Survival and prognostic factors in patients with synchronous ovarian and endometrial cancers and endometrial cancers metastatic to the ovaries

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Summary

Purpose: To compare the survival and prognostic factors of patients with synchronous primary ovarian and endometrial cancers, and endometrial cancers metastatic to the ovaries.

Patients and Methods: Fifty-three patients with synchronous primary ovarian and endometrial cancer and 64 patients with endometrial cancer metastatic to the ovaries were evaluated.

Results: Mean follow-up time was 47.2 months (18-170 months). There was no statistical difference in age, gravidity and parity between the two groups. Abnormal vaginal bleeding was the most common symptom in both groups. All patients were subjected to a surgical staging procedure. Overall survival of the synchronous group was significantly higher than that of the metastatic group (98 ± 12 vs 59 ± 6 months; p = 0.048). The significant prognostic factors for synchronous cancers after multivariate analysis were age, stage of ovarian cancer, grade of endometrial cancer, and adjuvant therapy status.

Conclusion: Patients with synchronous ovarian and endometrial cancers appear to have a good prognosis and should undergo primary surgical staging since the stage of tumors is a significant prognostic factor.

Key words: Ovarian carcinoma; Endometrial carcinoma; Synchronous tumors.

Introduction

Synchronous carcinomas involving both the ovary and uterus are relatively uncommon neoplasms and are found in 0.7-10% of patients with ovarian or endometrial cancer [1]. The co-existence of ovarian and endometrial cancer is still a diagnostic and therapeutic dilemma. There is much controversy with respect to diagnosing and managing of such cases since these cancers may represent either two synchronously occurring primary cancers or a single primary cancer with metastasis.

Although knowledge about prognostic factors and management of early stage in synchronous cancers exist in the literature [2, 3, 4], only a few reports were present for advanced stage diseases. The purpose of this study was to evaluate the prognostic factors and management in early and advanced synchronous ovarian and endometrial cancers and to compare them with those of endometrial carcinoma metastatic to the ovaries.

Materials and Methods

One hundred-seventeen patients admitted to the Gynecologic Oncology Division of Hacettepe University Hospital between 1982 and 2000 for synchronous ovarian and endometrial cancers (n = 53) and endometrial cancer metastatic to the ovaries (n = 64) were evaluated.

Data were obtained from patients' files, pathology reports, and gynecologic oncology follow-up forms. The patients were reviewed by dividing them into two groups. First, the synchronous group consisted of patients with primary ovarian and endometrial carcinoma, and second, the metastatic group consisted of patients with endometrial carcinoma metastatic to the ovaries. All patients were subjected to surgical staging (total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal cytology, omentectomy, pelvic and paraaortic lymph node dissection, multiple biopsies from different sites of the abdomen and tumoral debulking when necessary) assigned according to the classification of the International Federation of Gynecology and Obstetrics (FIGO) [5]. The differentiation between primary or metastatic cancers of the endometrium and ovary was made by using the pathological criteria of Ulbright and Roth [6]. The demographic features and histologic types, stages, and grades of tumors of the two groups were compared.

In 32 (60.3%) patients in the synchronous group, dissimilar histology of ovarian and endometrial carcinoma was found, while similar histology was found in the remaining 21 patients (39.6%). In the synchronous group, the most common histologic types were serous and endometrioid in the ovaries (34% and 32%, respectively) and endometrioid in the endometrium (94.3%). In the metastatic group, the most common histologic type was endometrioid adenocarcinoma (87%) (Table 1). Histological types of the synchronous group were subgrouped as endometrioid and non-endometrioid for statistical analysis.

In the synchronous group, 29 patients (55%) had Stage I, three patients (6%) had Stage II and 21 patients (40%) had Stage III ovarian cancer, and 44 (83%) had Stage I, three (5%) had Stage II, and six (11%) had Stage III endometrial cancer (Table 1). In the metastatic group, Stage III endometrial cancer was found in 60 patients (94%) and Stage IV in four patients (6%).

In the synchronous group, 33 patients (62%) had grade 1 ovarian cancer and 24 patients (45%) had grade 1 endometrial

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Table 1. — *Characteristics of demographic and clinical variables of patients in the synchronous and metastatic groups.*

Characteristics	Synchronous Group (n = 53)	Metastatic Group (n = 64)	Significance
Age	59 (24-72)	60.5 (29-81)	NS*
Gravidity	3 (0-12)	4 (0-12)	NS
Parity	2 (0-10)	3 (0-6)	NS
Nulliparity	3 (5.7%)	3 (4.7%)	NS
Menopausal status			
Premenopausal	12 (23%)	11 (17%)	
Postmenopausal	41 (77%)	53 (83%)	NS
Presenting symptoms			
Abnormal vaginal bleeding	32 (60%)	42 (66%)	
Pain	10 (19%)	7 (11%)	
Abdominal distention	5 (10%)	7 (11%)	
Abdominal mass	1 (2%)	6 (10%)	NS
Histological types (ovary/endometrium)			
Endometrioid	7 (32%) / 49 (92%)	56 (87%)	
Serous	18 (34%) / 1 (2%)	2 (3%)	
Granulosa	1 (2%) / -		
Clear cell	2 (4%) / -	4 (6%)	
Brenner	2 (4%) / -		
Mixed	6 (11%) /1 (2%)	1 (2%)	
Undifferentiated	6 (11%) /1 (2%)	1 (2%)	
Adenoacanthoma	- / 1 (2%)		
Stages			
I	29 (55%) / 44 (83%)		
II	3 (6%) / 3(5%)		
III	21 (40%) / 6 (11%)	60 (94%)	
IV	– / –	4 (6%)	
Grades			
1	24 (45%) / 33 (62%)	17 (27%)	
2	13 (24%) / 11 (21%)	26 (41%)	
3	16 (30%) / 9 (17%)	21 (33%)	
Adjuvant treatment			
Chemotherapy	35 (66%)	4 (6%)	
Radiotherapy	0	46 (72%)	
Chemotherapy+ +radiotherapy	9 (17%)	13 (20%)	
None	9 (17%)	1 (2%)	

* non-significant

cancer. However, only 17 patients (27%) in the metastatic group had grade 1 tumor (Table 1). For statistical comparisons, the higher stage and grade of the ovarian and endometrial cancers in the synchronous group were used.

Mean follow-up time was 47.2 months (18-170 months). Demographic data were analyzed with parametric and non-parametric methods as appropriate. Nominal variables were analyzed with chi-square or Fishers` exact test where appropriate. Survival analyses of the study groups were performed according to the stage, grade, and histological type of tumors, and adjuvant therapies. Kaplan-Meier survival analyses with the log-rank test were performed to calculate and compare the overall and 5-year survivals. The Cox-proportional hazard model was used to analyze the factors affecting survivals. A p value of < 0.05 was considered significant.

Results

Of the 117 patients, 53 had synchronous primary ovarian and endometrial carcinoma, and 64 had endometrial cancer metastatic to the ovaries. Patients diagnosed as having synchronous primary ovarian and endometrial carcinoma constituted 12% (53/443) of all endometrial malignancies and 4% (53/1300) of all ovarian malignancies encountered during the study period. Endometrial cancers metastatic to the ovaries accounted for 14.4% of all endometrial cancers.

Table 1 presents the demographic and selected clinical data of the synchronous and metastatic groups. There was no significant difference in the age, gravidity, parity, menopausal status, and presenting symptoms between the synchronous and metastatic groups. Abnormal vaginal bleeding was the most common symptom in both groups.

Figure 1 shows the overall survival curves of the synchronous and metastatic groups. The overall survival of the synchronous group was significantly higher than that of the metastatic group (98 ± 12 vs 59 ± 6 months, p = 0.048). The five-year survival rates of patients with synchronous and metastatic diseases were 61.7% and 42.8%, respectively. Figure 2 presents the overall survival curves of patients with endometrioid adenocarcinoma and non-endometrioid histologic types in the synchronous group. There was no significant difference in these overall survivals (106 ± 38 and 85 ± 27 months, respectively).

In the synchronous group, the 5-year survival of patients with Stage I cancer was significantly higher than those of Stage II and III cancers (75.6% vs 0% and 0%, respectively) (p = 0.001). In the metastatic group, 5-year survival of patients with Stage III disease was 42.4%. In the synchronous group the 5-year survival of patients was 81.2% for grade 1 cancers in both sites and 25.3% for grade 3 cancers. The 5-year survival rate of patients with grade 1 was significantly higher than those of the patients with grade 2 and 3. In the metastatic group, for patients with grades 1, 2 and 3, 5-year survival rates were 52.6%, 38.3% and 26.2%, respectively. Among patients with grades 1, 2 and 3 in the metastatic group, there were no significant differences in the 5-year survival rates.

The significant prognostic factors for synchronous

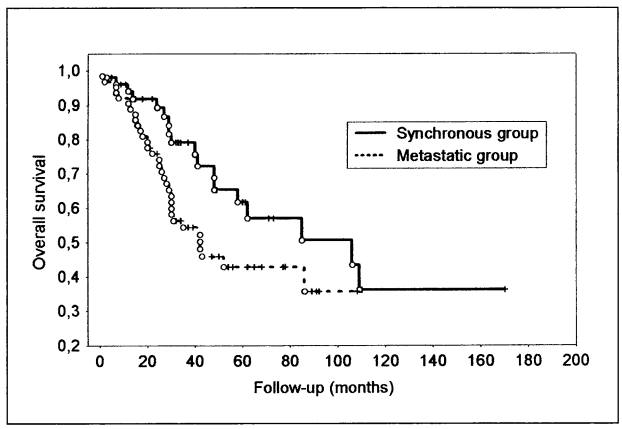

Figure 1. — Overall survival curves of synchronous and metastatic groups. Overall survival is significantly higher in the synchronous group (p = 0.048).

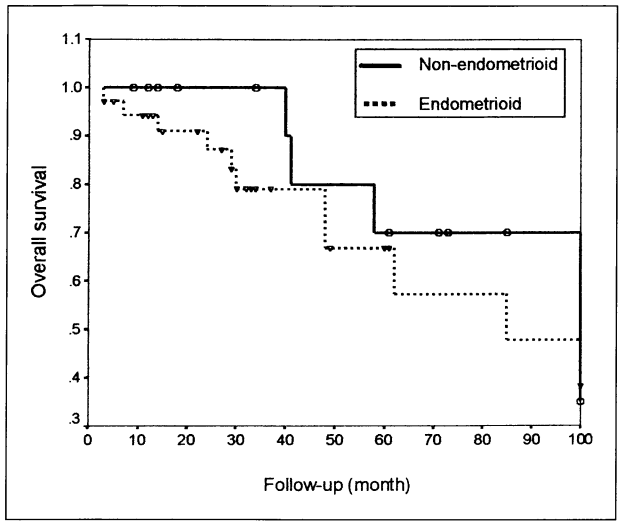

Figure 2. — Survival curves for endometrioid adenocarcinoma and non-endometrioid histologic subtypes in the synchronous group (p=0.07).

cancers after multivariate analysis were age, the stage of ovarian cancer and the grade of endometrial cancer (Table 2). In the metastatic group, age, parity, gravidity and menopausal status were not found to be the prognostic factors on the survival of patients (Table 3).

Discussion

The incidence of primary ovarian carcinoma in patients with endometrial cancer varies from 2% to 8.5% [7]. The incidence of endometrial cancer seen in ovarian cancer patients has been reported to be 1.6% and 20% [1, 8]. In this study, primary ovarian cancer was found in 12% of endometrial cancers and the incidence of primary endometrial cancer in patients with ovarian cancer was 4%.

Table 2. — *Cox proportional hazard model of synchronous ovarian and endometrial cancers.*

	Relative risk	95% CI for Relative risk	Significance
Age	1.5	1.9 - 2.1	0.015
Gravidity	0.9	0.5 - 1.8	0.880
Parity	1.7	0.6 - 5.0	0.346
Menopausal status	0.1	0.0 - 1.3	0.060
Type of ovarian cancer	1.3	0.9 - 1.6	0.079
Grade of ovarian cancer	0.3	0.9 - 1.5	0.153
Stage of ovarian cancer	12.5	2.5 - 62.1	0.002
Type of endometrial cancer	1.4	0.9 - 2.1	0.087
Grade of endometrial cancer	23.2	2.2 - 241.6	0.008
Stage of endometrial cancer	6.4	0.9 - 44.9	0.063

Table 3 — *Cox proportional hazard model of endometrial cancer metastatic to the ovaries.*

	Relative risk	95% CI for Relative risk	Significance
Age	1.0	0.979 - 1.1	0.226
Gravidity	1.1	0.793 - 1.4	0.673
Parity	0.9	0.562 - 1.5	0.698
Menopausal status	1.3	0.203 - 8.1	0.793

In the present study, there was no significant difference in the age at presentation or menopausal status between the synchronous and metastatic groups (Table 1). It has been reported that patients with synchronous ovarian and endometrial carcinomas were younger than those of the primary counterpart [3, 9, 10]. In the synchronous group, patients with endometrioid histologic types tended to be younger than patients with other histologic types. Because all histologic types were included in this study, the median age was higher than those of other studies.

In some previous reports, the most common ovarian histologic type for synchronous tumors was endometrioid adenocarcinoma [10, 11], in our study however, serous adenocarcinoma is as common as endometrioid adenocarcinoma consistent with Piura and Glezerman's series [3].

We found that the histological types of synchronous tumors had no significant effect on the survival of patients in contrast to some series reporting that histologic types were related with survival of patients with synchronous tumors [2].

Patients with synchronous cancer in the present study had a more advanced stage and grade of disease at diagnosis as compared to those with earlier reports [9, 10, 12]. Of patients in the synchronous group, 55% were Stage I, and 40% were Stage III. Also, in patients in the synchronous group, 30% of ovarian cancers were grade 3, whereas 17% of patients with endometrial cancers were grade 3.

The prognosis of the patients with synchronous ovarian and endometrial carcinoma has been suggested to be more favorable when compared to the survival of patients harboring the same neoplasms individually [9, 11]. In contrast to the literature, the prognosis of synchronous tumors did not seem to be better than primary cancers of endometrium in this study. The differences of survival rates between series may arise from patients with different stage and grade of tumor, and histologic types. In study of Pearly *et al.* [10], all of their patients had Stage I ovarian and endometrial cancers and only one patient had a grade 3 ovarian tumor, no patients had grade 3 endometrial cancer and there was 100% of survival rate at three years. Castro *et al.* [13] demonstrated that women with Stage I endometrial and ovarian tumors had a trend to a better disease-free survival (100% vs 68.6%, p = 0.07) than women with higher stage disease. In that study, only one patient (0.5%) had a grade 3 ovarian tumor and two patients (11%) had grade 3. We found that stage of ovarian cancer and grade of endometrial cancer were independent prognostic factors in patients with synchronous ovarian and endometrial carcinomas after multivariate analysis. Nonetheless, the patients with synchronous tumors should be evaluated for stage of ovarian cancer and grade of endometrial cancer.

Conservative surgical approaches (total abdominal hysterectomy and bilateral salpingo-oophorectomy alone) are proposed for management of synchronous ovarian and endometrial cancers by some authors [3, 9]. In their studies the patients who presented with early stage and low grade of tumors had not been subjected to a meticulous surgical staging including pelvic and para-aortic lymph node dissection [3, 9]. It might be therefore assumed that these patients may have been understaged. All patients in our study underwent surgical staging. In our opinion, the first step in appropriate management of patients with synchronous tumors should be the comprehensive surgical staging to determine the spread of tumor.

In conclusion, synchronous ovarian and endometrial tumors appear to have a good prognosis compared to endometrial carcinomas metastatic to the ovaries since they are low grade and early stage tumors. A careful surgical staging procedure is necessary to evaluate patients with synchronous ovarian and endometrial carcinoma and each primary tumor of the synchronous group should be separately evaluated for treatment modalities according to its stage and grade.

Conclusion

Synchronous ovarian and endometrial tumors appear to have a good prognosis compared to endometrial carcinomas metastatic to the ovaries since they are low grade and early stage tumors. Stage of ovarian cancer and grade of endometrial cancer are prognostic factors for patients with synchronous ovarian and endometrial carcinoma. Comprehensive surgical staging should be performed for patients with synchronous ovarian and endometrial carcinoma.

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