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Original Article

Prognosis for advanced-stage primary peritoneal serous papillary carcinoma and serous ovarian cancer in Taiwan

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Abstract

Objective: To compare the prognosis of patients with advanced-stage primary peritoneal serous papillary carcinoma (PSPC) or papillary serous ovarian cancer (PSOC).
Materials and Methods: This was a retrospective case–control study and included two study groups: one with stage III/IV PSPC ($n = 38$) patients and the other with PSOC ($n = 53$) patients. Patients were matched for histologic subtype (serous tumor), tumor stage, tumor grade, residual disease at the end of debulking surgery (primary or interval), and age (±5 years).
Results: Mean age was significantly greater for patients with PSPC (63.03 ± 11.88 years) than for patients with PSOC (55.92 ± 12.56 years, $p = 0.008$). Optimal debulking surgery was performed initially in 71.9% of PSPC patients and 66.0% of PSOC patients. In addition, 93.9% of PSPC patients and 92.3% of PSOC patients were treated with platinum–paclitaxel chemotherapy. The frequency of high-grade tumors was significantly higher in the PSPC (100%) than in the PSOC group (68.3%; $p < 0.001$). Progression-free survival (PFS) was similar in the PSPC [median 12 months, 95% confidence interval (CI) 7.3–16.7] and PSOC groups (median 16.7 months, 95% CI 12.9–20.4; $p = 0.470$). Overall survival was shorter in the PSPC (median 62 months, 95% CI 19.6–104.4) than in the PSOC group (median 77.5 months, 95% CI 69.7–85.2; $p = 0.006$, log-rank statistic).
Conclusion: PFS was similar for advanced-stage PSPC and PSOC patients. Since the PSPC patients tended to be older and have more high-grade tumors, OS was shorter for PSPC than for POSC patients. Thus, management of the two types of cancer should not differ.

Keywords: ovarian cancer; primary peritoneal serous papillary carcinoma; prognosis

Introduction

Primary peritoneal serous papillary carcinoma (PSPC) is a malignancy with diffuse involvement of the peritoneal surfaces while sparing or minimally involving the ovaries. It is histologically indistinguishable from epithelial ovarian cancer (EOC) and has similar clinical characteristics, spreading patterns, response to treatment, and survival rates. Previous reports have suggested that women with PSPC have epidemiological features similar to women with epithelial ovarian cancer, with the exception of an older age at diagnosis and an increased rate of obesity and lymph node spreading in stage III or IV primary PSPC [1].

There are numerous reports of very small series of patients with this disease, but larger series are rare. The study with the largest series (74 patients) was published 14 years ago [2]. This important study revealed the characteristics of patients with PSPC. Other retrospective studies compared the prognosis of PSPC to that of EOC [3–5]. To give more weight to the relevance of these retrospective studies, a few teams reported case–control studies that evaluated PSPC prognosis

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to determine whether the management of this tumor should be different from that for EOC [6–9].

A previous study suggested molecular similarities between PSPC and EOC [10]. The recommended treatment for serous PSPC is similar to that for serous ovarian carcinoma; however, optimal cytoreduction may be more difficult to achieve in women with PSPC because of widespread peritoneal disease without the presence of a predominant pelvic or ovarian mass. Although it has been shown to prolong survival, systemic chemotherapy in the relapsed or refractory setting is not curative [11].

To date, most of the studies evaluating PSPC have focused on western patients with high-grade serous tumors, with few reports on PSPC in Asia. Several questions concerning the management of EOC remain unclear. To study the prognosis of patients with PSPC, we conducted a retrospective analysis of cases treated in our institution and matched them with a control group of patients with EOC. The aim of this study was to evaluate the characteristics of patients with PSPC and to analyze the survival of these patients in Taiwan.

Materials and methods

This study included 38 PSPC patients and 53 patients with advanced-stage papillary serous ovarian cancer (PSOC) who had been admitted, treated, and followed up at the Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taiwan, between January 2000 and December 2010. Approval for the study was obtained from the hospital's ethics committee. The patients were selected on the basis of available histological material. The histological specimens were reviewed by a gynecological pathologist. Pathological specimens were assessed using the WHO criteria for histological subtype and nuclear grade.

The following clinical information was obtained directly from patients' hospital records: date of birth, date of diagnosis, operative findings, International Federation of Gynecology and Obstetrics (FIGO) stage based on the clinical examination and surgical exploration together with cytology results, cancer antigen 125 (CA125) levels at diagnosis and relapse, date of relapse, date of last follow-up, and date and cause of death.

The 38 advanced-stage PSPC patients had undergone debulking surgery. Optimal debulking surgery was defined as the presence of a residual tumor <1 cm in size after the procedure. By contrast, if the residual tumor was ≥ 1 cm, the surgery was then defined as suboptimal debulking. There was no significant difference in the optimal debulking rate between advanced-stage PSPC and PSOC patients (Table 1). Of the 33 PSPC who underwent chemotherapy, 31 (93.9%) were treated with six cycles of platinum–paclitaxel combination chemotherapy 2–3 weeks after initial surgery. There was no significant difference in the rate of platinum–paclitaxel chemotherapy between the PSPC and PSOC patients (Table 1). The chemotherapy regimen consisted of paclitaxel plus cisplatin or paclitaxel plus carboplatin. The PSOC patients were treated with six cycles of cisplatin-based combination chemotherapy (minimum total dose of cisplatin, 400 mg/m^2) 2–3 weeks after their initial surgery. Cisplatin-based combination chemotherapy consisted of either the CP regimen (cyclophosphamide plus cisplatin) or the CAP regimen (cisplatin, Adriamycin, and cyclophosphamide). After completing treatment, most patients were reviewed every 3–6 months for 5 years and annually thereafter.

Table 1
Patient characteristics.

	PSPC	PSOC	p
All patients	38	53	
Age (y)	63.03 ± 11.88	55.92 ± 12.56	0.008
FIGO stage			
IIIC	31 (81.6)	46 (86.8)	0.497
IV	7 (18.4)	7 (13.2)	
Histological type			
Papillary serous	38 (100)	53 (100)	1.000
Grade			
G2	0 (0)	13/41 (31.7)	<0.001
G3	38 (100)	28/41 (68.3)	
Cytoreduction			
Optimal	23/32 (71.9)	35 (66.0)	0.575
Suboptimal	9/32 (28.1)	18 (34.0)	
CA-125			
Positive	30/31 (96.8)	39/41 (95.1)	0.998
Negative	1/31 (3.2)	2/41 (4.9)	
Lymph node metastasis			
Positive	38 (100)	53 (100)	1.000
Negative	0 (0)	0/0 (0)	
Platinum–paclitaxel chemotherapy			
Yes	31/33 (93.9)	48/52 (92.3)	1.000
No	2/33 (6.1)	4/52 (7.7)	

Data are presented as n (%) or mean ± SD. PSOC = papillary serous ovarian cancer; PSPC = peritoneal serous papillary carcinoma.

Statistical analysis

The various clinicopathological parameters were analyzed by Fisher's exact test and the χ^2 test. Progression-free survival (PFS) was calculated from the date of surgery to the date of relapse or the date last seen, and overall survival (OS) was calculated from the date of diagnosis to the date of death or the date last seen. Survival curves were plotted using the Kaplan–Meier method. Statistical differences in survival between the groups were compared using the log-rank test. Statistical significance was set at $p < 0.05$.

Results

The mean age of patients with PSPC (63.03 ± 11.88 years) was significantly greater than for patients with PSOC (55.92 ± 12.56 years, $p = 0.008$). Some 31 (81.6%) of the PSPC patients had stage IIIc and seven (18.4%) had stage IV disease. Of the PSOC patients, 46 (86.8%) had stage IIIc and seven (13.2%) had stage IV disease (Table 1). All of the PSPC patients had grade 3 tumors, but only 28 (68.3%) of the PSOC patients had grade 3 tumors ($p < 0.001$) (Table 1).

The rate of optimal debulking surgery was 71.9% in the PSPC group and 66.0% in the PSOC but the difference was not significant ($p = 0.575$; Table 1). Survival curves were plotted using the Kaplan–Meier method. PFS in the PSPC group [median 12 months, 95% confidence interval (CI) 7.3–16.7]

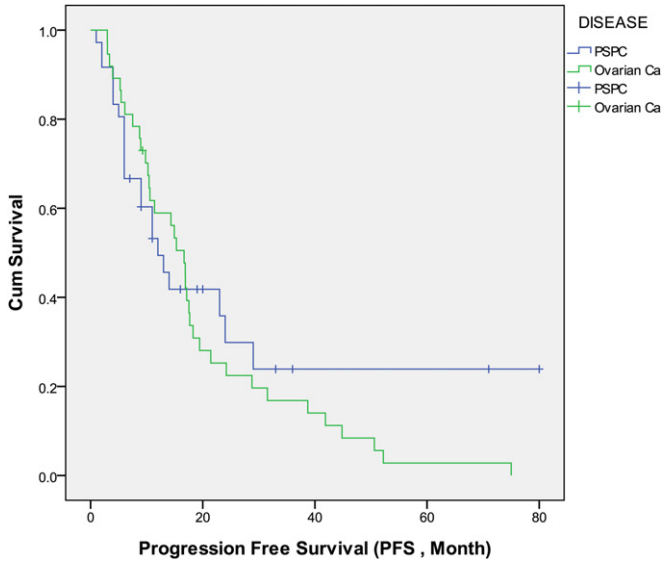

Fig. 1. Progression-free survival curves for peritoneal serous papillary carcinoma (PSPC) and papillary serous ovarian cancer (PSOC). PFS for PSPC patients (median 12 months, 95% confidence interval 7.3–16.7) was similar to that for PSOC patients (median 16.7 months, 95% confidence interval 12.9–20.4; $p = 0.470$).

was similar to that in the PSOC group (median 16.7 months, 95% CI 12.9–20.4; $p = 0.470$, log-rank statistic; Fig. 1). OS was shorter in the PSPC group (median 62 months, 95% CI 19.6–104.4) than in the PSOC group (median 77.5 months, 95% CI 69.7–85.2; $p = 0.006$, log-rank statistic; Fig. 2).

Discussion

Primary peritoneal carcinoma (PPC) is a malignancy with diffuse involvement of the peritoneal surfaces while sparing or minimally involving the ovaries [12]. It is histologically indistinguishable from EOC and has similar clinical characteristics, patterns of spreading, response to treatment, and survival rates [6,8,13]. Previous reports have suggested that women with PPC have epidemiological features similar to those of women with EOC, with the exception of an older age at diagnosis and a higher rate of obesity [14]. We found similar results. In our study, patients with PSPC were older than those with PSOC.

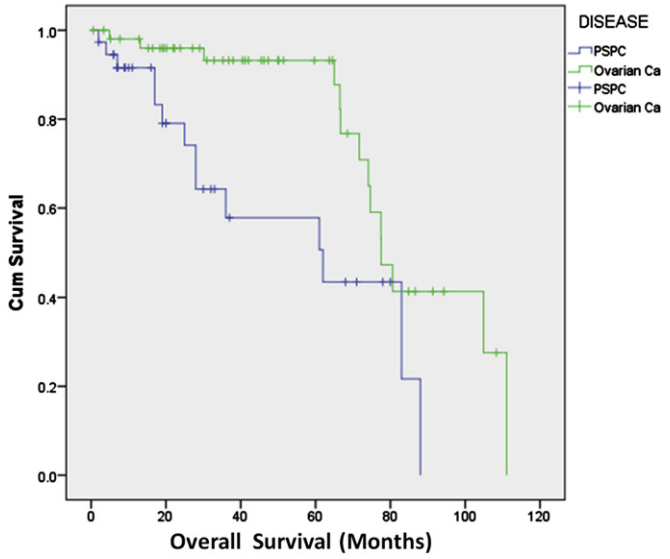

Fig. 2. Overall survival (OS) curves for peritoneal serous papillary carcinoma (PSPC) and papillary serous ovarian cancer (PSOC). OS in the PSPC group (median 62 months, 95% confidence interval 19.6–104.4) was shorter than in the POSC group (median 77.5 months, 95% confidence interval 69.7–85.2; $p = 0.006$, log-rank statistic).

According to a recent study, the median age at diagnosis of low-grade PPC was 51.7 years (range 27.1–82.4) [15]. Among the 46 patients (86.8%) who underwent primary surgery, optimal tumor reduction was achieved in 30 (65.2%). Some 48 patients (90.6%) received chemotherapy as part of their initial treatment. On completion of their primary treatment, 66.7% of patients had persistent or progressive disease. With a median follow-up of 66.1 months, the 5-year PFS was 16%, yet the 5-year OS was 69%. Similar to patients with low-grade serous ovarian carcinoma, patients with low-grade serous PPC have high rates of persistent disease on completion of primary treatment, despite a long OS [15]. However, in our study, PSPC was associated with a higher tumor grade in every case.

The recommended treatment for serous PPC is similar to that for serous ovarian carcinoma; however, optimal cytoreduction may be more difficult to achieve in women with PPC because of widespread peritoneal disease without the presence of a predominant pelvic or ovarian mass [9].

Cytoreductive surgery followed by combined platinum and taxane chemotherapy is the accepted standard treatment for patients with advanced EOC [16]. Three large randomized Phase III studies comparing intraperitoneal (IP) to intravenous (IV) cisplatin-based chemotherapy for patients with small-volume residual disease reported favorable survival results for IP intervention [17,18]. Furthermore, pharmacological data now show that more than two-thirds of free platinum enters the systemic circulation after IP carboplatin administration. Miyagi et al demonstrated that the area under the curve (AUC) for 24-hour free platinum in serum was identical for IP and IV administration [19]. Concentrations may be even higher in retroperitoneal lymph nodes [20]. Thus, in future work, we will study the role of the IP regimen in treating PSPC.

This retrospective case-matched comparison confirms that PFS in patients with PSPC is similar to that in patients with advanced-stage PSOC. Chiou et al reported similar results [21]. Therefore, the therapeutic response to debulking surgery and platinum–paclitaxel chemotherapy may well be similar for these two diseases. However, the OS for patients with PSPC was poor compared to that for POSC patients. The possibility of poor OS increases with age and the rate of poor tumor grade is higher in PSPC. Thus, management of PSPC should not be different from that of advanced-stage POSC.

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