นิพนธ์ต้นฉบับ . Original Article

อัตราการรอดชีพและปัจจัยที่มีผลต่ออัตราการรอดชีพของผู้ป่วยมะเร็งรังไข่ระยะแรกที่ได้รับการรักษาในโรงพยาบาลสวรรค์ประชารักษ์

ธิดาพร ยศวิมลวัฒน์*
กลุ่มงานสูติ-นรีเวชกรรม โรงพยาบาลสวรรค์ประชารักษ์ จังหวัดนครสวรรค์

Survival Rate and Factors Affecting on Survival of Early-Stage Epithelial Ovarian Cancer Patients at Sawanpracharak Hospital

Tidaporn Yotwimonwat*
Department of Obstetrics and Gynecology, Sawanpracharak Hospital, Nakornsawan Province

Received: 17 January 2024 / Review: 18 January 2024 / Revised: 5 February 2024 / Accepted: 12 February 2024

บทคัดย่อ

หลักการและวัตถุประสงค์: แม้ว่าอัตราการรอดชีวิตของโรคมะเร็งรังไข่ชนิดเยื่อบุผิวระยะแรกจะสูงกว่าโรคมะเร็งระยะลุกลามอย่างมาก แต่ประมาณร้อยละ 20 ถึง 30 ของผู้ป่วยเหล่านี้จะเสียชีวิตจากโรคมะเร็ง วัตถุประสงค์หลักเพื่อศึกษาอัตราการรอดชีพ 5 ปี วัตถุประสงค์รองเพื่อศึกษาปัจจัยที่มีผลต่อการรอดชีพของผู้ป่วยมะเร็งรังไข่ชนิดเยื่อบุผิวระยะแรก

วิธีการศึกษา: เป็นการศึกษา retrospective cohort study กลุ่มประชากรคือ ผู้ป่วยที่ได้รับการวินิจฉัยมะเร็งรังไข่ชนิดเยื่อบุผิวระยะแรกที่ได้รับการรักษาที่โรงพยาบาลสวรรค์ประชารักษ์ระหว่าง 1 มกราคม พ.ศ. 2551 ถึง 31 ธันวาคม พ.ศ. 2561 โดยเก็บรวบรวมข้อมูลจากเวชระเบียน การวิเคราะห์ข้อมูลใช้สถิติเชิงพรรณนา, Kaplan Meier survival curve, Log rank test และ Cox proportional hazard model โดยกำหนดระดับนัยสำคัญที่ $p < 0.05$

ผลการศึกษา: ผู้ป่วยมะเร็งรังไข่ชนิดเยื่อบุผิวระยะแรก 151 ราย ที่มัธยฐานระยะเวลาในการติดตาม 101 เดือน อัตราการปลอดโรคและรอดชีพที่ 5 ปีของมะเร็งรังไข่ระยะแรก เท่ากับร้อยละ 79.3 และ 80.2 มะเร็งรังไข่ระยะ 1 มีอัตราการปลอดโรคและรอดชีพที่ 5 ปีเท่ากับร้อยละ 81.3 และ 83.4 ระยะที่ 2 เท่ากับร้อยละ 71.9 และ 71.7 ตามลำดับ ปัจจัยที่มีผลต่ออัตราการปลอดโรคและรอดชีพที่ 5 ปีแย่ลงอย่างมีนัยสำคัญทางสถิติ ได้แก่ คะแนนประเมินสภาพร่างกาย (ECOG PS) 2, 3 (HR 8.84, 95% CI 2.88-27.07, p<0.001), (HR 10.68, 95% CI 3.99-28.57, p<0.001) และมะเร็งชนิด clear cell (HR 9.01, 95% CI 1.91-42.39, p=0.005), (HR 5.16, 95% CI 1.44-18.49, p=0.012). สตรีที่ได้รับการรักษาด้วยยาเคมีบำบัดชนิด carboplatin (HR 5.79, 95% CI 1.12-29.61, p=0.036) และ carboplatin ร่วมกับ cyclophosphamide (HR 3.64, 95% CI 1.22-10.89, p=0.021) มีอัตราการปลอดโรคและการรอดชีพที่ 5 ปี ต่ำกว่าผู้ที่ได้รับการรักษาด้วย carboplatin ร่วมกับ paclitaxel ตามลำดับ.

สรุป: มะเร็งรังไข่ชนิดเยื่อบุผิวระยะแรกเป็นมะเร็งที่มีอัตราการปลอดโรคและรอดชีพที่ดี ถ้าได้รับการผ่าตัดและยาเคมีบำบัดที่เพียงพอ

คำสำคัญ: มะเร็งรังไข่ชนิดเยื่อบุผิวระยะแรก, อัตราการรอดชีพ, ปัจจัยพยากรณ์โรค

*Corresponding author: Tidaporn Yotwimonwat, E-mail: ytidaporn@gmail.com

Abstract

Background and Objective: Although the survival rate of early-stage epithelial ovarian cancer is higher than advanced-stage cancer, approximately 20% to 30% of these patients succumb to the disease. The main objective is to study the 5-year survival rate, with secondary objectives focusing on factors influencing the survival of patients with early-stage epithelial ovarian cancer.

Methods: This research is a retrospective cohort study of a population comprising patients diagnosed with early-stage epithelial ovarian cancer who received treatment at Sawanpracharak Hospital between January 1, 2008, and December 31, 2018. Data were collected from medical records, and statistical analysis involved descriptive statistics, Kaplan-Meier survival curve, Log-rank test, and Cox proportional hazard model with a significance level set at $p < 0.05$.

Results: Among 151 patients with early-stage epithelial ovarian cancer, with a median follow-up time of 101 months, the 5-year disease-free and overall survival rates were 79.3% and 80.2%, respectively. Stage 1 ovarian cancer had a 5-year disease-free and overall survival rate of 81.3% and 83.4%, while stage 2 had rates of 71.9% and 71.7%, respectively. In the multivariate analysis, the results indicate that ECOG PS 2,3 (HR 8.84, 95% CI 2.88-27.07, p<0.001), (HR 10.68, 95% CI 3.99-28.57, p<0.001), and clear cell cancer (HR 9.01, 95% CI 1.91-42.39, p=0.005), (HR 5.16, 95% CI 1.44-18.49, p=0.012), serve as independent predictive factors for a poorer 5-year disease-free survival (DFS) and overall survival (OS). Women who were administered the carboplatin regimen (HR 5.79, 95% CI 1.12-29.61, p=0.036) and the carboplatin plus cyclophosphamide regimen (HR 3.64, 95% CI 1.22-10.89, p=0.021) exhibited lower 5-year progression-free survival (PFS) and 5-year OS compared to those who received the carboplatin plus paclitaxel regimen, respectively.

Conclusion: Early-stage epithelial ovarian cancer demonstrates favorable disease-free and overall survival rates when treated with adequate surgery and chemotherapy.

Keywords: early-stage epithelial ovarian cancer, survival rate, prognostic factors.

Introduction

Ovarian cancer is the third most common gynecological cancer, following cervical and endometrial cancers. It ranks second in causing mortality, surpassed only by cervical cancer.[1] Due to vague and nonspecific symptoms, over 70% of patients present with advanced disease, leading to significantly lower survival rates. Approximately 25-30% of patients with epithelial ovarian cancer (EOC) present with early-stage disease (International Federation of Gynecology and Obstetrics [FIGO] stage I–II), which is a phase with favorable treatment outcomes.

The primary treatment for early-stage ovarian cancer is surgery, with the goal of completely removing the disease and determining the surgical stage. Surgical staging is essential to guide subsequent treatment with appropriate postoperative adjuvant therapy. For cases where fertility preservation is desired, it is possible to retain the uterus and unaffected ovary, especially in stage IA grade 1 cases.

The National Comprehensive Cancer Network[2] provides guidelines for the treatment of early-stage epithelial ovarian cancer, recommending that low-risk patients, specifically those in stage IA and IB grade 1 after surgical staging, may not require postoperative chemotherapy. These patients typically have a highly favorable prognosis, with a long-term disease-free survival rate reaching up to 90%. For high-risk patients with characteristics such as clear cell carcinoma, grade 3 and some grade 2 tumors, stage IC, and stage 2, the chances of disease recurrence are higher, reaching 30-40%, and a 5-year mortality rate of 25-30%. Therefore, these patients are recommended to undergo platinum-based chemotherapy for 4-6 cycles to improve their prognosis.

Although generally patients with early-stage epithelial ovarian cancer exhibit favorable treatment outcomes, there is a notable difference in recurrence rates among those considered high-risk, ranging from 15% to over 40%, as reported in various studies.[3-6] This is attributed to the fact that early-stage ovarian cancer is less commonly diagnosed than advanced-stage cases, resulting in fewer studies on survival rates and influencing factors. The studies conducted in other countries encompass diverse populations, including stage IC and stage 2 ovarian cancers, which exhibit 5-year survival rates ranging from 60-70%, in contrast to stage IA cases, which have a 90% 5-year survival rate. The FIGO 2014 staging criteria have been updated, emphasizing the different patterns of tumor rupture and positive cytology. Therefore, it is crucial to identify risk factors for disease recurrence to tailor treatment strategies for optimal outcomes.

The studies revealed that prognostic factors for the disease include the disease stage, tumor grade, residual tumor, age, performance status, positive cytology, and the type of cancer cell.[7-10] However, there is still no study on survival rates and prognostic factors specifically for early-stage ovarian cancer patients in Thailand. The objective of this study is to investigate the clinicopathological characteristics, survival rates, and prognostic factors for the survival of early-stage epithelial ovarian cancer patients. This information is intended to be used as data for future studies to contribute to the development of surgical and treatment strategies for future ovarian cancer patients.

Materials and Methods

This research employed a retrospective cohort study design, focusing on the target population of patients with early-stage epithelial ovarian cancer in Sawanpracharak Hospital. The study included patients diagnosed in stages 1 and 2 between January 1, 2008, and December 31, 2018.

Inclusion criteria involved patients who received both treatment and diagnosis of epithelial ovarian cancer and had their diagnoses confirmed in the hospital's pathology reports during the specified period. The study concluded with the final status of life or the end of the study on December 31, 2023. Exclusion criteria consisted of patients with ovarian cancer diagnosed in conjunction with cancers in other locations, those diagnosed with borderline ovarian cancer, patients with mucinous ovarian cancer originating from other organs, patients with mixed-cell type epithelial ovarian cancer, and patients with incomplete data.

The definition of surgical staging consisted of removal of the affected ovary or ovaries ;removal of the uterus; careful inspection and palpation of all peritoneal surfaces and biopsy sampling of any suspicious areas, such as adhesions adjacent to the

primary tumor; peritoneal washing for cytology analysis; omentectomy; blind peritoneal biopsy sampling of the right hemidiaphragm, the right and left paracolic gutters, the pouch of Douglas, the bladder peritoneum, and the pelvic side walls; removal of para-aortic and pelvic lymph nodes. Adjuvant therapy consisted of platinum-based chemotherapy (with or without cyclophosphamide or paclitaxel) in accordance with clinical and pathological characteristics.

The total number of patients during the study period was 151. Following ethical approval from the Research Ethics Committee (Approval No. COA. 16/2567), data were collected from patient medical records in the hospital's computerized database. Information included general patient data and treatment history, as well as diagnostic details recorded on predefined forms. The follow-up period commenced from the date of confirmed cancer diagnosis and continued until the patient's demise or the end of the study on December 31, 2023. Patients unable to be tracked for vital status were considered censored. Censoring also applied to patients who passed away due to causes unrelated to ovarian cancer. Confirmation of death and determination of its cause were obtained through the examination of patient medical records and civil registration data.

Statistical analysis involved descriptive statistics, Kaplan-Meier survival curves for survival analysis, log-rank tests for group comparisons, and Cox proportional hazard regression for identifying factors affecting disease-free survival and overall survival. Results were presented as hazard ratios and 95% confidence intervals and statistical significance was set at $p < 0.05$.

Results

From the study, a total of 151 patients with early-stage ovarian cancer were identified, with an average age of 55 years (range: 28-79 years). Most patients had Eastern Cooperative Oncology Group (ECOG) performance status scores of 1 (79.5%) and 2 (15.2%). Among the total patients, 132 (87.5%) underwent complete surgical staging, whereas 15 patients (9.9%) required re-staging following an initial incomplete operation. Out of all patients, 119 (78.8%) were in stage 1, with stage IC being the most prevalent at 62.2%. Meanwhile, 32 patients (21.2%) were in stage 2, distributed between Stage IIA (9.9%) and Stage IIB (11.3%). The most frequently encountered cancer cell types were clear cell (33.8%), followed by serous (27.2%), mucinous (22.5%), and endometrioid (16.6%). For patients in stages IA-IB, mucinous (48%) and endometrioid (20%) were the common cell types. In stage IC, clear cell (42.6%) dominated, followed by serous (22.3%). In stages IIA-IIB, serous cell type was predominant (50%), followed by clear cell (21.9%). The distribution of cancer grades found 17.9% grade 1, 15.2% grade 2, and 13.9% grade 3. Out of the 151 patients in total, 36.4% had ascites, 47.7% experienced intraoperative rupture, 55% exhibited dense adhesions, and 25.8% showed positive cytology, primarily in patients with ascites (46.1%). Out of 151 patients, 140(92.7%) underwent surgery with no residual tumor, 4 patients had residual tumor less than or equal to 1 cm, and only 4.6% had residual tumor greater than 1 cm. High-risk group patients received carboplatin with paclitaxel chemotherapy, constituting 78.8% of the cases (Table 1).

Table 1 Patient and clinicopathologic characteristics of early-stage epithelial ovarian cancer.

Variables	N (N=151)	%
Age: Mean (Min-Max), (years)	55 (28 – 79)	
< 60	109	72.2
≥ 60	42	27.8
ECOG Performance status		
0	3	2.0
1	120	79.5
2	23	15.2
3	5	2.6
CA 125 (units/ml)		
≤ 35	29	19.2
> 35	89	58.9
Missing	33	21.9
FIGO stage		
IA	24	15.9
IB	1	0.7
IC1	28	18.5
IC2	39	25.8
IC3	27	17.9
IIA	15	9.9
IIB	17	11.3
Histology		
1 Clear cells	51	33.8
2 Serous	41	27.2
3 Mucinous	34	22.5
4 Endometrioid	25	16.6
Tumor grade		
1	27	17.9
2	23	15.2
3	21	13.9
Not grade	29	19.2
Clear cell	51	33.8
Presence of Ascites		
No	96	63.6
Yes	55	36.4
Dense Adhesion		
No	68	45.0
Yes	83	55.0
Cytology		
Negative	85	56.3
Positive	39	25.8
Not done	27	17.9
Ruptured capsule		
Unruptured	52	34.4
Accidental ruptured	72	47.7
Ruptured	27	17.9
Endometriosis		
No	109	72.2
Yes	42	27.8
Biopsy seeding		
No	118	78.1
Yes	33	21.9
Type of Surgery		
Complete surgical staging	132	87.5
Incomplete staging (re-staging)	15	9.9
Inadequate staging surgery*	4	2.6
Residual Tumor		
No RT	140	92.7
Optimal Surgery (≤ 1 cm)	4	2.6
Suboptimal Surgery (> 1 cm)	7	4.6
Chemotherapy		
1 No	9	6.0
2 PT	119	78.8
3 PC	15	9.9
4 Carboplatin	8	5.3
Site of Recurrence (in 5 yr.)		
1. Local Recurrence	6	19.3
2. Peritoneal Metastasis	12	38.7
3. LN Metastasis	5	16.1
4. Distant Metastasis	8	25.8

ECOG: Eastern Cooperative Oncology Group

FIGO: the International Federation of Gynecology and Obstetrics

*No lymph node dissection performed

Table 2 Progressive-free survival and overall survival by patient characteristics.

	N (N=151)	PFS % 5yr	PFS p-value	OS % 5yr	OS p-value		N (N=151)	PFS % 5yr	PFS p-value	OS % 5yr	OS p-value
Age group, yrs.						**Grade**					
< 60	109	78.7	0.95	81.2	0.695	G1,2	50	87.9	0.032	87.3	0.022
≥ 60	42	80.9		80.3		G 3, Clear cell	72	73.2		75.7	
ECOG PS						**Ascites**					
0-1	123	85.3	0.000	87.6	0.000	No	96	75.9	0.112	78.8	0.111
2-3	28	52.1		50.8		Yes	55	85.2		84.8	
FIGO Stage						**Capsule Ruptured**					
IA or IB	25	96.0	0.056	96.0	0.143	Unruptured	52	80.7	0.717	82.6	0.655
IC	94	77.3		80.1		AR	72	76.1		78.2	
IIA-IIB	32	71.9		71.7		Ruptured	27	85.2		85.0	
Type of EOC*						**Dense Adhesion**					
Type I	109	80.7	0.802	80.7	0.897	No	68	88.0	0.043	89.2	0.029
Type II	31	76.8		75.6		Yes	83	72.3		74.3	
Undefined	11	72.7		81.8		**Cytology**					
Histology						Negative	85	86.8	0.000	88.9	0.001
1 Endometrioid	25	95.8	0.014	95.7	0.008	Positive	39	64.1		66.3	
2 Mucinous	34	91.0		90.9		**Optimal Surgery**					
3 Serous	41	72.8		74.4		Optimal (≤ 1 cm)	144	81.8	0.000	83.6	0.000
4 Clear cells	51	68.6		72.4		Suboptimal (> 1 cm)	7	28.6		21.4	
NCC VS Clear cell						**Chemotherapy****					
Non-Clear cell	100	84.8	0.013	85.4	0.006	PT	118	81.3	0.011	88.9	0.001
Clear cell	51	68.6		72.4		PC	15	72.7		66.3	
						Carboplatin	8	37.5			

*Type I EOC: low-grade serous, mucinous, endometrioid, clear cell, transitional cell carcinomas and Type II EOC includes high-grade serous carcinomas, undifferentiated carcinomas and carcinosarcomas.

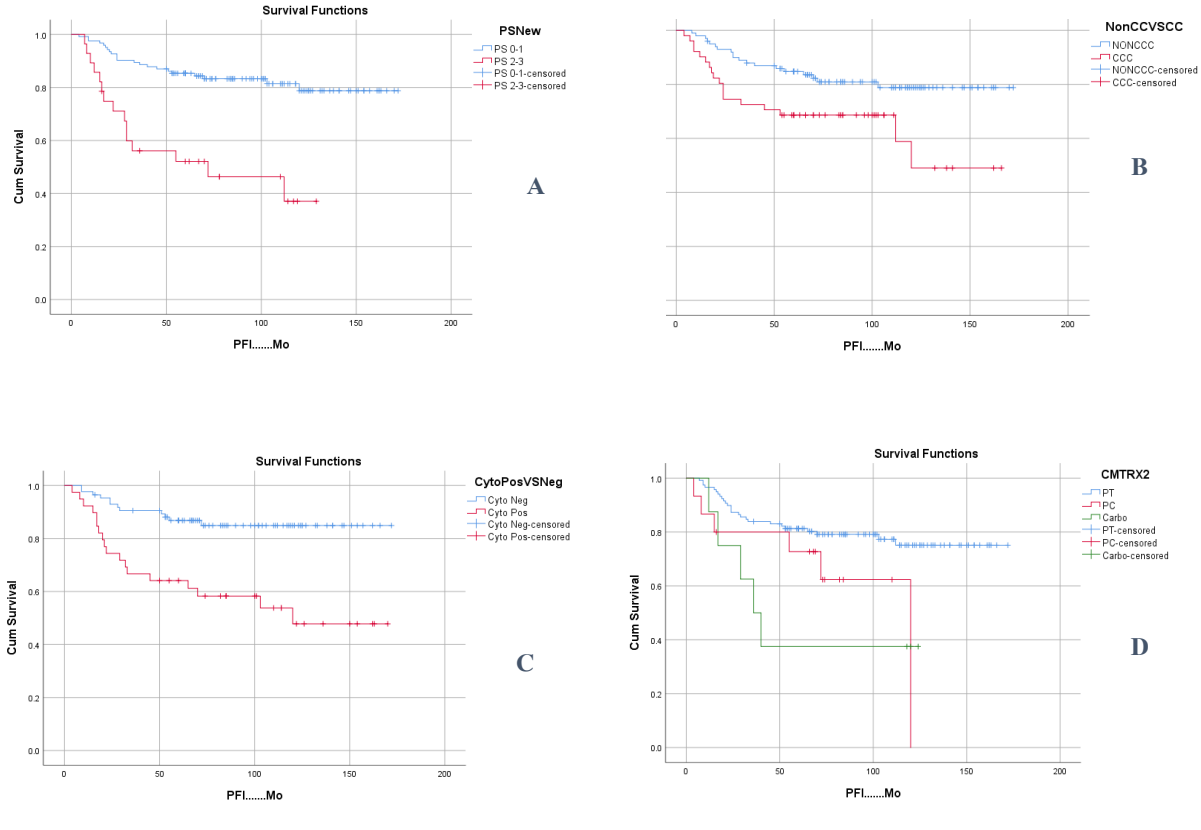
**PT: Carboplatin and Paclitaxel, PC: Carboplatin and Cyclophosphamide

Table 3 Multivariate analysis of predictive factors influencing disease free survival and overall survival in patients early-stage ovarian cancer

Variable	Disease Recurrence			Death		
	Adj. HR	95% CI	p-value	Adj. HR	95% CI	p-value
ECOG PS*						
0-1	1			1		
2-3	8.84	2.88-27.07	< 0.001	10.68	3.99-28.57	< 0.001
Histology						
Non clear cell	1			1		
Clear cell	9.01	1.91-42.39	0.005	5.16	1.44-18.49	0.012
Cytology						
Negative	1					
Positive	2.86	1.15-7.12	0.024			
Chemotherapy**						
PT	1			1		
PC	2.79	0.73-10.64	0.132	3.64	1.22-10.89	0.021
Carboplatin	5.79	1.12-29.61	0.036	4.53	0.87-23.61	0.073

*ECOG: Eastern Cooperative Oncology Group

**PT: Carboplatin and Paclitaxel, PC: Carboplatin and Cyclophosphamide



Figures 1 Comparison of disease-free survival rates based on performance status 2 and 3(A), clear cell type cancer versus non-clear cell type(B), positive versus negative cytology(C), and types of chemotherapy received (D)

In this study, the median follow-up duration was 101 months. Out of 151 patients, 37 experienced disease recurrence, and 45 patients died. The 5-year disease-free survival rate and overall survival rate for early-stage ovarian cancer were 79.3% and 80.2%, respectively. For stage 1 ovarian cancer, the 5-year disease-free survival rate and overall survival rate were 81.3% and 83.4%, respectively. Specifically, stage IA-IB had the highest 5-year disease-free survival rate at 96.0% and an overall survival rate of 96.0%. Stage IC had a 5-year disease-free survival rate of 77.3% and an overall survival rate of 80.1%, while Stages IIA-IIB had the lowest rates at 71.9% and 71.7%, respectively. The 5-year disease-free survival rates between both stages were not statistically different. A subgroup analysis was performed for patients in stage IC, and according to FIGO 2014, IC1 had a 5-year disease-free survival rate of 82.1% and an overall survival rate of 80.4%. for IC2, the rates were 81.4% and 86.7%, respectively. However, patients in IC3 had the lowest 5-year disease-free survival rate at 66.7% and an overall survival rate of 70.4%, which was statistically significantly lower than IC1 and IC2 (p=0.048).

The 5-year disease-free survival rate and overall survival rate analysis compared type I and type II EOC were not significantly different. The cell type with the highest 5-year disease-free survival rate was endometrioid, at 95.8%, and overall survival rate at 95.7%. Mucinous followed closely, with a 5-year disease-free survival rate of 91.0% and an overall survival rate of 90.9%. Serous and clear cell types had relatively lower rates, with serous at 72.8% and 74.4%, and clear cell having the lowest rates at 68.6% and 72.4%, respectively. Comparing the clear cell group with the non-clear cell group showed statistically significant lower rates in the clear cell group (p=0.013, p=0.001).

Patients who had residual disease less than or equal to 1 cm after surgery had a 5-year disease-free survival rate of 81.8% and an overall survival rate of 83.6%. In contrast, those with residual disease greater than 1 cm had significantly worse rates at 28.6% and 21.4%, respectively (p=0.001). Additionally, patients with performance status 2 and 3, grade 3 cancer cells, dense adhesions, and positive cytology, as well as those who received carboplatin or carboplatin with cyclophosphamide chemotherapy, had significantly poorer 5-year disease-free survival and overall survival rates (Table2). Figures 1 show a comparison of disease-free survival rates based on performance statuses 2 and 3, clear cell type cancer versus non-clear cell type, positive versus negative cytology, and types of chemotherapy received.

In the multivariate analysis (Table 3) evaluating factors influencing the disease-free survival and overall survival rates of early-stage ovarian cancer patients, the following factors were identified. For disease-free survival, significant factors included performance status 2 and 3 (Adj. HR = 8.84; 95% CI: 2.88-27.07), clear cell type cancer (Adj. HR = 9.01; 95% CI: 1.91-42.39), positive cytology (Adj. HR = 2.86; 95% CI: 1.15-7.12), and receipt of carboplatin chemotherapy (Adj. HR = 5.79; 95% CI: 1.12-29.61). Regarding overall survival, noteworthy factors included performance status 2 and 3 (Adj. HR = 10.68; 95% CI: 3.99-28.57), clear cell type cancer (Adj. HR = 5.16; 95% CI: 1.44-18.49), and receipt of carboplatin with cyclophosphamide chemotherapy (Adj. HR = 3.64; 95% CI: 1.22-10.89).

Discussion

In this study, it was found that the 5-year disease-free survival and overall survival rates for early-stage epithelial ovarian cancer were 79.3% and 80.2%, respectively. For stage 1 ovarian cancer, the 5-year disease-free survival and overall survival rates were 81.3% and 83.4%, and for stage 2, they were 71.9% and 71.7%, respectively. These findings align with the study conducted by Chan et al[4], who analyzed data from GOG protocols 95 and 157, involving 506 patients. This population resembled ours, with the highest proportion in stage IC and clear cell type. In Chan et al[4] study, the 5-year disease-free survival and overall survival rates for early-stage ovarian cancer were 76.0% and 82.0%, respectively, with stage 1 having a 5-year disease-free survival rate of 84%, and stage 2 having rates of 65.9% and 76.3%, respectively. The 5-year disease-free survival and overall survival rates for stage IC ovarian cancer in our study were 77.3% and 80.1%, respectively, consistent with the GOG study, which reported rates of 77.8% and 83.7%, respectively.

However, our results differed from the study conducted by Hsieh et al[11], which shared similar population characteristics. Hsieh et al reported higher 5-year disease-free survival and overall survival rates for stage IC ovarian cancer at 82.8% and 91.5%, respectively. This difference may be attributed to a better prognosis of clear cell type cancer in their Taiwanese study compared to other cell types. This contrasts with the clear cell type in our study, which showed the least favorable prognosis. Wei et al[12] also reported higher 5-year disease-free survival rates for stages 1 and IC ovarian cancer at 86.5% and 81%, respectively. In their subgroup analysis of the IC group according to FIGO 2014, they found no statistically significant differences in the 5-year disease-free survival and overall survival rates among IC1 (70/85), IC2 (85/98), and IC3 (89/90). This contrasts with our study's results, where the 5-year disease-free survival rates for IC3 were significantly lower at 66.7% and 70.4% compared to IC1 and IC2 (p = 0.048), leading to an overall decrease in the disease-free survival rates for stage IC.

This study found that ovarian cancer stages IA-IB have the highest 5-year disease-free and overall survival rates, primarily attributed to the favorable prognosis of mucinous cell types. These findings align with previous studies[10,13], suggesting that mucinous tumors, often detected in early stages, contribute to more straightforward surgical interventions. Our study revealed a predominance of clear cell type, followed by serous type, notably in stages IC and II, with both cell types demonstrating relatively low 5-year disease-free survival and overall survival rates. These findings align with previous studies[4,14], suggesting that the prognosis of clear cell is similar to serous histology. When comparing the 5-year disease-free survival and overall survival rates between the clear cell group (68.6% and 72.4%), significantly lower rates were observed than for the non-clear cell group (84.8% and 85.4%) (p=0.013, p=0.001), consistent with a study conducted in Thailand on stage IC ovarian clear cell carcinoma.[15] These findings support the notion that molecular analyses and cell of origin studies suggest that type I tumors of the dualistic model of epithelial carcinogenesis are quite heterogeneous and have very different precursors and molecular profiles.[16]

In addition, this study noted that patients who underwent surgery with residual disease equal to or less than 1 cm exhibited superior 5-year disease-free survival and overall survival rates compared to those with residual disease exceeding 1 cm. Wei et al. similarly reported 5-year disease-free survival rates for residual disease equal to or less than 1 cm and more than 1 cm as 80% vs. 50% and 92% vs. 69%, respectively.[12]

The prognostic factors influencing disease-free survival and overall survival in early-stage epithelial ovarian cancer are the performance status, clear cell type, and receiving chemotherapy with carboplatin and paclitaxel. On the other hand, the crucial factor affecting disease-free survival alone is positive cytology. Previous studies have consistently identified the disease stage as a significant factor affecting disease-free survival and overall survival.[4,10-12,17] However, this study found that the disease stage only had a specific impact when analyzing univariate variables. This might be due to a relatively small quantity of early-stage ovarian cancer patients in this study, and the 5-year disease-free survival rate for stage 2 ovarian cancer was relatively high at 71.9%, compared to other studies ranging from 44% to 65%.[4,11,12,17] Correspondingly, some authors indicated that the stage was not influential if optimal treatment were administrated.[18] Clear cell ovarian cancer emerged as a factor associated with an increased risk of recurrence and decreased overall survival, consistent with several studies.[3-5,19] In contrast, Hsieh et al reported a favorable prognosis for clear cell type.[11] Positive cytology is a factor affecting disease-free survival, consistent with these studies that found the presence of cancer cells in the abdominal fluid is associated with a higher risk of recurrence within the abdominal cavity.[4,10] The majority of studies have found that administering chemotherapy with carboplatin and paclitaxel results in better treatment outcomes than other platinum-based regimens.[2,20] This corroborates with the current study. Several studies have also reported that age is a crucial factor affecting recurrence and overall survival.[4,10,17] However, this study found that performance status is a critical factor, consistent with the study by Trilsch et al[21], which identified the performance status as a crucial factor affecting

disease-free survival, not just age. This finding is further supported by additional studies.[22-24]

Since the introduction of FIGO 2014, this study represents the first investigation into the survival rates and factors influencing the survival of patients with early-stage epithelial ovarian cancer in Thailand. The strength of this study lies in the fact that nearly all patients, 97.4%, underwent surgical staging, and 93% had surgery resulting in no residual tumor. The choice of the chemotherapeutic regimen was determined based on the patients' age, medical condition, chemotherapy toxicities, and the presence of low-grade tumors such as mucinous types. The majority of high-risk patients received chemotherapy with carboplatin and paclitaxel. Over a 5-year period, 20.7% of patients experienced recurrence, with 80% of recurrences occurring in the abdominal cavity and metastasizing to other organs. An association was observed with clear cell type, which showed a poorer prognosis and response to chemotherapy. Patients who underwent both adequate surgery and received sufficient chemotherapy exhibited 5-year disease-free survival and overall survival rates comparable to results from international studies. However, the study's limitations include its retrospective design and a relatively small population due to the low incidence of early-stage ovarian cancer. Additionally, the study collected data only from patients treated by a single gynecologic oncologist during the period covered by the study.

In clinical application, the findings of this study serve as valuable insights for advancing surgical procedures and patient care in the future. They contribute foundational data for hospitals to enhance the quality of their services and serve as a reference for future studies and research on ovarian cancer.

In the early stages, ovarian cancer exhibits favorable rates of disease-free and overall survival when adequate surgical intervention, combined with sufficient chemotherapy, is administered. The outcomes of clinical trials, such as GOG 268, which explores the combination of temsirolimus with carboplatin and paclitaxel as the first-line treatment, and GOG 254, investigating the use of sunitinib for recurrent patients, should be closely monitored. These trials have the potential to contribute valuable insights that may improve future treatment outcomes. Additionally, collaborative prospective studies involving multiple institutions may be required to obtain a sufficiently large sample size, providing clear insights into the factors influencing disease-free and overall survival.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71(3):209-49. doi: 10.3322/caac.21660.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Ovarian cancer/Fallopian Cancer/Primary Peritoneal Cancer. Version 1.2021. [Accessed on January 29, 2020]. Available at: https://www.nccn.org/professionals/physician_gls.
3. Vergote I, De Brabanter J, Fyles A, Bertelsen K, Einhorn N, Sevelda P, et al. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. Lancet 2001;357(9251):176-82. doi: 10.1016/S0140-6736(00)03590-X.
4. Chan JK, Tian C, Monk BJ, Herzog T, Kapp DS, Bell J, et al. Prognostic factors for high-risk early-stage epithelial ovarian cancer. A Gynecologic Oncology Group Study. Cancer 2008(10);112:2202-10. doi: 10.1002/cncr.23390
5. Ahmed FY, Wiltshaw E, A'Hern RP, Nicol B, Shepherd J, Blake P, et al. Natural history and prognosis of untreated stage I epithelial ovarian cancer. J Clin Oncol 1996;14(11):2968-75. doi: 10.1200/JCO.1996.14.11.2968.
6. Schueler JA, Cornelisse CJ, Hermans J, Trimbos JB, van der Burg ME, Fleuren GJ. Prognostic factors in well-differentiated early-stage ovarian cancer. Cancer 1993;71(3):787-95. doi: 10.1002/1097-0142(19930201)71:3<787:aid-cncr2820710322>3.0.co;2-2.
7. Dembo AJ, Davy M, Stenwig AE, Berle EJ, Bush RS, Kjorstad K. Prognostic factors in patients with stage I epithelial ovarian cancer. Obstet Gynecol 1990;75(2):263-73. PMID: 2300355.

8. Sjovall K, Nilsson B, Einhorn N. Different types of rupture of the tumour capsule and the impact on survival in early ovarian cancer. Int J Gynecol Cancer 1994;4(5):333-6. doi: 10.1046/j.1525-1438.1994.04050333.x
9. Sevelda P, Dittich C, Salzer H. Prognostic value of the rupture of the capsule in stage I epithelial ovarian carcinoma. Gynecol Oncol 1989;35(3):321-2. doi: 10.1016/0090-8258(89)90071-1.
10. Tognon G, Carnazza M, Ragnoli M, Calza S, Ferrari F, Gambino A, et al. Prognostic factors in early-stage ovarian cancer. Ecancermedicalscience 2013;7:325. doi: 10.3332/ecancer.2013.325.
11. Hsieh SF, Lau HY, Wu HH, Hsu HC, Twu NF, Cheng WF. Prognostic factors of early-stage epithelial ovarian carcinoma. Int J Environ Res Public Health 2019;16(4):637. doi: 10.3390/ijerph16040637
12. Wei W, Li N, Sun Y, Li B, Xu L, Wu L, et al. Clinical outcome and prognostic factors of patients with early-stage epithelial ovarian cancer. Oncotarget 2016;118(14):23862-70. doi: 10.18632/oncotarget.13317
13. Manchana T, Kobwitaya K. Survival outcomes for different subtypes of epithelial ovarian cancer. Clin Res Obstetr Gynecol 2018;1(1):1-7.
14. Schnack TH, Høgdall E, Nedergaard L, Høgdall C. Demographic clinical and prognostic factors of primary ovarian adenocarcinomas of serous and clear cell histology-A comparative study. Int J Gynecol Cancer 2016;26(1):82-90. doi: 10.1097/IGC.0000000000000585.
15. Thaweekul Y, Lertkhachonsuk R, Khemapech N, Manchana T, Sirisabya N, Worasethsin P, et al. Treatment outcome of stage Ic ovarian clear cell carcinoma compared to non-clear cell type. Chulalongkorn Medical Journal 2010;54(3):213-23. doi: CHULA.CMJ.54.3.4
16. Salazar C, Campbell IG, Gorringe KL. When Is "Type I" ovarian cancer not "Type I"? Indications of an out-dated dichotomy. Front Oncol 2018;21(8):654. doi: 10.3389/fonc.2018.00654.
17. Ditto A, Maggiore UL, Bogani G, Martinelli F, Chiappa V, Evangelista MT, et al. Predictive factors of recurrence in patients with early-stage epithelial ovarian cancer. Int J Gynecol Obstet 2019;145(1):28-33. doi: 10.1002/ijgo.12769.
18. Trimbos JB, Vergote I, Bolis G, Vermorken JB, Mangioni C, Madronal C, et al. Impact of adjuvant chemotherapy and surgical staging in early-stage ovarian carcinoma: European Organisation for Research and Treatment of Cancer-Adjuvant Chemotherapy in Ovarian Neoplasm Trial. J Natl Cancer Inst 2003;95(2):113–25. PMID: 12529344
19. Sugiyama T, Kamura T, Kigawa J, Terakawa N, Kikuchi Y, Kita T, et al. Clinical characteristics of clear cell carcinoma of the ovary: a distinct histologic type with poor prognosis and resistance to platinum-based chemotherapy. Cancer 2000;88(11):2584-9. PMID: 10861437
20. Adams G, Zekri J, Wong H, Walking J, Green JA. Platinum-based adjuvant chemotherapy for early-stage epithelial ovarian cancer: single or combination chemotherapy? BJOG 2010;117(12):1459-67. doi: 10.1111/j.1471-0528.2010.02635.x
21. Trillsch F, Woelber L, Eulenburg C, Braicu I, Lambrechts S, Chekerov R, et al. Treatment reality in elderly patients with advanced ovarian cancer: a prospective analysis of the OVCAD consortium. J Ovarian Res 2013;6(1):42. doi: 10.1186/1757-2215-6-42
22. Bun S, Yunokawa M, Ebata T, Kato MK, Shimoi T, Kato T, et al. Feasibility of initial treatment in elderly patients with ovarian cancer in Japan: A retrospective study. Int J Clin Oncol 2019;24(9):1111-8. doi: 10.1007/s10147-019-01449-3
23. Fourcadier E, Tretarre B, Gras-Aygon C, Ecarnot F, Daures J, Bessaoud F. Under-treatment of elderly patients with ovarian cancer: A population-based study. BMC Cancer 2015;15:937. doi: 10.1186/s12885-015-1947-9.
24. Yoshikawa K, Fukuda T, Uemura R, Matsubara H, Wada T, Kawanishi M, et al. Age-related differences in prognosis and prognostic factors among patients with epithelial ovarian cancer. Mol Clin Oncol 2018;9(3):329-34. doi: 10.3892/mco.2018.1668

SMJ