Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2024**; 51(2): 31
https://doi.org/10.31083/j.ceog5102031

Original Research

Effectiveness of Lymph Node Dissection in Women over Age 70 with Stage I Ovarian Cancer

Genping Huang[1,*], Guoping Zhu[1], Cheng Chen[1,*]

[1]Department of Gynecology, First affiliated Hospital of Huzhou Normal College, 313000 Huzhou, Zhejiang, China
*Correspondence: 15952178460@163.com; 21718429@zju.edu.cn (Genping Huang); 12208421@qq.com (Cheng Chen)
Academic Editor: Michael H. Dahan
Submitted: 24 September 2023 Revised: 10 November 2023 Accepted: 27 November 2023 Published: 4 February 2024

Abstract

Background: Considering the possibility of surgical intervention affecting the survival benefit of elderly patients, the relationship between lymph node dissection and the survival of elderly patients with stage I ovarian cancer (OC) was retrospectively analyzed. **Methods**: This was a retrospective cohort study using the database in Surveillance, Epidemiology and End Results (SEER) which was queried to identify 8191 women with stage I OC treated with surgery from 1975 to 2016. Frequencies and percentages were presented to describe the categorical data. Pearson χ^2 test was used to compare the correlation between the patient characteristics and lymph node dissection. Kaplan–Meier test was used to analyze the relationship between overall survival (OS) and patients at all age levels. The log-rank test was used for pairwise comparisons of OS. Cox proportional hazard regression analyses were performed to determine the association between lymph node dissection status and the OS in women with stage I OC. **Results**: There were 8191 stage I OC patients in this study. Among all patients undergoing lymph node dissection, 11.23% patients were older than 70 years. However, 17.44% of the patients over 70 years of age did not undergo lymph node dissection. Lymph node conservation was associated with a higher mortality risk compared to lymph node dissection. Kaplan–Meier analysis revealed that patients had a worse prognosis with lymph node conservation in people older than 70 years. Univariate and multivariate analysis showed that age and lymph node dissection both remained independent prognostic factors for improved OS with stage I OC. **Conclusions**: Lymph node dissection was an independent predictor of improved long-term OS in stage I OC patients and had a significant benefit in women over age 70.

Keywords: lymph node dissection; prognosis; elderly; ovarian cancer

1. Introduction

Ovarian Cancer (OC) is the most lethal gynecological malignancy [1], and has the highest mortality rate among female reproductive tract malignancies [2]. Early diagnosis and staging determine the prognosis of the disease. The proportion of patients with early-stage ovarian cancer is increasing as diagnostic and treatment technologies continue to improve. As life expectancy continues to increase, this results in an increase in the proportion of elderly patients with OC. Advances in the treatment of ovarian cancer, such as advanced surgical procedures, intravenous chemotherapy with carboplatin and paclitaxel, and abdominal chemotherapy, have led to an increase in 5-year survival rates from 34.8% in 1975 to 44.6% in 2011 [3]. However, the treatment progress of ovarian cancer is still significantly worse than that of other types of solid tumors [4]. Greater than 10 years ago, an analysis of the European research on adjuvant chemotherapy for ovarian malignant tumors demonstrated that the surgical staging of patients with early ovarian malignant tumors improved tumor-free survival and overall survival [5]. This finding has led to national and international guidelines for the treatment of early ovarian malignancies recommending surgical staging [6,7], including hysterectomy, bilateral salpingo-oophorectomy, omentectomy, cytological examination, peritoneal biopsy, and pelvic and paraaortic lymphadenectomy. The purpose of definitive surgery is to completely remove the tumor, determine the pathological diagnosis and staging of ovarian cancer, determine the histological subtype and grade of the disease, and determine the risk factors, in order to select the appropriate follow-up treatment (including chemotherapy and treatment duration, etc.). Based on the Surveillance, Epidemiology and End Results (SEER) database, this study evaluated the clinicopathological features and prognostic factors of early ovarian cancer and to provide new ideas for the therapeutic benefits of lymph node dissection in the clinical diagnosis and treatment of early ovarian cancer in women over age 70.

2. Methods

2.1 Study Population

Ovarian cancer cases were identified through the SEER program of the National Cancer Institute, which included data of 27.8% of the US population from 11 states and 7 areas. The information was accessed from the SEER database, and the requirement for informed consent was exempted by the University of Southern California Institutional Review Board. Data were extracted from the SEER18 Regs Research Data as well as Hurricane Katrina Impacted Louisiana Cases (1975–2016) using SEER*STat

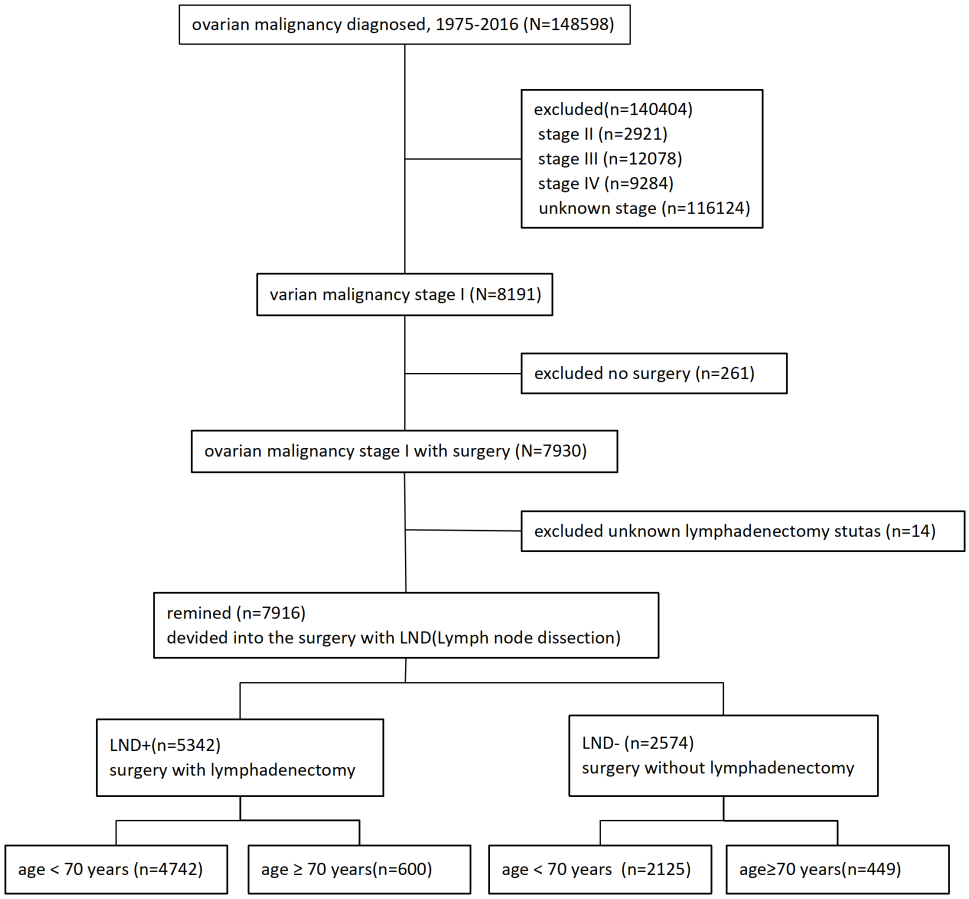

Fig. 1. Selection criteria. Stage I ovarian cancer treated by surgery. LND, lymph node dissection.

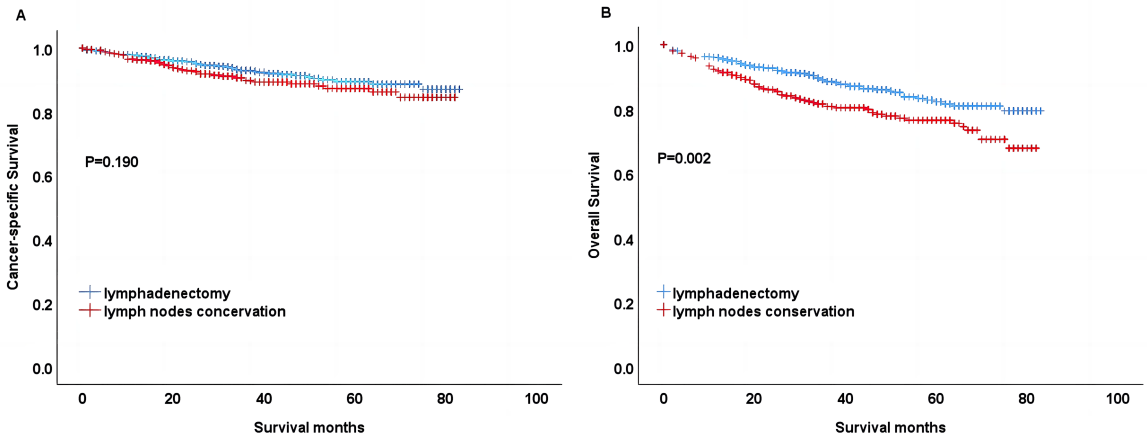

Fig. 2. Kaplan–Meier survival curves showing the CSS (A) and OS (B) analysis of patients over 70 years of age with intraoperative lymph node dissection. CSS, cancer-specific survival; OS, overall survival.

8.3.6 (http://www.seer.cancer.gov). The inclusion criteria for the SEER 18 registries included: (1) the pathological diagnosis was primary ovarian cancer; (2) the 7th edition of the American Joint Committee on Cancer (AJCC), stage T1 ovarian cancer; (3) surgical treatment of the primary lesion; (4) clear follow-up data. The exclusion criteria for the SEER 18 registries included: (1) unilateral and bilateral tumor unknown; (2) unknown SEER stage; (3) survival status of the patient unknown; (4) unknown survival time; (5) unknown tumor node metastasis (TNM) stage; (6) unknown lymph node dissection; and (7) multiple primary tumors. According to inclusion and exclusion criteria, 7916 patients were finally included, as shown in Fig. 1.

Table 1. Patient Demographics (N = 7916).

Demographic	Value (%)
Age (years)	
<60	5289 (66.81)
61–69	1578 (19.93)
70–79	727 (9.18)
≥80	322 (4.07)
Race	
White	6270 (79.21)
Black	595 (7.52)
Other	976 (12.33)
Unknown	75 (0.94)
SEER registry	
Midwest	410 (5.18)
Northeast	1345 (16.99)
South	1914 (24.18)
West	4247 (53.65)
Marital status	
Married	3883 (49.05)
Single	3655 (46.17)
Unknown	378 (4.78)
Laterality	
Right	3631 (45.87)
Left	3594 (45.40)
Bilateral	639 (8.07)
Unknown	52 (0.66)
Tumor grade	
Grade I	1730 (21.85)
Grade II	1722 (21.75)
Grade III	1500 (18.95)
Grade IV	877 (11.08)
Unknown	2087 (26.36)
Lymph node detection	
No nodes were examined	2553 (32.25)
Nodes were examined	5217 (65.90)
Undefined	146 (1.84)
Lymph node metastasis	
All nodes examined are negative	5347 (67.55)
No nodes were examined	2552 (32.24)
Undefined	17 (0.21)
LND	
LND+	5342 (67.48)
LND−	2574 (32.52)

SEER, Surveillance, Epidemiology and End Results; LND+, lymph node dissection; LND–, no lymph node dissection.

2.2 Clinicopathological Data and Observational Indicators

Demographic characteristics included age at diagnosis, specific year, race, place of SEER registration, and marital status. The pathological features of the tumor, including the location of the primary tumor, histological grade, lymph node metastasis and lymph node resection are shown in Table 1. The tumor stage was determined by the 7th edition AJCC ovarian cancer TNM stage. Histological classification was based on the World Health Organization (WHO) standards for ovarian cancer, and histological classification included Grade I, Grade II, Grade III, and Grade IV. According to the extent of surgical intervention, the patients were divided into lymph node resection group and lymph node preservation group. The follow-up period was extended to 31 December 2019. The main outcome measures included overall survival (OS) and cancer-specific survival (CSS). OS time is defined as the time interval from the time of pathological diagnosis of the patient to the time of death. CSS time was defined as the time interval from when a patient was pathologically diagnosed with ovarian cancer to the time the patient died of ovarian cancer.

2.3 Statistical Analysis

SPSS for Windows version 25.0 (IBM SPSS Inc, Chicago, IL, USA) was used for statistical analysis and chi-square test was used to compare the characteristic distribution of baseline data. The influencing factors of lymph node metastasis were analyzed by logistic regression. Survival information and survival curves were obtained by Kaplan–Meier survival analysis. Univariate and multivariate Cox regression models were used to analyze the independent prognostic factors. All statistical analyses were the two-side test, and $p < 0.05$ was considered to be statistically significant.

3. Results

3.1 Baseline Characteristics of Patients with Stage I Ovarian Cancer

Baseline data of all patients are shown in Table 2. A total of 7916 patients were included according to the inclusion criteria, among whom intraoperative lymph node dissection was performed at the same time: 1135 patients (71.9%) aged 61–69, 456 patients (62.7%) aged 70–79, and 144 patients (44.7%) aged 80 years or older. Among the patients who underwent surgery, there was a difference in overall survival when lymph node dissection was performed in patients older than 70 years.

3.2 Survival Analysis

Kaplan–Meier survival curve analysis: Fig. 2A showed that there was no significant correlation between intraoperative lymph node dissection and specific survival (CSS) in stage I ovarian cancer patients over age 70 (p = 0.190). Fig. 2B showed that there was a significant correlation between intraoperative lymph node dissection and OS in stage I ovarian cancer patients over age 70 (p = 0.002).

Univariate and multivariate analyses were performed using Cox proportional hazard method. Univariate analysis showed that age ≥70 years, histological grade, and lymph node dissection were influencing factors for OS and CSS in stage I ovarian cancer ($p < 0.05$). In univariate analysis,

Table 2. Baseline characteristics of patients with Stage I ovarian cancer (N = 7916).

Characteristics	LND+	LND–	Adjusted OR	95% CI		*p*
				Upper limit	Lower limit	
Age (years)						
<60	3607 (68.2)	1682 (31.8)	1			
61–69	1135 (71.9)	443 (28.1)	0.911	0.801	1.035	0.153
70–79	456 (62.7)	271 (37.3)	1.369	1.153	1.609	<0.001
≥80	144 (44.7)	178 (55.3)	2.779	2.19	3.526	<0.001
Race						
White	4338 (69.2)	1932 (30.8)	1			
Black	294 (49.4)	301 (50.6)	2.057	1.721	2.458	<0.001
Other	665 (68.1)	311 (31.9)	1.083	0.931	1.259	0.303
Unknown	45 (60.0)	30 (40.0)	1.569	0.974	2.526	0.064
SEER registry						
Midwest	287 (70.0)	123 (30.0)	1			
Northeast	968 (72.0)	377 (28.0)	0.864	0.672	1.111	0.255
South	1217 (63.6)	697 (36.4)	1.339	1.054	1.702	0.017
West	2870 (67.6)	1377 (32.4)	1.204	0.958	1.515	0.112
Marital status						
Married	2769(71.3)	1114 (28.7)	1			
Single	2314 (63.3)	1341 (36.7)	1.256	1.135	1.39	<0.001
Unknown	259 (68.5)	119 (31.5)	1.062	0.838	1.345	0.618
Laterality						
Right	2459 (67.7)	1172 (32.3)	1			0.471
Left	2400 (66.8)	1194 (33.2)	1.05	0.949	1.161	0.349
Bilateral	454 (71.0)	185 (29.0)	0.965	0.797	1.168	0.713
Unknown	29 (55.8)	23 (44.2)	1.412	0.794	2.511	0.24
Tumor grade						
Grade I	1165 (67.3)	565 (32.7)	1			<0.001
Grade II	1244 (72.2)	478 (27.8)	0.773	0.666	0.896	0.001
Grade III	1078 (71.9)	422 (28.1)	0.768	0.657	0.897	0.001
Grade IV	668 (76.2)	209 (23.8)	0.598	0.494	0.724	<0.001
Unknown	1187 (56.9)	900 (43.1)	1.534	1.34	1.757	<0.001
Survival						
Alive	4902 (68.4)	2264 (31.6)	1			
Dead	440 (58.7)	310 (41.3)	1.393	1.183	1.64	<0.001

OR, odds ratio; 95% CI, 95% confidence interval.

$p < 0.05$ factors were incorporated into multivariate Cox proportional risk model regression analysis, and the results suggested that age ≥70 years, histological grade and lymph node dissection were independent prognostic risk factors for OS ($p < 0.05$). Age ≥70 years and histological grade were independent prognostic risk factors for CSS ($p < 0.05$) (Table 3).

4. Discussion

In the treatment of early ovarian cancer, the initial staging operation is very important [8]. In clinical practice, whether the surgical scope of early ovarian cancer requires systematic lymph node dissection has been a controversial issue [9]. According to statistics, the lymph node positive rate of early ovarian cancer is approximately 13%–20% [10]. In the current guidelines for ovarian cancer, the mainstream view is to recommend intraoperative lymph node dissection for early stage patients. In a retrospective analysis of over 6000 patients, Chan *et al*. [11] concluded that lymph node dissection improved the 5-year survival rate of Federation International of Gynecology and Obstetrics (FIGO) Stage I patients from 87.0% to 92.6% ($p < 0.001$). On the contrary, other investigators found that there was no significant difference in progression-free survival between patients with early ovarian cancer undergoing lymph node dissection and those who did not receive lymph node dissection [12]. Some researchers believe that systematic lymph node dissection could not only not prolong the progression-free survival of patients with early ovarian cancer, but also increase the incidence of complications. Other investigators have proposed that lymph node dissection prolongs the operative time and hospital stay, and

Table 3. Univariate analysis.

Characteristic	Overall survival			Cause specific survival		
	HR	95% CI	*p*	HR	95% CI	*p*
Age (years)						
<60			<0.001			<0.001
61–69	0.189	0.151–0.235	<0.001	1.251	0.973–1.609	0.08
70–79	0.301	0.235–0.386	<0.001	1.944	1.457–2.593	<0.001
≥80	0.519	0.401–0.674	<0.001	2.392	1.605–3.564	<0.001
Race						
White			0.095			0.004
Black	1.356	1.066–1.724	0.013	1.746	1.291–2.362	<0.001
Other	0.987	0.787–1.237	0.908	1.103	0.815–1.492	0.527
Unknown	0	0–1.143×10^{48}	0.871	0	0–6.118×10^{67}	0.906
SEER registry						
Midwest			0.003			0.078
Northeast	1.652	1.069–2.554	0.024	1.582	0.853–2.935	0.146
South	2.03	1.332–3.095	0.001	2.027	1.116–3.681	0.02
West	1.64	1.086–2.478	0.019	1.851	1.035–3.311	0.038
Marital status						
Married			<0.001			<0.001
Single	1.465	1.265–1.698	<0.001	1.445	1.182–1.768	<0.001
Unknown	0.899	0.607–1.333	0.597	0.616	0.325–1.165	0.136
Laterality						
Right			0.05			0.001
Left	1.036	0.889–1.206	0.653	1.19	0.961–1.471	0.111
Bilateral	1.405	1.103–1.789	0.006	1.912	1.401–2.61	<0.001
Unknown	1.023	0.423–2.475	0.959	1.289	0.411–4.039	0.664
Tumor grade						
Grade I			<0.001			<0.001
Grade II	1.346	1.046–1.731	0.021	1.807	1.223–2.671	0.003
Grade III	2.3	1.819–2.908	<0.001	3.558	2.479–5.106	<0.001
Grade IV	2.575	1.985–3.341	<0.001	4.141	2.812–6.098	<0.001
Unknown	1.371	1.075–1.749	0.011	1.986	1.365–2.89	<0.001
LND						
LND+						
LND–	1.592	1.377–1.842	<0.001	1.241	1.01–1.526	0.04
Multivariate Analysis						
Characteristic	Overall survival			Cause specific survival		
	HR	95% CI	*p*	HR	95% CI	*p*
Age (years)						
<60			<0.001			<0.001
61–69	1.547	1.283–1.864	<0.001	1.186	0.919–1.529	0.19
70–79	2.581	2.107–3.162	<0.001	1.831	1.369–2.448	<0.001
≥80	4.167	3.304–5.255	<0.001	1.901	1.261–2.865	0.002
Race						
White			0.129			0.006
Black	1.346	1.047–1.729	0.02	1.764	1.284–2.423	<0.001
Other	1.087	0.863–1.37	0.478	1.093	0.803–1.487	0.573
Unknown	0	0–1.143×10^{48}	0.897	0	0–2.04×10^{70}	0.911
SEER registry						
Midwest			0.002			0.142
Northeast	1.623	1.049–2.512	0.001	1.599	0.861–2.97	0.137
South	1.856	1.215–2.836	0.61	1.872	1.028–3.411	0.04
West	1.651	1.091–2.498	0.034	1.875	1.046–3.36	0.035

Table 3. Continued.

Characteristic	Overall survival			Cause specific survival		
	HR	95% CI	*p*	HR	95% CI	*p*
Marital status						
Married			0.03			0.002
Single	1.301	1.116–1.517	0.004	1.367	1.11–1.683	0.003
Unknown	0.902	0.607–1.341	0.018	0.634	0.334–1.205	0.164
Laterality						
Right			<0.001			0.02
Left	1.011	0.868–1.178	0.042	1.16	0.937–1.437	0.172
Bilateral	1.255	0.982–1.603	<0.001	1.654	1.206–2.268	0.002
Unknown	0.979	0.404–2.375	<0.001	1.162	0.369–3.654	0.798
Tumor grade						
Grade I			0.025			<0.001
Grade II	1.3	1.009–1.674	0.318	1.791	1.21–2.649	0.004
Grade III	2.087	1.647–2.645	0.889	3.346	2.324–4.818	<0.001
Grade IV	2.361	1.814–3.074	0.069	3.951	2.672–5.844	<0.001
Unknown	1.323	1.036–1.69	0.963	1.933	1.326–2.818	0.001
LND						
LND+	1.441	1.239–1.677	<0.001	1.197	0.965–1.484	0.102
LND–						

HR, hazard ratio.

increases the incidence of surgical complications [13]. The scope of comprehensive staging surgery mainly includes pelvic and para-aortic lymph node dissection, large mesh membrane resection, random peritoneal biopsy and ascites cytology. For patients over age 70, systematic lymph node dissection is not necessary when performing comprehensive staging surgery, avoiding the possibility of extensive surgery and prolonged surgical time may affect the survival benefit of patients. Moreover, the proportion of complications in patients with lymph node dissection is significantly increased, including intraoperative bleeding, postoperative hematoma formation, infection, adjacent organ and nerve injury, and tumor dissemination, especially in patients over age 70. Therefore, in order to determine whether patients over age 70 with early ovarian cancer could benefit from lymph node dissection, survival period analysis was performed on patients with early ovarian cancer age $\geq$70 years. The results demonstrated that the prognosis was poor without lymph node dissection, and lymph node dissection was an independent prognostic factor affecting the overall survival of patients over age 70 ($p < 0.001$).

There are some limitations to this study. First, this study was a retrospective clinical study over a large time span. The improvement in surgical instruments and better trained surgeons have affect the survival benefits to patients. This study was based on the prognosis of ovarian cancer in the United States, which may be different from the real situation of ovarian cancer in China. Therefore, it is necessary to conduct a multi-center with a large-sample size on the Chinese population in order to obtain results applicable to Chinese women.

5.Conclusions

In our study, lymph node dissection was found to be an independent predictor of improved long-term OS in patients with stage I ovarian cancer, with a significant benefit in older women. Therefore, we need to carefully consider the choice of surgical methods in order to obtain a more beneficial prognosis.

Abbreviations

CI, confidence interval; EC, endometrial cancer; HR, hazard ratio; LND+, lymph node dissection; LND–, no lymph node dissection; OR, odds ratio; OS, overall survival; SEER, Surveillance, Epidemiology, and End Results.

Availability of Data and Materials

The data sets generated and analyzed during the current study are available in the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute.

Author Contributions

GH and CC designed the research study. GH and GZ performed the research. All authors analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The SEER data are public and free of charge so no ethical review and individual consent are required.

Acknowledgment

Thanks to all the peer reviewers for their opinions and suggestions.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Verdecchia A, Angelis GD, Capocaccia R. Estimation and projections of cancer prevalence from cancer registry data. Statistics in Medicine. 2002; 21: 3511–3526.

[2] Siegel RL, Miller KD, Jemal A. Cancer statistics. 2020. CA: A Cancer Journal for Clinicians. 2020; 70: 7–30.

[3] Wright JD, Chen L, Tergas AI, Patankar S, Burke WM, Hou JY, *et al*. Trends in Relative Survival for Ovarian Cancer from 1975 to 2011. Obstetrics and Gynecology. 2015; 125: 1345–1352.

[4] Goff B. Measuring ovarian cancer care: why are we still failing? Gynecologic Oncology. 2015; 136: 1–2.

[5] 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. JNCI Journal of the National Cancer Institute. 2003; 95: 113–125.

[6] Wagner U, Harter P, Hilpert F, Mahner S, Reuß A, Du Bois A, *et al*. S3-guideline on diagnostics, therapy and follow-up of malignant ovarian tumours. Geburtshilfe und Frauenheilkunde. 2013; 73: 874–889.

[7] González Martín A, Redondo A, Jurado M, De Juan A, Romero I, Bover I, *et al*. GEICO (Spanish Group for Investigation on Ovarian Cancer) treatment guidelines in ovarian cancer 2012. Clinical and Translational Oncology. 2013; 15: 509–525.

[8] Winter-Roach BA, Kitchener HC, Dickinson HO. Adjuvant (post-surgery) chemotherapy for early stage epithelial ovarian cancer. The Cochrane Database of Systematic Reviews. 2009; CD004706.

[9] Colombo N, Sessa C, du Bois A, Ledermann J, McCluggage WG, 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. Annals of Oncology. 2019; 30: 672–705.

[10] Heitz F, Harter P, Ataseven B, Heikaus S, Schneider S, Prader S, *et al*. Stage-and histologic subtype-dependent frequency of lymph node metastases in patients with epithelial ovarian cancer undergoing systematic pelvic and paraaortic lymphadenectomy. Annals of surgical oncology. 2018; 25: 2053–2059.

[11] Chan JK, Munro EG, Cheung MK, Husain A, Teng NN, Berek JS, *et al*. Association of lymphadenectomy and survival in stage I ovarian cancer patients. Obstetrics & Gynecology. 2007; 109: 12–19.

[12] Maggioni A, Benedetti Panici P, Dell'Anna T, Landoni F, Lissoni A, Pellegrino A, *et al*. Randomised study of systematic lymphadenectomy in patients with epithelial ovarian cancer macroscopically confined to the pelvis. British Journal of Cancer. 2006; 95: 699–704.

[13] Polan RM, Rossi EC, Barber EL. Extent of lymphadenectomy and postoperative major complications among women with endometrial cancer treated with minimally invasive surgery. American Journal of Obstetrics and Gynecology. 2019; 220: 263.e1–263.e8.