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ORIGINAL RESEARCH

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Adjuvant chemotherapy is not associated with improved overall survival with stage I endometrioid ovarian cancer patients in a SEER cohort

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Abstract

The objectives of this study was to investigate the prognostic significance of adjuvant chemotherapy in early-stage endometrioid ovarian cancer (EnOC) patients, especially those with grade II stage IA and IB and grade I stage IC, that are not explicitly recommended in the current National Comprehensive Cancer Network (NCCN) guidelines. This was a retrospective cohort study based on the Surveillance, Epidemiology and End Results (SEER) database, comprising 875 cases diagnosed with stage I EnOC from 2010 to 2018, of whom 441 (50%) and 434 (50%) received and did not receive chemotherapy, respectively. The Kaplan-Meier method was used for survival analysis, and the Cox multivariate regression analysis was performed to identify independent prognostic factors. Stratified survival analysis for adjuvant chemotherapy based on the recommendations of the NCCN Guidelines in stage I EnOC patients with different substages and grades showed that in this cohort adjuvant chemotherapy did not improve the survival of any of the stage I stratified substages group (p = 0.076, HR: 0.600, 95% CI: 0.342–1.054). Age ≥60 (p = 0.000, HR: 3.609, 95% CI: 2.156–6.039) and elevated CA125 (p = 0.028, HR: 2.480, 95% CI: 1.103–5.577) were independent risk factors associated with worse survival in stage I EnOC patients. In conclusion, chemotherapy would be unnecessary for stage I EnOC patients to improve the overall survival no matter substage and grade in our cohort.

Keywords

Adjuvant chemotherapy; Stage I; Endometrioid carcinoma; SEER Program

1. Introduction

Among women, the ovarian cancer-related disability-adjusted life years were estimated ranking sixth globally, while breast cancer ranking first [1]. In 2020, there were an estimated 313,959 new cases of ovarian cancer and 207,252 related death worldwide [2]. Ovarian cancer is among the five leading causes of cancer deaths in women in the United States [3]. Approximately 90% of ovarian cancers are of the epithelial type, of which endometrioid ovarian cancer (EnOC) has a relatively better prognosis, especially in early-stage patients [4]. The 5-year cause-specific survival of stage I and stage II are reported to be 95% and 84%, respectively [5, 6].

However, due to the good prognosis of EnOC, there is a lack of consensus on the necessity of adjuvant treatment in early-stage EnOC patients [7–10]. A prospective randomized clinical trial that investigated the prognostic effects of chemotherapy in highly or moderately differentiated patients with stage IA and IB ovarian cancer, assigned to groups receiving no chemotherapy or receiving melphalan orally, found no significant difference in their 5-year disease-free survival (91% *vs.* 98%, p = 0.41) or overall survival (94% *vs.* 98%, p = 0.43) [11]. However, a retrospective study based on data from the National Cancer Data Base (NCDB) from 2004 to 2014 reported that chemotherapy had greater survival benefits in early-stage EnOC patients (Hazard ratio (HR): 0.68, 95% Confidence interval (CI): 0.55–0.84). Subgroup analysis showed that the administration of chemotherapy was associated with better overall survival (OS) for patients with stage IA/IB (p = 0.017; 5-year OS rates: 95% *vs.* 92.3%) or IC (p = 0.002; 5-year OS rates: 89.1% *vs.* 90.8%) [8]. Another retrospective study that used data before 2013 also reached a conclusion as they found that adjuvant chemotherapy was not associated with improved survival in stage IA (n = 2062) or IB (n = 209) of any grade or stage IC grade I (n = 441) or II (n = 557) EnOC patients [10]. However, since the recommendations of adjuvant chemotherapy for early-stage EnOC were recently updated in the National Comprehensive Cancer Network (NCCN) Guidelines (Version 3.2022) [12], the conclusions from the above analysis might not be applicable as they were not conducted by combining the substage and grade according to current NCCN Guidelines. Thus, the results contradict each other and may not be consistent with the NCCN Guidelines recommendations [13].

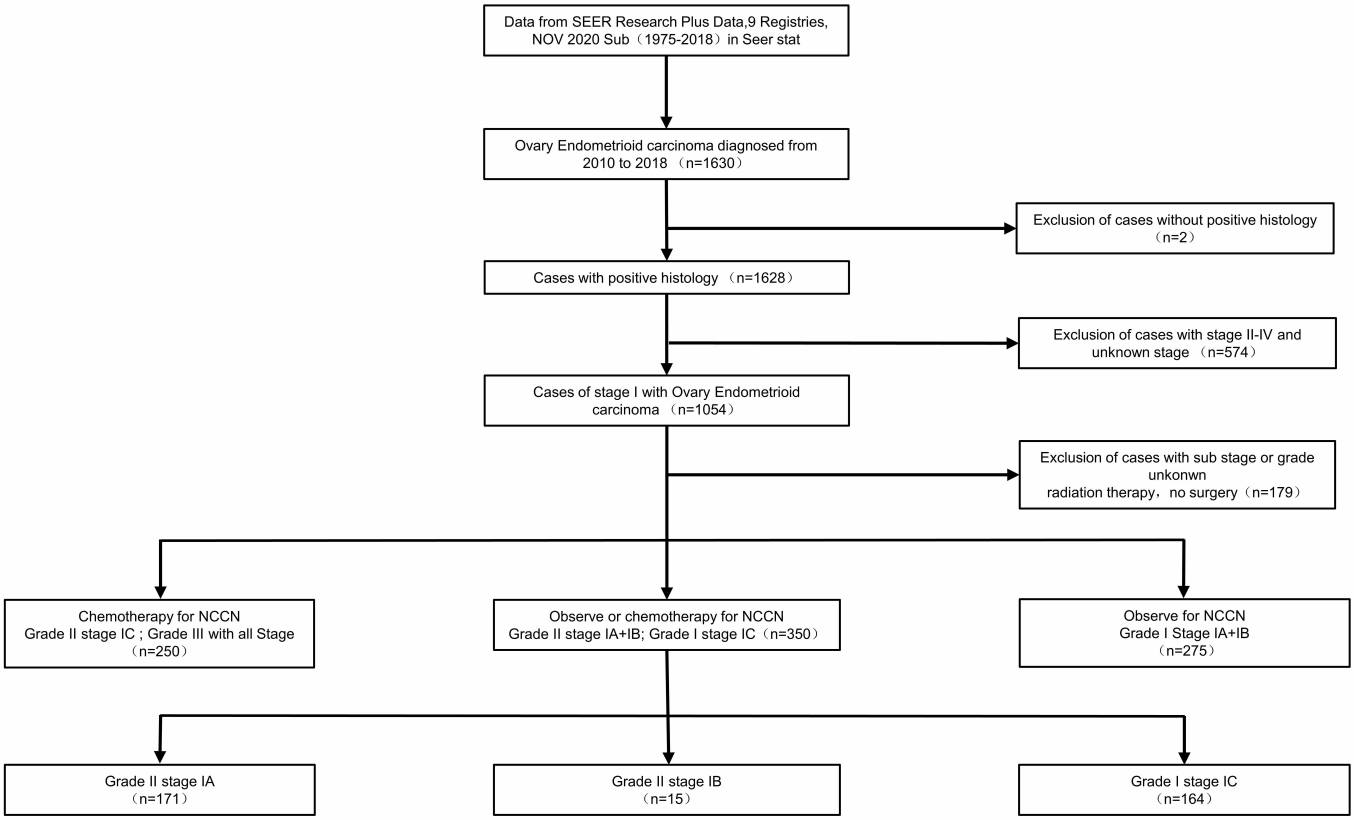

FIGURE 1. Flow diagram of patients' selection. SEER: Surveillance, Epidemiology and End Results; NCCN: National Comprehensive Cancer Network.

The purpose of this study was to explore the prognostic impact of chemotherapy on patients with early-stage EnOC using the latest data from the Surveillance, Epidemiology, and End Results (SEER) database, especially in grade II stage IA, IB and grade I stage IC patients, among whom adjuvant chemotherapy is not specifically recommended in the current NCCN Guidelines (Version 3.2022).

2. Material and methods

2.1 Data collection

This was a retrospective cohort study based on the SEER database, which enrolled eligible stage I EnOC patients to investigate the prognostic significance of adjuvant chemotherapy. The SEER database is supported by the National Cancer Institute and is a publicly available database. SEER currently collects information on cancer cases from various locations and sources throughout the United States, covering approximately 48.0% of the U.S. population. The SEER*Stat (Surveillance Research Program, National Cancer Institute SEER*Stat software, seer.cancer.gov/seerstat) version. 8.3.9 software, downloaded from the SEER official website, was used to extract targeted cases. Database from SEER Research Plus Data, 9 registries, NOV 2020 Sub (1975–2018), was chosen to obtain cases diagnosed with EnOC between 2010 and 2018.

The ICD-O-3/WHO 2008 site code "Ovary" and ICD-O-3 Hist/Behav morphology Codes "8380–8383" were used to identify the EnOC cases. Those with radiation therapy, classified as stage II–IV, stage or grade unknown, did not undergo surgery, and without histopathological diagnosis were excluded. The following data were extracted: patients' demographics (age at diagnosis and race), tumor characteristics (stage, tumor differentiation and CA125 level), treatments (surgery, chemotherapy, and radiotherapy), and survival status.

2.2 Statistical analysis

Data analysis was performed with the IBM SPSS software for Windows or Macintosh, version 23 (IBM Corp., Armonk, N.Y., USA). Overall survival (OS) curves were plotted using the Kaplan-Meier method. The Kaplan-Meier method, with both univariate and multifactorial Cox regression, was used to screen for OS prognostic factors in thyroid cancer patients, and all variables were used to construct prognostic models. Cox multivariate regression analysis was performed on risk factors that were statistically significant in univariate analysis or that influenced prognosis according to clinical experience. The statistical significance of the Alpha level was set at 0.05. The results are shown as HR with 95% CI. Death was considered the study endpoint event.

3. Results

3.1 Patient demographics

A total of 875 eligible patients who met the inclusion criteria were identified. Our analysis showed that with a median follow-up time of 53 months (95% CI: 49.569–56.431), the

five-year survival rate of stage I patients was 94%. By the end of the follow-up, no more than half of the patients met the endpoint event.

According to the latest NCCN Guidelines (Version 3.2022) for ovarian cancer [12], observation is recommended for EnOC grade I stage IA and IB patients (n = 275, 31%), adjuvant chemotherapy is recommended for all substages of stage IC grade II and grade III patients (n = 250, 29%), and observation or chemotherapy is recommended for grade II stage IA and IB and grade I stage IC (n = 350, 40%) (Fig. 1).

In this selected population, 314 (36%) patients were ≥60 years old, while the remaining 561 (64%) were younger. The vast majority of patients were White (n = 708, 81%). There were 441 patients (50%) who received chemotherapy and 434 (50%) who did not receive chemotherapy (or unclear data). Compared with other substages of stage I, the number of stage IB patients was the least, with only 30 cases (3%), which made subsequent statistical analysis difficult. There were 484 (55%) and 361 (41%) stage IA and IC patients, and there were 439 (50%), 317 (36%) and 119 (14%) patients in grades I, II and III, respectively. The number of patients with elevated pretreatment CA125 was greater than those within the normal range (501 (57%) *vs.* 144 (16%)) (Table 1).

3.2 Univariate and multivariate regression survival analysis

Univariate analysis of all stage I EnOC patients showed that age ≥60 (p = 0.000) was a statistically significant factor for overall survival, while no significant difference was observed for chemotherapy (p = 0.076) or other factors such as grade, substage and pretreatment CA125 on overall survival (Table 2, Fig. 2).

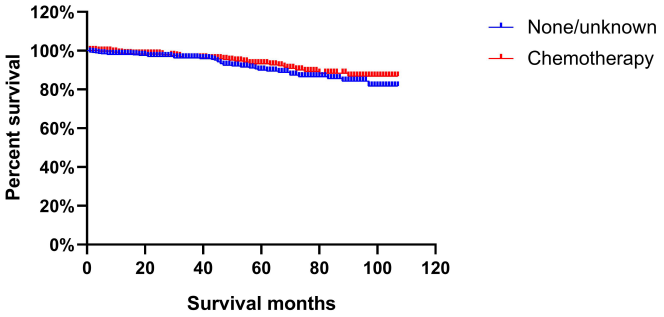

FIGURE 2. Kaplan-Meier survival curves for stage I EnOC.

To explore how the clinical factors might jointly affect the overall survival of the patients, multivariate Cox regression analysis involving these factors was performed. The result showed that the prognosis of (the space between years and in) patients ≥60 years old (p = 0.000, HR: 3.609, 95% CI: 2.156–6.039) was relatively poor. Different from the univariate analysis results, after adjusting for age, the results suggested that elevated CA125 was an independent prognostic risk factor for overall survival (p = 0.028, HR: 2.480, 95% CI: 1.103–5.577), while race, substage and grade were not associated with increased mortality and was not statistically significant for overall survival.

Thus, these findings indicated that age <60 and negative CA125 were protective factors that could prolong the survival of stage I EnOC patients.

3.3 Impact of chemotherapy on survival

Our results confirmed that chemotherapy did not significantly improve the survival of patients with grade I IA and IB (p = 0.452, HR: 1.547, 95% CI: (0.497–4.815) (Tables 3,4, Fig. 3A), which was consistent with the NCCN Guidelines and previous literature [10, 12–15].

An in-depth study was performed on patients recommended for observation or chemotherapy in the NCCN Guidelines, namely, those classified as grade II stage IA and IB and grade I stage IC. For grade II stage IA patients, chemotherapy cannot improve the survival of patients (p = 0.062, HR: 602, 95% CI: 0.337–1.075) (Fig. 3B). For grade I stage IC patients, chemotherapy cannot increase the overall survival of patients as well (p = 0.339, HR: 1.963, 95% CI: 0.493–7.817) (Fig. 3C). Owing to the small proportion of grade II stage IB patients (n = 15, 1.4%), their treatment association with survival could not be performed.

For patients with grade II stage IC and those of all substages of grade III who are recommended to undergo chemotherapy by the NCCN Guidelines, our statistical analysis showed that their survival after receiving chemotherapy was not significantly improved (p = 0.645, HR: 0.806, 95% CI: 0.322–2.019) (Fig. 3D).

It is confirmed that EnOC patients with stage I may not benefit from chemotherapy.

4. Discussion

Ovarian cancer is a general term for a series of diseases that share one common anatomical site of occurrence. The risk factors, clinical course and treatment response of EnOC are different from other ovarian cancers [16, 17]. Patients with early-stage EnOC were shown to have better prognoses [6]; thus, their need for postoperative adjuvant chemotherapy remains inconclusive.

Previous clinical trials mostly focused on the effects of chemotherapy regimens and cycles on the survival of early-stage epithelial ovarian cancer, including EnOC. A prospective randomized clinical trial explored the effect of chemotherapy on 81 well-differentiated or moderately differentiated IA and IB epithelial ovarian cancer patients who were assigned to oral melphalan or no chemotherapy. They found no significant difference in the 5-year disease-free survival rate (91% *vs.* 98%; p = 0.41) or overall survival rate (94% *vs.* 98%; p = 0.43) between the two groups [18]. Another clinical trial (NCT00002477) performed from 1990–2000 investigated the impact of chemotherapy on the survival of patients with stage I and II ovarian cnt within subgroups of age, tumor stage, histolancer. They reported that the survival of patients with adjuvant chemotherapy was not statistically differeogic cell type or cell differentiation [11]. An analysis had explored the potential benefit of 6 *vs.* 3 cycles of chemotherapy in women with early-stage high-risk epithelial ovarian cancer of which EnOC accounts for 25%.The analyses of relative risk of disease

TABLE 1. Patient demographics.

Characteristics	Chemotherapy (n = 441)	No Chemotherapy or unknown (n = 434)
Age (yr)		
≥60	139 (32%)	175 (40%)
<60	302 (68%)	259 (60%)
Race		
Black	19 (4%)	21 (5%)
White	355 (80%)	353 (81%)
Other	64 (15%)	55 (13%)
Unknown	3 (1%)	5 (1%)
FIGO* stage at diagnosis		
IA	161 (37%)	323 (74%)
IB	19 (4%)	11 (3%)
IC	261 (59%)	100 (23%)
Pathological Grade		
1	157 (36%)	282 (65%)
2	189 (43%)	128 (29%)
3	95 (22%)	24 (6%)
Analyzed subgroups		
Grade I stage IA and IB	50 (11%)	225 (52%)
Grade I stage IC	107 (24%)	57 (13%)
Grade II stage IA	80 (18%)	91 (21%)
Grade II stage IB	10 (2%)	5 (1%)
Grade II stage IC or grade III of all substages	194 (44%)	56 (13%)
Lymphadenectomy (No. of lymph nodes)		
0	66 (15%)	78 (18%)
1–10	134 (30%)	117 (27%)
11–20	122 (28%)	112 (26%)
21–30	75 (17%)	75 (17%)
>30	44 (10%)	52 (12%)
Survival status		
Alive	413 (94%)	395 (91%)
Dead	28 (6%)	39 (9%)
Timing of chemotherapy		
Systemic therapy after surgery	437 (99%)	/
Systemic therapy before surgery	1 (0%)	/
Systemic therapy both before and after surgery	3 (1%)	/
Surgery		
Confined to (fallopian) ovaries	25 (6%)	40 (9%)
Hysterectomy	277 (63%)	296 (68%)
Cytoreductive surgery	93 (21%)	55 (13%)
Omentectomy	229 (52%)	217 (50%)
CA125** (pretreatment)		
Positive/elevated	287 (65%)	214 (49%)
Negative/normal	56 (13%)	88 (20%)
Borderline	1 (0%)	1 (0%)
Missing	97 (22%)	131 (30%)

**FIGO: The International Federation of Gynecology and Obstetrics; **CA125: Carbohydrate antigen 125.*

TABLE 2. Univariate and multivariate regression analysis for overall survival.

Variables	Univariate analysis		Multivariate analysis	
	p-value	HR (95% CI)	*p*-value	HR (95% CI)
Age (yr)				
<60	1.000		1.000	
≥60	0.000	3.645 (2.211–6.010)	0.000	3.609 (2.156–6.039)
Grade				
I	1.000		1.000	
II	0.333	1.305 (0.761–2.236)	0.576	1.171 (0.672–2.041)
III	0.051	1.912 (0.998–3.664)	0.058	1.985 (0.977–4.033)
Stage				
IA	1.000		1.000	
IB	0.418	1.531(0.546–4.293)	0.246	1.856 (0.653–5.273)
IC	0.727	0.914 (0.552–1.514)	0.757	1.091 (0.627–1.899)
CA125 (pretreatment)				
Negative/normal	1.000		1.000	
Positive/elevated	0.152	1.795 (0.806–3.996)	0.028	2.480 (1.103–5.577)
Borderline	0.968	0.000 (0.000–∞)	0.974	0.000 (0.000–∞)
Others	0.323	1.553 (0.649–3.719)	0.141	1.935 (0.804–4.659)
Cytoreductive surgery				
Yes	1.000			
No	0.654	1.174 (0.582–2.371)	0.358	1.398 (0.685–2.852)
Chemotherapy				
No/unknown	1.000		1.000	
Yes	0.114	0.676 (0.416–1.099)	0.076	0.600 (0.342–1.054)

HR, Hazard ratio; CI, Confidence interval; CA125, Carbohydrate antigen 125.

TABLE 3. Guidelines-based stratified survival analysis between adjuvant chemotherapy and survival.

Combination of grade and substage	Univariate analysis		Multivariate analysis	
	p-value	HR (95% CI)	*p*-value	HR (95% CI)
Grade I stage IA and IB	0.717	1.231 (0.401–3.779)	0.452	1.547 (0.497–4.815)
Grade I stage IC	0.543	1.504 (0.403–5.607)	0.339	1.963 (0.493–7.817)
Grade II stage IA	0.012	0.203 (0.059–0.703)	0.062	0.602 (0.337–1.075)
Grade II stage IC, grade III with all substage	0.294	0.619 (0.252–1.518)	0.645	0.806 (0.322–2.019)

HR, Hazard ratio; CI, Confidence interval.

TABLE 4. No. of events in the guidelines-based stratified groups.

No. of events in stratified groups (%)	Chemotherapy		No Chemotherapy or unknown	
	Alive	Dead	Alive	Dead
Grade I stage IA and IB	46 (92%)	4 (8%)	212 (94%)	13 (6%)
Grade I stage IC	102 (95%)	5 (5%)	53 (93%)	4 (7%)
Grade II stage IA	77 (96%)	3 (4%)	76 (84%)	15 (16%)
Grade II stage IB	9 (90%)	1 (10%)	5 (100%)	0 (0%)
Grade II stage IC, grade III with all substage	179 (92%)	15 (8%)	49 (88%)	7 (13%)

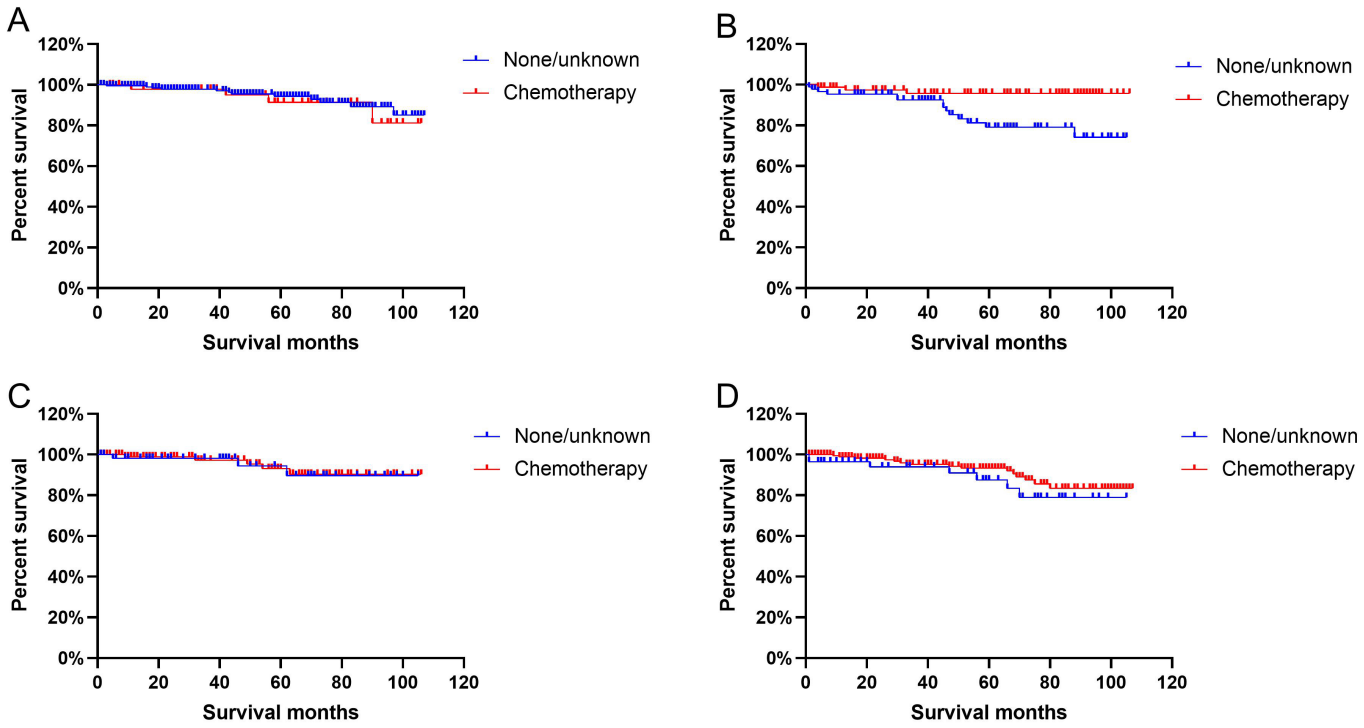

FIGURE 3. Kaplan-Meier survival curves for EnOC patients with stratified groups. (A) Kaplan-Meier survival curves for EOC patients with stage IA and IB of grade I; (B) Kaplan-Meier survival curves for EOC patients with stage IA grade II; (C) Kaplan-Meier survival curves for EOC patients with stage IC grade I; (D) Kaplan-Meier survival curves for EOC patients with stage IC grade II and any substage of grade III.

recurrence for EnOC patients receiving six versus three cycles of treatment showed no significantly difference. (HR: 1.07, 95% CI: 0.47–2.44) [19] Based on our existing knowledge from literature review, previously performed clinical trials did not specifically perform chemotherapy for EnOC patients, especially those with early-stage disease.

Numerous studies have been performed on the necessity of adjuvant chemotherapy for early-stage EnOC patients based on cancer databases. A retrospective study using the SEER database for ovarian cancer patients treated from 2000 to 2013 reported that chemotherapy was not associated with a survival benefit in stage IA and IB of any grade and stage IC grade I or II patients [10]. Li *et al.* [14] also used SEER data for patients treated from 2004 to 2015 and concluded that chemotherapy could not prolong the 5-year overall survival of patients with early-stage serous and EnOC (HR, 1.092; 95% CI, 0.954–1.249; $p = 0.201$). Nasioudis *et al.* [8] used the NCDB data for cases from 2004–2014 and observed that the administration of chemotherapy was associated with better survival benefits in patients with stage IA/IB (HR: 0.66, 95% CI: 0.49–0.88) and IC (HR: 0.71, 95 % CI: 0.52–0.98) EnOC. However, the above studies did not combine grade and stage to explore the effect of adjuvant chemotherapy on the prognosis following the recommendations of the latest NCCN Guidelines (Version 3.2022) [12] for ovarian cancer, and thus their obtained conclusions were contradictory to each other and not fully inconsistent with the current NCCN Guidelines.

The present study was a retrospective study of a large sample based on the SEER database from the most recent years, which provides a statistical-evidence basis for the impact of adjuvant chemotherapy for early-stage EnOC. According to the NCCN Guidelines in Version 3.2022 of ovarian cancer, the EnOC patients recommended for observation are grade I stage IA–IB patients, while for adjuvant chemotherapy are grade II stage IC and grade III patients in all substages, for observation or chemotherapy are grade II stage IA and IB, grade I stage IC. However, in the European Society for Medical Oncology (ESMO) and European Society of Gynaecologial Oncology (ESGO) consensus conference recommendations on ovarian cancer [20], no adjuvant chemotherapy was suggested for fully staged patients with stage IA grade I–II EnOC while for those with stage IB–IC grade I–II was optional and recommended for patients stage IA–IC grade III. Based on our stratified analysis, adjuvant chemotherapy only improve the overall survival of grade II stage IA patients aged ≥60 years. And the results are inconsistent with NCCN and ESMO-ESGO recommendations. Based on our stratified analysis, chemotherapy does not improve outcomes in stage I patients regardless of substage, grade and surgical range. And the results are inconsistent with NCCN guideline recommendations for patients of grade II stage IC, grade III with all substage. However, we also observed that age <60 and negative CA125 were beneficial factors associated with prolonging the survival of stage I EnOC patients.

However, there were some limitations that should be fully recognized for information obtained from the SEER database. We acknowledge the data limitations for the chemotherapy fields in the data. Additionally, mixing 'No chemotherapy' with 'Unknown chemotherapy status' may have decreased the observed effects of chemotherapy EnOC.

According to the NCCN guidelines, patients with ovarian, fallopian tube and primary peritoneal cancer should undergo genetic risk evaluation and germline and somatic testing (if not previously done). Furthermore, the Society of Gynecologic Oncology (SGO) [21] and NCCN guidelines [12] recommend that all women diagnosed with ovarian, fallopian tube or peritoneal carcinoma, regardless of age or family history, should receive genetic counseling and be offered genetic testing. Post-primary treatment recommendations for stage II–IV and grade 2–3 tumor and germline breast cancer susceptibility gene (*BRCA)* genes analysis are recommended. The presence of the pathogenic variant in *BRCA* genes is important for possible additional therapy with poly ADP-ribose polymerase (PARP) inhibitors, and genetic counseling should be offered to all living patients' offspring. However, these information are not currently unavailable in the SEER database [22].

5. Conclusions

The study suggested that adjuvant chemotherapy does not improve outcomes in stage I patients regardless of substage and grade.Further, age <60 and negative CA125 were favorable factors for the survival of stage I EnOC patients. Future clinical trials or molecular typing studies should seek the necessity of chemotherapy for EnOC patients.

ABBREVIATIONS

BRCA, Breast cancer susceptibility gene; CA125, Carbohydrate antigen 125; CI, Confidence interval; DFS, Disease-free survival; EnOC, Endometrioid ovarian cancer; ESGO, European Society of Gynaecologial Oncology; ESMO, the European Society for Medical Oncology; FIGO, The International Federation of Gynecology and Obstetrics; GOG, Gynecologic Oncology Group; HR, Hazard ratio; NCBD, National Cancer Data Base; NCCN, National Comprehensive Cancer Network; NOS, Not other specified; ORR, Objective response rates; OS, Overall survival; PARP, poly ADP-ribose polymerase; PBC, Platinum-based chemotherapy; PFS, Progression-free survival; RFS, Recurrence-free survival; SEER, Surveillance, Epidemiology and End Results; SGO, the Society of Gynecologic Oncology.

AUTHOR CONTRIBUTIONS

WJ and JL—designed the research study. RNM—performed the research. RM, JWL and MMS—analyzed the data. JL and RNM—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Based on the SEER website https://www.cancer.gov/policies/accessibility, the National Cancer Institute (NCI) provides access to all individuals seeking information on http://www.cancer.gov, including individuals who are disabled.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Global Burden of Disease 2019 Cancer Collaboration, Kocarnik JM, Compton K, Dean FE, Fu W, Gaw BL, Harvey JD, *et al*. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis for the global burden of disease study 2019. JAMA Oncology. 2022; 8: 420–444.

[2] 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: A Cancer Journal for Clinicians. 2021; 71: 209–249.

[3] Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. CA: A Cancer Journal for Clinicians. 2021; 71: 7–33.

[4] Huang CY, Cheng NM, Wang PH. Risk factors associated with epithelial ovarian cancer in women with endometriosis. Taiwanese Journal of Obstetrics & Gynecology. 2020; 59: 353–355.

[5] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2018; 68: 394–424.

[6] Torre LA, Trabert B, DeSantis CE, Miller KD, Samimi G, Runowicz CD, *et al*. Ovarian cancer statistics, 2018. CA: A Cancer Journal for Clinicians. 2018; 68: 284–296.

[7] Pierson WE, Peters PN, Chang MT, Chen LM, Quigley DA, Ashworth A, *et al*. An integrated molecular profile of endometrioid ovarian cancer. Gynecologic Oncology. 2020; 157: 55–61.

[8] Nasioudis D, Latif NA, Simpkins F, Cory L, Giuntoli RL 2nd, Haggerty AF, *et al*. Adjuvant chemotherapy for early stage endometrioid ovarian carcinoma: an analysis of the National Cancer Data Base. Gynecologic Oncology. 2020; 156: 315–319.

[9] Kumar A, Le N, Tinker AV, Santos JL, Parsons C, Hoskins PJ. Early-stage endometrioid ovarian carcinoma: population-based outcomes in british columbia. International Journal of Gynecologic Cancer. 2014; 24: 1401–1405.

[10] Oseledchyk A, Leitao MM Jr, Konner J, O'Cearbhaill RE, Zamarin D, Sonoda Y, *et al.* Adjuvant chemotherapy in patients with stage I endometrioid or clear cell ovarian cancer in the platinum era: a surveillance, epidemiology, and end results cohort study, 2000–2013. Annals of Oncology. 2017; 28: 2985–2993.

[11] Trimbos JB, Parmar M, Vergote I, Guthrie D, Bolis G, Colombo N, *et al*. International collaborative ovarian neoplasm trial 1 and adjuvant chemotherapy in ovarian neoplasm trial: two parallel randomized phase III trials of adjuvant chemotherapy in patients with early-stage ovarian carcinoma. Journal of the National Cancer Institute. 2003; 95: 105–112.

[12] Satoh T, Hatae M, Watanabe Y, Yaegashi N, Ishiko O, Kodama S, *et al*.

Outcomes of fertility-sparing surgery for stage I epithelial ovarian cancer: a proposal for patient Selection. Journal of Clinical Oncology. 2010; 28: 1727–1732.

[13] Hall E, Finch A, Jacobson M, Rosen B, Metcalfe K, Sun P, *et al*. Effects of bilateral salpingo-oophorectomy on menopausal symptoms and sexual functioning among women with a *BRCA1* or *BRCA2* mutation. Gynecologic Oncology. 2019; 152: 145–150.

[14] Li S, Zhu Z. Chemotherapy is not necessary for early-stage serous and endometrioid ovarian cancer after undergoing comprehensive staging surgery. Journal of Ovarian Research. 2020; 13: 91.

[15] Dinkelspiel HE, Tergas AI, Zimmerman LA, Burke WM, Hou JY, Chen L, *et al*. Use and duration of chemotherapy and its impact on survival in early-stage ovarian cancer. Gynecologic Oncology. 2015; 137: 203–209.

[16] Vaughan S, Coward JI, Bast RC Jr, Berchuck A, Berek JS, Brenton JD, *et al*. Rethinking ovarian cancer: recommendations for improving outcomes. Nature Reviews Cancer. 2011; 11: 719–725.

[17] Köbel M, Kalloger SE, Boyd N, McKinney S, Mehl E, Palmer C, *et al*. Ovarian carcinoma subtypes are different diseases: implications for biomarker studies. PLoS Medicine. 2008; 5: e232.

[18] Young RC, Walton LA, Ellenberg SS, Homesley HD, Wilbanks GD, Decker DG, *et al*. Adjuvant therapy in stage I and stage II epithelial ovarian cancer. Results of two prospective randomized trials. The New England Journal of Medicine. 1990; 322: 1021–1027.

[19] Chan JK, Tian C, Fleming GF, Monk BJ, Herzog TJ, Kapp DS, *et al*. The potential benefit of 6 *vs.* 3 cycles of chemotherapy in subsets of women with early-stage high-risk epithelial ovarian cancer: an exploratory analysis of a gynecologic oncology group study. Gynecologic Oncology. 2010; 116: 301–306.

[20] Colombo N, Sessa C, Bois AD, Ledermann J, McCluggage W, McNeish I, *et al*. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. International Journal of Gynecologic Cancer. 2019; 29: 728–760.

[21] Crafton SM, Cohn DE, Llamocca EN, Louden E, Rhoades J, Felix AS. Fertility-sparing surgery and survival among reproductive-age women with epithelial ovarian cancer in 2 cancer registries. Cancer. 2020; 126: 1217–1224.

[22] Hollis RL, Thomson JP, Stanley B, Churchman M, Meynert AM, Rye T, *et al.* Molecular stratification of endometrioid ovarian carcinoma predicts clinical outcome. Nature Communications. 2020; 11: 4995.

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