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Comparison Of Early-Stage High-Grade Serous Primary Fallopian Tube Cancers and Epithelial Ovarian Cancers: A Multicenter Study

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Keywords

Primary fallopian tube cancer · Epithelial ovarian cancer · High-grade serous cancer

Summary

Introduction: We compared the disease free-survival (DFS) and overall survival (OS) rates of patients with high-grade serous primary fallopian tube cancer (HG-sPFTC) and high-grade serous epithelial ovarian cancer (HG-sEOC). **Methods:** 22 early-stage cancer patients (International Federation of Gynecology and Obstetrics (FIGO) stages I–II) with HG-sPFTC were retrospectively evaluated. In addition, 44 control patients diagnosed with HG-sEOC were matched to these patients with respect to tumor stage at diagnosis. All patients underwent complete surgical staging, followed by adjuvant chemotherapy. Kaplan-Meier curves were used to generate survival data. **Results:** The mean age of HG-sPFTC patients was 59.4 ± 6.2 years, and that of HG-sEOC patients 55.2 ± 11.0 years (p = 0.002). All patients underwent 6 cycles of platinum-based adjuvant chemotherapy. All operations were optimal. The 5-year DFSs were 77.3% for HG-sPFTC patients and 75% for HG-sEOC patients (p = 1.00).The 5-year OS rates were 81.8% in women with HG-sPFTC and 77.3% in those with HG-sEOC (p = 0.75). **Conclusion:** The DFS and OS rates of patients with early-stage (FIGO stages I and II) HG-sPFTC and HG-sEOC were similar. The surgical and adjuvant therapy management of these malignancies should be similar.

Introduction

Epithelial ovarian cancer (EOC) is the second most common gynecological malignancy and the fifth most frequent cause of death from cancer in women worldwide [1]. However, the incidence varies greatly among different countries. High-grade serous carcinoma is the most frequent (75%) and most aggressive histotype of EOC. In contrast, primary fallopian tube cancer (PFTC) is a rare gynecological malignancy, accounting for < 1% of all female genital tract cancers. As is true of EOC, serous histology is the most common pathological presentation of PFTC (45–90%) [1–3].

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Histological, morphological, and molecular data suggest that serous carcinoma and ovarian serous carcinoma of the fallopian tube are, in fact, a single entity [2]. High-grade serous cancer may reflect seeding of the peritoneal cavity by malignant cells from the fimbriated end of the fallopian tube [1].

Studies on the clinical outcomes of early-stage PFTC patients have yielded conflicting results; the survival times have been better than [4], similar to [5–8], or worse than, those of patients with EOC [9]. However, most cited studies enrolled patients with heterogeneous cancers (serous, mucinous, and endometrial), and patients differing in terms of cancer type. Furthermore, the study durations, imaging technologies used, chemotherapeutic regimens prescribed, and surgical techniques employed, also differed markedly.

The aim of our present multicenter, retrospective case-control study was to compare demographic characteristics and survival times between patients with early-stage high-grade serous EOC (HG-sEOC) and serous PFTC (HG-sPFTC).

Methods

The databases of 9 gynecological oncology departments – those of the Izmir Tepecik Education and Research Hospital, the Ege University School of Medicine, the Eskisehir Osmangazi University School of Medicine, the Ankara University School of Medicine, the Antalya Akdeniz University School of Medicine, the Adana Cukurova University School of Medicine, the Istanbul Bakırkoy Dr Sadi Konuk Education and Research Hospital, the Uludag University School of Medicine, and the Zekai Tahir Burak Education and Research Hospital – were reviewed to identify patients with pathologically proven HG-sPFTC and HG-sEOC who underwent surgical staging between 1 January 1996 and 31 December 2013. The study was performed in accordance with the ethical standards of the Helsinki Declaration, and was approved by the ethics committee of the Izmir Tepecik Education and Research Hospital.

We retrospectively evaluated 22 cases with early-stage (International Federation of Gynecology and Obstetrics (FIGO) stages I–II) HG-sPFTC, and 44 HG-sEOC patients. Controls were selected from the computer database of the gynecological oncology unit and matched by the FIGO stages when the tumors were diagnosed, the type of surgery, the type of first-line chemotherapy, and the type of chemotherapy given during recurrence. All patients underwent complete surgical staging (pelvic washing, peritoneal biopsy, omentectomy, bilateral pelvic and para-aortic lymph node dissection, and total abdominal hysterectomy with bilateral salpingo-oophorectomy).

We used the PFTC diagnostic criteria of Huet et al. [10] as modified by Sedlis [11]. All slides were reviewed by expert pathologists from each institution. The clinical data collected from medical, surgical, pathological, and chemotherapeutic reports included demographic characteristics, presenting symptoms, serum cancer antigen (CA) 125 levels, the date of surgery, the type of surgical procedure employed, the presence or absence of residual tumor tissue after surgery, the numbers of excised and positive lymph nodes, the presence or absence of ascites, the first-line chemotherapy prescribed, the date of any recurrence, the date of the last medical examination, and the date of death.

Debulking was considered optimal when the maximum residual tumor diameter was < 1 cm. All patients were scheduled for follow-up every 3 months for the first 2 years, every 6 months for the next 3 years, and annually thereafter. Computed tomography or magnetic resonance imaging was performed annually. Survival data were analyzed in December 2013.

Survival analysis employed the Kaplan-Meier method; the results were compared using the log-rank test. Disease-free survival (DFS) was defined as the time from the date of primary surgery to the detection of recurrence or the last follow-up. Overall survival (OS) was defined as the time from the date of primary surgery to death or the last follow-up. The χ^2 test and Student's *t*-test were used to compare unpaired data. Cox's regression was employed to identify factors affecting survival; the results are presented as hazard ratios (HRs). All statistical analyses were performed using Med-Calc software. A p value < 0.05 was considered to indicate statistical significance.

Table 1. Characteristics of patients with FIGO stages I or II high-grade serous fallopian tube cancer (case group) and high-grade, serous ovarian cancer (control group)

	Case group	Control group	p value
n	22	44	
Age, years (mean ± SD)	59.4 ± 6.2	55.2 ± 11.0	0.002
Postmenopausal, n (%)	19 (86.4)	33 (75.0)	0.35
Nulliparity, n (%)	3 (13.6)	7 (15.9)	1.00
CA-125, U/ml (mean ± SD)	92.5 ± 65.2	155.2 ± 113.1	0.01
Bilateral disease, n (%)	2 (9.1)	6 (13.6)	0.70
Stage, n (%)			1.00
IA	14 (63.6)	28 (63.6)	
IB	2 (9.1)	4 (9.1)	
IC	5 (22.7)	10 (22.7)	
II	1 (4.5)	2 (4.5)	
No. of removed lymph nodes, mean ± SD*			
Pelvic	15.9 ± 6.4	17.1 ± 5.8	0.42
Para-aortic	13.0 ± 3.7	14.2 ± 4.1	0.25
First-line chemotherapy, n (%)	22 (100.0)	44 (100.0)	1.00
Recurrence, n (%)	4 (18.2)	10 (22.7)	0.75
Recurrence site, n			
Pelvis	1	3	
Spleen	-	2	
Peritoneal surface	1	2	
Recto-sigmoid colon	1	2	
Isolated aortic lymph node	1	1	
Duration of follow-up, months (mean ± SD)	60.1 ± 17.7	54.5 ± 16.2	0.20
Disease-free survival, months (mean ± SD)	55.6 ± 21.5	49.5 ± 18.9	0.24
Overall survival, months (mean ± SD)	60.1 ± 17.7	54.5 ± 16.2	0.20
5-year survival rate, n (%)	19 (86.4)	36 (81.8)	0.73

FIGO = International Federation of Gynecology and Obstetrics, HG-sPFTC = high-grade serous fallopian tube cancer, HG-sEOC = high-grade serous ovarian cancer, SD = standard deviation.

Results

We studied 124 patients with PFTC. 22 patients with HG-sPFTC of FIGO stages I and II, and 44 HG-sEOC patients, underwent complete surgical staging. Their demographic and surgical characteristics are listed in table 1. The mean age of patients with HG-sPFTC was 59.4 ± 6.2 years, and that of HG-sEOC patients 55.2 ± 11.0 years (p = 0.002). The mean Ca-125 level of the HG-sEOC group was higher than that of the HG-sPFTC group (179.0 ± 118.0 vs. 118.5 ± 82.0 IU/l; p = 0.01). All patients underwent 6 cycles of adjuvant chemotherapy (175 mg/m^2 paclitaxel + 5–6 AUC carboplatin). 2 patients in the HG-sEOC and 2 in the HG-sPFTC groups underwent unilateral salpingo-oophorectomy

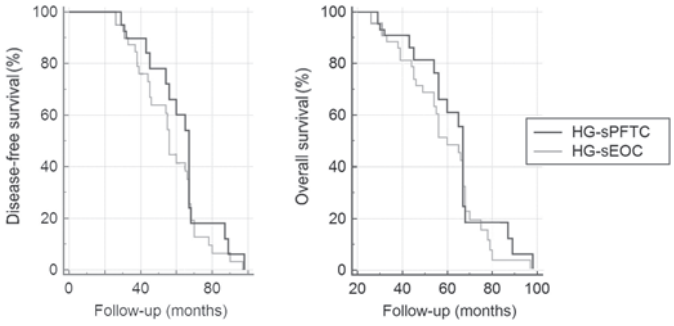

Fig. 1. a Disease-free survival (DFS) curves of patients with FIGO stages I and II high-grade serous fallopian tube cancer (HG-sPFTC) and high-grade serous ovarian cancer (HG-sEOC). **b** Overall survival (OS) curves of patients with FIGO stages I and II HG-sPFTC and HG-sEOC.

as the first operation. Additional surgical procedures were performed in gynecological oncology clinics. All operations were optimal. All patients with recurrent disease received paclitaxel and carboplatin.

The mean DFS was 55.0 ± 21.7 months in patients with HG-sPFTC and 49.5 ± 18.9 months in patients with HG-sEOC (HR 1.3; 95% confidence interval (CI) 0.7–2.3; p = 0.28) (fig. 1a). The mean OS rates of HG-sPFTC and HG-sEOC patients were 60.1 ± 17.7 and 54.5 ± 16.2 months, respectively (HR 1.3; 95% CI 0.7–2.2; p = 0.32) (fig. 1b). The 5-year DFS rates were 77.3% for HG-sPFTC patients and 75% for HG-sEOC patients (p = 1.00). The 5-year OS rates were 81.8% in women with HG-sPFTC and 77.3% in those with HG-sEOC (p = 0.75).

Discussion

In the present case-control study, we evaluated patients with high-grade serous cancers of the ovary and fallopian tubes; we compared DFS and OS rates. To the best of our knowledge, this is the first study to directly compare patients with serous ovarian and fallopian tube cancer. We identified only 6 relevant prior studies on a systematic search of the databases (PubMed, OvidSP, Google Scholar, and Scopus). Medline was also searched from January 1966 to July 2016, using the MeSH terms epithelial ovarian cancer, fallopian tube carcinoma, and outcome.

The origin of EOC remains controversial. Recent studies strongly suggest that HG-sEOCs arise from the fallopian tubal epithelium rather than the ovary per se [1]; thus, PFTC spreads within the abdominal cavity. Traditionally, management options follow the guidelines used to treat EOC. However, no optimal treatment for PFTC has been identified; the disease is rare [12].

In 1994, Rosen et al. [7] studied 68 PFTC and 194 early-stage EOC patients, and found that the 5-year survival rate of PTFC patients was poorer than that of EOC patients (50.8 vs. 77.5%). In contrast, 1 trial comparing 50 early-stage PCFT patients with 97 early-stage EOC patients found that the 5-year OS and DFS were better in PTFC than EOC patients (95 vs. 76% and 79 vs. 65 %, respectively) [5]. Conversely, a very large retrospective case-control study compared the outcomes of 1,567 patients with PFTC and 54,249 patients with EOC, finding that PFTC patients enjoyed a better OS than EOC patients. A recent retrospective study including 428 women with stage I PFTC (n = 43) and EOC (n = 385) concluded that the survival rates were similar [8].

There are many reasons why the results of previous studies may conflict. Some studies included patients of all cancer grades (I, II, and III) and histological types (serous, mucinous, endometrioid, and clear cells). Also, neither the surgical procedure nor the adjuvant chemotherapy prescribed were standardized. Some trials did not include a standardized pathological review or information on adjuvant treatment.

All of our patients had early-stage, high-grade serous cancer, underwent complete optimal surgical staging, and were prescribed the same platinum-based chemotherapy. We found that the DFS and OS rates were similar in HG-sPFTC and HG-sEOC patients. Therefore, we suggest that the principal treatment guidelines should be identical for patients with either condition.

The potential limitations of our study include its retrospective nature, the absence of data on BRCA mutations, and the small sample size. Retrospective cohort studies are subject to both selection and recall biases and the effects of unknown confounding variables, which may, in turn, negatively affect the accuracy of the results. Despite these limitations, the similarities in the demographic characteristics of our study populations, the availability of good follow-up data, and the use of the same treatment regime (complete surgical staging with adjuvant chemotherapy) suggest that our results are valid, mitigating any possible weaknesses.

In conclusion, the DFS and OS rates of patients with early-stage (FIGO stages I and II) HG-sPFTC and -sEOC were similar. Clinicians should use similar surgical approaches, and prescribe similar adjuvant therapies, when managing these malignancies.

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Disclosure Statement

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