Brief Communication

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Comparison of the Prognostic Outcome between High-Grade Ovarian Sertoli-Leydig Cell Tumors (SLCTs) and Low-Grade SLCTs

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The purpose of the current study was to compare prognostic outcomes between patients with high-grade ovarian Sertoli-Leydig cell tumors (SLCTs) and those with other low-grade SLCTs. We retrospectively reviewed medical records for 24 patients pathologically diagnosed with SLCTs between 2006 to 2019 at two institutions. The patients were grouped according to pathological grade: SLCT was classified as grade 1, well differentiated; grade 2, intermediated differentiated; or grade 3, poorly differentiated (Meyer's classification). Statistical analysis was performed to compare survival outcomes according to pathological grade. The median patient age was 42.5 years (range 16–75). Eighteen patients (75%) were International Federation of Gynecology and Obstetrics stage I, and none were diagnosed in stage IV. Nine patients (37.5%) were grade 3, and 15 patients (63.5%) were grades 1–2. When comparing clinical baseline characteristics of the grade 1–2 group with those of the grade 3 group, only serum CA125 level at diagnosis was significantly higher in the grade 3 group (38.34 vs. 382.29, p=0.002). Five patients experienced recurrence of grade 3 disease, while no recurrence was reported in grade 1–2 disease. Four of the five recurrent patients died. In result, grade 3 ovarian SLCT showed significantly poorer prognosis than grade 1–2 disease (overall survival, hazard ratio=14.25, 95% confidence interval=1.881–108.0; log-rank p=0.010). Our findings were consistent with the concept that patients with stage I/grade 1–2 tumors have a good prognosis without adjuvant chemotherapy. Since grade 3 ovarian SLCT appears to be relatively more fatal than grade 1 or 2, patients with grade 3 SLCT might require more aggressive surgical intervention and post-treatment surveillance.

Key Words: Ovarian Sertoli-Leydig cell tumors, prognosis, chemotherapy

Ovarian Sertoli-Leydig cell tumors (SLCTs) are the most frequently observed low-grade malignancies.[1-3] SLCTs have been classified into well differentiated (grade 1), intermediate differentiation (grade 2), and poorly differentiated tumors (grade 3).[4-7] Although surgery plays the most pivotal role in the management of patients with SLCT, postoperative adjuvant platinum-based chemotherapy is indicated in advanced tumors and in poorly differentiated SLCTs. Clinical data evaluating the benefit of chemotherapy and the optimal regimen, however, are limited, with most of the literature consisting of anecdotal case reports.[8,9] We hypothesized that adjuvant chemotherapy could be safely avoided in patients with low-grade SLCTs and would lead to more successful clinical results, thereby improving fertility and prognostic outcomes. The present study was approved by Institutional Review Board for Human Research of Yonsei University Hospital (ethic code: 4-2020-0395). The medical records of 24 patients who were pathologically diagnosed with SLCTs of the ovary were reviewed. All patients were treated at two institutes from 2006 to 2019.[10] Based

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on a histopathological review, the cases were divided into one of the three SLCT categories: grade 1 tumors were well differentiated and contained a significant component of Leydig cells, as well as Sertoli cells. Grade 2 tumors exhibited intermediate differentiation, and tumors were composed of immature Sertoli cells typically arranged in a diffuse pattern. Grade 3 tumors were poorly differentiated, and increased mitotic activity and only a few Leydig cells were found (Fig. 1).[11] The median patient age was 42.5 years (range 16–75). The age distribution of the patients with grade 3 disease was not significantly different from those with grade 1–2 disease. International Federation of Gynecology and Obstetrics stages were as follows: 18 (75.0%) with stage I, 4 (16.7%) with stage II, 2 (8.3%) with stage III, and none with stage IV. Six patients (25.0%) had grade 1 tumors, 9 (37.5%) had grade 2 tumors, and 9 (37.5%) had grade 3 tumors. Two cases contained heterologous elements: patients had IA/G3 and IIIC/G3 diseases, respectively. Overall, 9 patients (37.5%) had grade 3 and 15 patients (63.5%) had grade 1–2 disease. When comparing clinical baseline characteristics of patients with grade 1–2 disease with those with grade 3 disease, only serum CA125 level at diagnosis was significantly higher in the grade 3 group (38.34 vs. 382.29, p=0.002) (Table 1). Fertility-preservation intervention was performed in 14 (58.3%) patients (laparoscopic approach in six cases), while definitive surgery was executed in 10 (47.7%) patients. Ten patients had staging surgery that included total abdominal or laparoscopic hysterectomy with bilateral salpingo-oophorectomy. Additionally, 8 of 24 patients underwent pelvic lymph node dissections. Eight of the 24 patients underwent laparoscopic surgery, and 16 patients underwent laparotomies. Nine

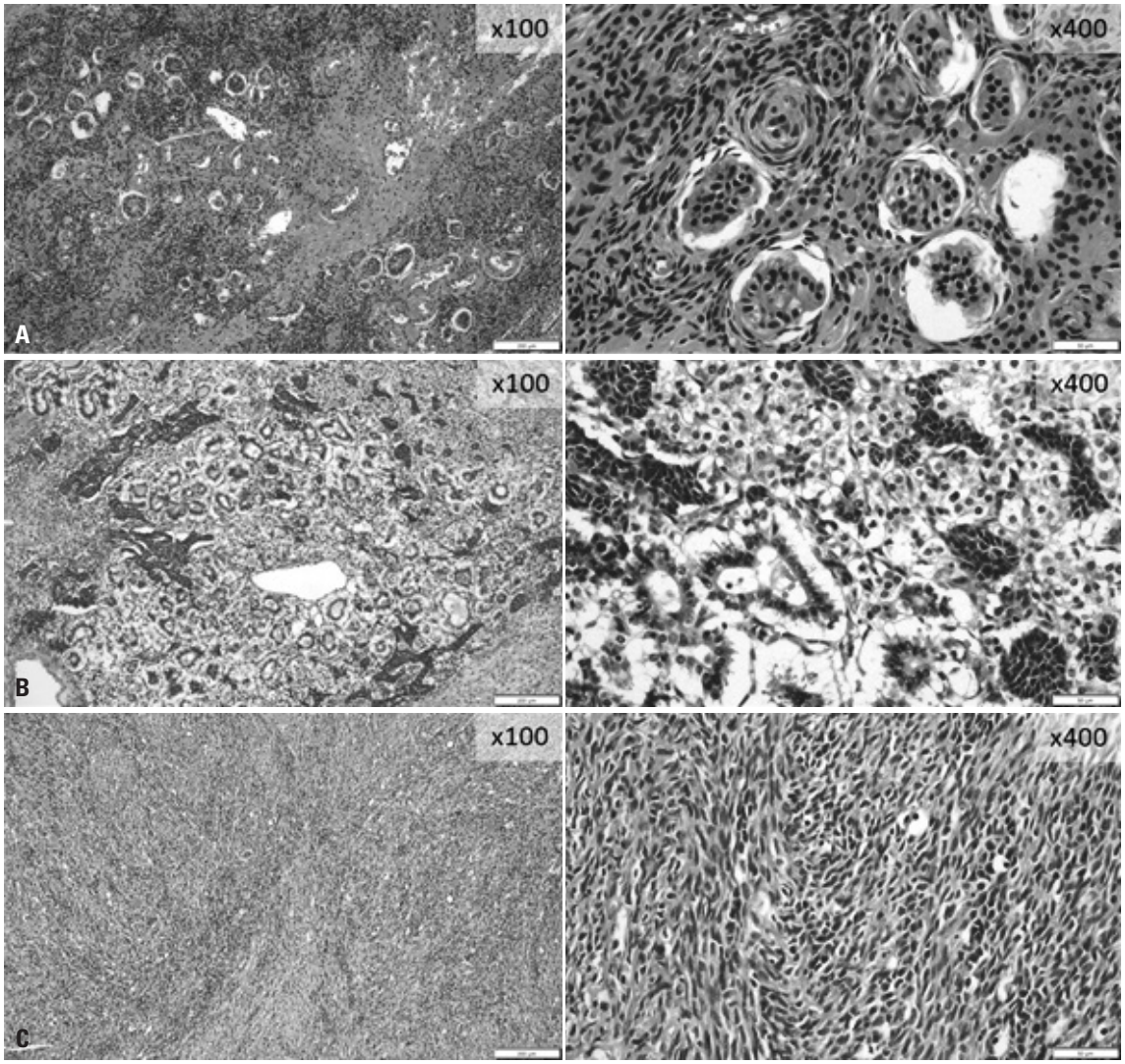

Fig. 1. Pathologic comparison of ovarian Sertoli-Leydig cell tumor by pathologic grade. (A) Grade 1. Tubules of Sertoli cell and clusters of Leydig cell in intervening stroma are shown. Sertoli cells with oval to round nuclei and Leydig cells with eosinophilic cytoplasm are characterized. No atypia or mitotic activity is observed. (B) Grade 2. Typical diffuse or lobulated architectural pattern and alternating hypo and hypercellularity are observed. Hyperchromatic, oval or spindled nuclei with mild to moderate atypia are characterized. (C) Grade 3. Diffuse sheets of immature cells with moderate to marked nuclear atypia are observed. Increased mitotic activity and few Leydig cells are found.

Table 1. Baseline and Disease Characteristics

	Grade 1–2 (n=15)	Grade 3 (n=9)	Total (n=24)	*p* value
Age (yr)				0.164
Mean±SD	48.40±18.27	36.48±19.32	54.04±19.13	
Median (range)	51 (20–72)	31 (16–75)	42.50 (16–75)	
BMI (kg/m²)				0.153
Mean±SD	28.01±4.44	22.78±3.55	2409±4.36	
Median (range)	24.89 (19.03–35.86)	22.68 (17.40–28.72)	23.07 (17.40–35.86)	
Parity				0.246
Mean±SD	1.27±1.22	0.67±0.87	1.04±1.12	
Median (range)	2 (0–4)	0 (0–2)	1 (0–4)	
Menopause, n (%)				0.423
Premenopause	7 (46.7)	6 (66.7)	13 (54.2)	
Postmenopause	8 (53.3)	3 (33.3)	11 (45.8)	
FIGO stage, n (%)				0.112
I	13 (86.7)	5 (55.6)	18 (75.0)	
II	2 (13.3)	2 (22.2)	4 (16.7)	
III	0 (0)	2 (22.2)	2 (8.3)	
IV	0 (0)	0 (0)	0 (0)	
LN metastasis, n (%)				0.320
Negative	14 (93.3)	8 (88.9)	22 (91.7)	
Positive	1 (6.7)	1 (11.1)	2 (8.4)	
CA-125 (U/mL)				0.002
Mean±SD	38.34±42.55	382.29±550.48	167.32±368.01	
Median (range)	24.30 (7.5–157.3)	134.40 (4.0–1512.9)	27.85 (4.0–1521.9)	

BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; LN, lymph node.

Table 2. Adjuvant Chemotherapy and Prognostic Outcome

Stage	n	Adjuvant chemotherapy		Recurrence		Status	
		Yes	No	Yes	No	NED	DOD
I G1	5	0	5	0	5	5	0
I G2	8	0	8	0	8	8	0
I G3	5	4	1	1	4	4	1
II G1	1	0	1	0	1	1	0
II G2	1	1	0	0	1	1	0
II G3	2	2	0	2	0	1	1
III G3	2	2	0	2	0	0	2
Total	24	9	15	5	19	20	4

NED, no evidence of disease; DOD, died of disease.

patients were given adjuvant chemotherapy after surgery, consisting of a bleomycin, etoposide, and cisplatin regimen in eight cases and a combined paclitaxel and cisplatin regimen in one case. Fourteen patients who had IA/grade 1, IA/grade 2, or IC disease were not administered postoperative chemotherapy. Five of the 24 patients experienced disease recurrence, and four patients died from recurrence after surgery. Of note, the tumors from these 2 patients were pathologically re-diagnosed as Sertoli-form endometrioid carcinoma. The other 20 patients remain alive without evidence of recurrence at the time of reporting (Table 2). The 5 patients with recurrence all had grade 3 disease, and no recurrence was reported in grade 1–2 disease. As a result, grade 3 ovarian SLCT showed significantly poor prognosis than grade 1–2 disease (overall survival, hazard ratio=14.25, 95% confidence interval=1.881–108.0; log-rank p= 0.010) (Fig. 2).

The present study was performed to compare prognostic outcomes between patients with high-grade SLCTs and those with other low-grade SLCTs. Our results revealed that patients with stage I/ grade 1–2 tumors have an excellent prognosis without adjuvant chemotherapy. Since grade 3 ovarian SLCT appears to be relatively more fatal than grade 1 or 2, grade 3 SLCT may warrant more aggressive surgical intervention and postoperative chemotherapy. Overall, the prognoses of patients

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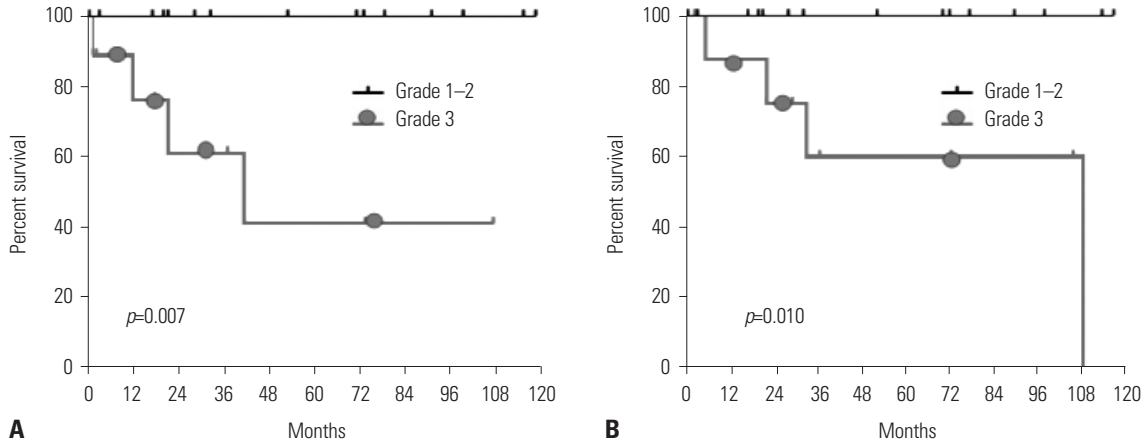

Fig. 2. Kaplan-Meier curves of progression-free survival (A) and overall survival (B) between patients with high-grade SLCTs (n=9) and low-grade SLCTs (n=15). SLCTs, Sertoli-Leydig cell tumors.

were favorable in our study, even for patients who did not receive adjuvant chemotherapy, and laparoscopy was a feasible approach to treat this disease.

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AUTHOR CONTRIBUTIONS

Conceptualization: Young Tae Kim and Maria Lee. Data curation: Kyung Jin Eoh and Junsik Park. Formal analysis: Kyung Jin Eoh and Junsik Park. Funding acquisition: Young Tae Kim. Investigation: Junsik Park and Hye Min Kim. Methodology: Kyung Jin Eoh, Junsik Park, and Young Tae Kim. Project administration: Young Tae Kim and Maria Lee. Resources: Young Tae Kim and Maria Lee. Software: Kyung Jin Eoh and Junsik Park. Supervision: Young Tae Kim and Maria Lee. Validation: Kyung Jin Eoh and Young Tae Kim. Visualization: Kyung Jin Eoh and Hye Min Kim. Writing—original draft: Kyung Jin Eoh. Writing—review & editing: Young Tae Kim. Approval of final manuscript: all authors.

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