-value of less than 0.05 was considered statistically significant.

RESULTS

Clinical characteristics are shown in Table 1. According to different parity groups, the most common group was 5 or more 23(54.8%). The most common age group was 50-59 years (40.5%).

Table 1: Clinical characteristics

	Frequency	Valid (%)
Parity		
0	8	19.0
1-2	7	16.7
3-4	4	9.5
≥ 5	23	54.8
Total	42	100.0
Age (years)		
<30	6	14.3
30-39	3	11.9
40-49	10	23.8
5059	17	40.5
≥ 60	4	9.5
Total	42	100.0

Table 2: Pathologic characteristics

	Frequency	Valid (%)
Histologic grade		
1	12	28.6
2	25	59.5
3	5	11.9
FIGO stage		
I	13	31.0
II	5	11.9
III	21	50.0
IV	3	7.1
Histologic type		
Epithelial	36	85.70
Endometrioid	3	7.14
Serous	29	69.40
Mucinous	4	9.52
Germ cell	4	9.50
Dysgerminoma	2	4.76
Immature teratum	2	4.76
Granulosa	2	4.76
Lymph node status		
Negative	36	85.50
Positive	6	14.30
Omental involvement	21	50.00
Ascites	22	52.40
Malignant cells in asciteic fluid	13	59.00

Pathologic characteristics are shown in Table 2. The predominant histologic type was epithelial (85.7%). The most common stage and grade of tumor were, respectively; III and 2. Of 22 (52.4) patients with ascites, 13 (59%) had malignant cells in the ascitic fluid. Patients with ascites were statistically more likely to have malignant cells in ascitic fluid compared to the patients with no ascites ($p = 0.005$). About 21 (50%) of patients had omental involvement. This results shows that 50% of patients had advanced disease.

Ascitic fluid status correlation among the grade, stage and cell type of tumors are shown in Table 3. Ascites was present in 16.6% of grade 1. Sixty four percent of grade 2 and 80% of grade 3 ($p = 0.004$), however there was no significant difference between tumor grade and prescence of malignant cells on ascetic

fluid (p = 0.122). Ascites was present in 7.6, 20, 80.9 and 100% of patients with stage I, II, III and IV disease, respectively (p = 0.005) and also patients with advanced stages were statistically more likely to have ascetic fluid with malignant cells than early stages (p = 0.005). Ascites was present in 55.5 and 33.3% of patients with epithelial and nonepithelial tumors, respectively (p = 0.072). Patients with epithelial tumors were not statistically more likely to have malignant ascites compared to the nonepithelial tumors (p = 0.091).

The correlation of age with FIGO stage, tumor grade and histologic type of tumor are shown in Table 4. When evaluating all grades of tumor, there was no detectable difference in grade among the 5 age groups, (p = 0.8). However, the most common age group in grade 1, 2 and 3 was 50-59 age group. The age group differences between different stages were not significant, (p = 0.52), but stage I was common in age group of <30 and other stages were common in older patients. There were no differences between tumor cell types and different age groups, (p = 0.11).

Grade, histologic type and parity by cancer stages are shown in Table 5. Tumor grade increased with stage (p = 0.005). There were no differences between the cancer stages with respect to tumor histologic type and parity.

The correlation of tumor grade with histologic type, omental and lymph node involvements are shown in Table 6. There were no statistically differences between the tumor grades and different histologic types (p = 0.848). Patients with grade 3 were statistically more likely to have omental involvement (8.3 vs. 64 vs. 80%, p = 0.002). Fourteen percent of all patients had lymph node involvement with no difference in incidence among the 3 grade groups (p = 0.333).

Table 3: FIGO stage, grade and histologic type by ascites with respect to the peritoneal cytology

		Malignant cells on ascites fluid		
	Ascites total	Positive n (%)	Negative n (%)	p-value
Histologic grade				
1	2	1 (50)	1 (50)	0.122
2	16	10 (62.5)	6 (37.5)	
3	4	2 (50)	2 (50)	
FIGO stage				
I	1	-	1(100)	0.005
II	1	-	1(100)	
III	17	11 (64.7)	6 (35.3)	
IV	3	2 (66.6)	1 (33.4)	
Histologic type				0.091
Epithelial	20	13 (65)	7 (35)	
Non Epithelial	2	-	2 (100)	

Table 4: FIGO Stage, grade and histologic type by age

	Age<30 n (%)	Age 30-39 n (%)	Age 40-49 n (%)	Age 50-59 n (%)	Age>60 n (%)	Total	p-value
Grade							
1	2 (16.6)	1 (8.3)	3 (25)	4 (33.3)	2 (16.6)	12	0.8
2	4 (16)	4 (16)	6 (24)	10 (40)	1 (4)	25	
3	-	-	1 (20)	3 (60)	1 (20)	5	
FIGO Stage							
I	4 (30.7)	1 (7.6)	3 (23)	3 (23)	2 (15.3)	13	0.52
II	-	1 (20)	2 (40)	2 (40)	-	5	
III	2 (9.5)	3 (14.2)	5 (23.8)	9 (42.8)	2 (9.5)	21	
IV	-	-	-	3 (100)	-	3	
Histologic type							
Epithelial	3 (8.3)	5 (13.8)	8 (22.2)	17 (47)	3 (8.3)	36	0.11
Germ cell	3 (75)	-	1 (25)	-	-	4	
Sex cord stromal	-	-	1 (50)	-	1 (50)	2	
Total	6	5	10	17	4	42	

Table 5: Grade, histologic type and parity by stage

	Stage					
	I n (%)	II n (%)	III n (%)	IV n (%)	Total	p-value
Grade						
1	10(83)	1(8.3)	1(8.3)	-	12	0.005
2	3(12)	4(16)	16(64)	2(8)	25	
3	-	-	4(80%)	1(20)	5	
Histologic type						
Epithelial	8(22.2)	5(13.88)	20(55.5)	3(8.33)	36	0.146
Germ cell	3(75)	-	1(25)	-	4	
Sex cord stromal	2(100)	-	-	-	2	
Parity						
Nullipara	4(50)	2(25)	2(25)	-	8	0.276
1-2	2(28.5)	-	5(71.5)	-	7	
3-4	-	-	4(100)	-	4	
≥ 5	7(30.4)	3(13)	10(43.4)	3(13)	23	

Table 6: Pathologic charachteristics by tumor grade

	Stage				
	1 n (%)	2 n (%)	3 n (%)	Total	p-value
Histologic type					
Epithelial	10(27.7)	21(58.3)	5(13.8)	36	0.848
Germ cell	1(25)	3(75)	-	4	
Sex cord stromal	1(50)	1(50)	-	2	
Omental involvement	1(4.76)	16(76.1)	4(19)	21	0.002
Lymph node involvement	-	5(83.3)	1(16.6)	6	0.333

DISCUSSION

The great variability in survival of patients with ovarian cancer has prompted numerous investigations into which clinical factors influence survival (Sorbe *et al*., 1982; Sigurdsson *et al*., 1983; Lund *et al*., 1990; Neijt *et al*., 1991).

Review of the recent literature reveals various clinical and pathologic variables reported to be of prognostic significance. The GOG has identified age, performance status, histologic grade, cell type, cis-platinum-based chemotherapy, stage, ascites and size and number of residual lesions after primary cytoreductive surgery as significant prognostic factors in ovarian carcinoma (Omura *et al*., 1991; Hoskins *et al*., 1992, 1994).

More recently, Chi *et al*. (2001) in their multivariate analysis identified three factors as having prognostic significance: Age at time of diagnosis, presence or absence of ascites and size of residual disease remaining after primary cytoreductive surgery (Chi *et al*., 2001).

Our study showed that the most common age group of patients at time of diagnosis was 50-59 (40.5%) years with mean age of 46 years (range, 18-75) (Table 1). Brun *et al*. (2000), studied on long-term results and prognostic factors in 287 patients with epithelial ovarian cancer. Their analysis found that the most common age group was group of >60 years (49%), which is dissimilar to ours. It seems that different results of these studies may because they studied only on epithelial ovarian cancer whereas this study relied on all cell type of ovarian cancers. They showed that the most common stage and grade were stage III (52%) and grade 2 (38%). The results are similar to our study.

Of 42 patients, 22 (52.4%) had ascites. About 13(59%) of 22 patients having ascites, had malignant cells on ascitic fluid ($p = 0.005$). Shen and Mannel (2002) found 41 (73%) ascites in 56 patients with ovarian malignancy. They concluded that ovarian malignancies in the early stages (I and II) produced ascites only in 17% of the cases and in the advanced stages (III or IV), 89% produced ascites. Relationship between patients having ascites with respect to the peritoneal cytology and histopathologic characteristics are shown in Table 3. Our results are similar to those of Ayhan *et al*. (2007) who showed patients with advanced stages (III-IV) were statistically more likely to have malignant cells on ascetic fluid than the patients with early stages (I-II). In their study there was no detectable difference in presence of malignant cells on ascitic fluid in different tumor grades. The results are similar to our study.

Our data show that there are not distinct differences between younger and older populations with regard to histopathologic characteristics such as: grade, stage and cell type. Although, 60% of grade 3 tumors were in age group of 50-59 years versus 33% of grade 1 and the most common age group in epithelial and germ cell tumors were 50-59 and <30 years, respectively. Tsai *et al*. (2001) in their study on 19 epithelial ovarian cancer in patients age <21 years found that 79% of patients had stage I disease and 21% had stage III disease. Bozas *et al*. (2006) found that, age < or = 40 was correlated with low tumor grade ($p = 0.009$) and small volume of residual disease after primary surgery ($p = 0.020$). Our results are dissimilar to their study. It seems that different results of these studies may because, we studied all histologic type of ovarian cancers.

Ayhan *et al*. (2008) in their study on clinico-pathological correlation of metastiatic lymph node (LN) numbers in patients with ovarian carcinoma found that 31 (95%) patients had grade 1, 85 (25.9%) had grade 2 and the remaining 212 (64.6%) had grade 3 disease. Distribution of tumor grades was not significant among the groups ($p = 0.6$). The results are similar to those of our study which showed no significant difference in LN involvement in 3 groups of tumor grade ($p = 0.333$).

CONCLUSION

Will attentive in present study on 42 patients, which tumor stage and grade were high, establishing a population based cancer registry organization in our country 1st to evaluate exact epidemiology of ovarian carcinoma and second for improvement of women's attitude about the frequency and primary diagnostic methods particularly regular annually examination are essential.

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