Evaluation of the prognostic value of lymphadenectomy in low-grade serous ovarian cancer: A case-control multicenter retrospective study

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Abstract

ABSTRACT Objective: To evaluate the effect of lymphadenectomy on clinical outcome in patients with low-grade serous ovarian cancer (LGSOC). Design: Case-control multicenter retrospective study. Setting: University Hospital-based research center. Population: 147 patients with LGSOC. Methods: Propensity score matching (PSM) algorithm was used to balance the basic characteristics of patients with lymphadenectomy or not, and the Kaplan-Meier analysis was used to evaluate the impact of clinical prognosis. Finally, univariate and multivariate Cox proportional hazards regression analysis were performed to analyze the high-risk factors associated with clinical prognosis. Main outcome measures: Disease-free survival (DFS) and overall survival (OS). Results: A total of 147 women from 4 medical centers were enrolled. In the before matching cohort, 101 (68.7%) patients underwent lymphadenectomy. Fifty-two (35.4%) patients experienced recurrence, and 25 (17%) patients died. Kaplan-Meier analysis showed that there was no significant difference in DFS(P=0.058) and OS(P=0.067) in the after matching cohort. Cox proportional hazard regression analysis showed age (P=0.012), the International Federation of Gynecology and Obstetrics (FIGO) stage (P=0.031) and effective cytoreductive surgery (P=0.044) were 3 high-risk factors associated with recurrence. Age (P=0.031) and effective cytoreductive surgery (P=0.009) were 2 high-risk factors associated with death. Conclusions: Lymphadenectomy seems not to provide a significant benefit neither DFS nor OS in our study. Age, the FIGO stage and effective cytoreductive surgery are high-risk factors associated with clinical prognosis in LGSOC patients.

Introduction

Ovarian cancer is the eighth most common malignancy in women. According to the Global Cancer Data Report of 2020, there are 313,959 new cases of ovarian cancer (8th female malignancy, 3.4%) and 207,252 deaths (8th female malignancy, 4.7%).[1] In the histological classification, epithelial ovarian cancer accounts for 90%, of which serous ovarian cancer is the most common and is divided into high-grade serous ovarian cancer (HGSOC) and low-grade serous ovarian cancer (LGSOC) according to the two-tier grading system.[2-6]LGSOC accounts for about 6-10% of epithelial ovarian cancer.[5,7,8,9,10] Compared with HGSOC, LGSOC is diagnosed at a younger age with a better prognosis, and relative chemoresistance.[9,11-15]

Due to LGSOC is a rare ovarian malignant tumor, clinical guidance for LGSOC patients is mainly based on

retrospective studies, and subgroup analysis of ovarian cancer clinical trials.[16-18]During clinical treatment, the surgical management of ovarian cancer requires at least hysterectomy, bilateral salpingoophorectomy, omentectomy, and visible resection of metastatic lesions.[15,19,20] At the same time, primary maximal cytoreductive surgery is paramount importance for clinical prognosis of LGSOC patients.[7,19] Previous studies have reported that about 20-70% patients with ovarian cancer have lymph node metastasis, with the proportion gradually increasing with International Federation of Gynecology and Obstetrics (FIGO) stage.[19,21-23] However, whether to perform lymphadenectomy during cytoreductive surgery is still inconclusive. The large randomized trial LION study which published in 2019, reported that systematic pelvic and para-aortic lymphadenectomy in patients with advanced ovarian cancer had no survival benefit and increased postoperative complications.[24] Due to the low morbidity of LGSOC, majority of patients in the LION study were HGSOC, and there is still no conclusive clinical evidence on the clinical benefit of lymphadenectomy for patients with LGSOC.[25,26]

The aim of present study is to use the propensity score matching (PSM) analysis to further evaluate the prognostic value of lymphadenectomy in LGSOC patients with different FIGO stages.[27] Our results could provide a more individualized reference for surgical scheme options during clinical precision treatment.

Patients and methods

Study population

We retrospectively reviewed 147 LGSOC patients from 4 medical centers, including Qilu Hospital of Shandong University, the Affiliated Hospital of Qingdao University, Women's Hospital School of Medicine Zhejiang University, and Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology from 2010 to 2020. All patients had a clear pathological diagnosis of LGSOC, and the initial treatment was surgical management.

Data collection

Clinical characteristics, such as age at diagnosis, tumor size, pre-operative serum carbohydrate antigen 125 (CA-125) level (IU/ml), the FIGO stage (2014),[27] surgical method and range, intraoperative pathology, ascites, postoperative routine pathology, postoperative pathological staging and adjuvant therapy, duration of follow-up and survival outcomes, were included in the analysis. The size of the largest residual tumor and postoperative pathological staging were evaluated according to the surgical records and related pathological results. The maximum diameter of residual tumor was <1 centimeter (cm) for effective cytoreductive surgery, and [?]1 cm for other residual tumor with maximum diameter.

Endpoints

The primary end points were disease-free survival (DFS) and overall survival (OS). DFS was defined as the time period from surgery to the first occurrence of disease progression, recurrence, or death due to the disease. If none of the above events occurred, it was the time of the last follow-up. OS was calculated as the time from surgery to death, or the last follow-up time if the patient was currently alive.

Statistical analysis

The flow chart was shown in **Figure S1** . Patients were divided into lymphadenectomy group and no lymphadenectomy group according to whether pelvic and/or para-aortic lymphadenectomy was performed during the operation. The Chi-square test was used to compare the clinical characteristics of the two groups. In order to scientifically balance the differences in clinical characteristics between the two groups of patients and better evaluate the impact of lymphadenectomy on the clinical outcomes of patients, we adopted PSM algorithm. The characteristics which P value <0.20 after the Chi-square test were matched by PSM, and 0.02 was set as the match tolerance. These propensity scores were utilized to match patients in lymphadenectomy and no lymphadenectomy at a 1:1 fixed ratio.

The Kaplan-Meier analysis was used to evaluate the effect of lymphadenectomy on DFS and OS in the before and after matching cohorts. The univariate Cox proportional hazard regression analysis was used

for screening of high-risk factors which associated with DFS and OS. After that, characteristics with the P value <0.15 were enrolled in the multivariate Cox proportional hazard regression analysis. The results were described as the hazard ratio (HR), 95% confidence interval (CI), and P value.

Finally, in order to further evaluate the impact of lymphadenectomy on DFS and OS in LGSOC patients of different FIGO stages, we conducted subgroup analysis. Patients were divided into FIGO I and II stage group, FIGO III and IV stage group, and performed the above-mentioned PSM analysis. The Kaplan-Meier analysis was used to explore the effect of lymphadenectomy on DFS and OS of patients with different FIGO stages.

All statistical analysis was conducted with SPSS (version 25.0). The$P$ value <0.05 is considered statistical significant.

Results

Clinical characteristics of patients

This study included 147 patients with LGSOC from 4 medical centers. The median age was 47 years (range 21-79 years), and 88 (59.4%) patients were still premenopausal. There were 48 (32.7%) patients in FIGO stage I, 11 (7.5%) patients in stage II, 80 (54.4%) patients in FIGO stage III, and 8 (5.4%) patients in stage IV. One hundred and seven (72.8%) patients received effective cytoreductive surgery, and 40 (27.2%) patients had maximum diameter of residual tumor >1cm after surgery. A total of 101 patients (68.7%) who underwent pelvic and/or para-aortic lymphadenectomy, and 28 (27.7%) of them had pathologic evidence of lymph node metastasis. Platinum-based adjuvant chemotherapy was observed in 126 (85.7%) patients. Fifty-two patients (35.4%) had experienced disease progression or recurrence, of which 45 patients (86.5%) in FIGO stage III or IV. Median DFS time was 84 months. Twenty-five patients (17%) died postoperatively due to disease or other complications, of which 22 patients (88%) in FIGO stage III or IV. The median OS time was 90 months.

Propensity score matching analysis

Table 1 shows the characteristics of patients in the before and after propensity score matching cohorts. In the before PSM cohort, significant statistical differences were observed in age (P =0.024), FIGO stage (P =0.007), CA-125 level (P =0.023), operation method (P =0.088), and adjuvant therapy (P =0.081). The two groups of patients were matched by PSM in the 1:1 ratio. A total of 86 women were selected into the after matching cohort, 40 (46.5%) patients underwent lymphadenectomy, and 46 (53.5%) patients did not. The basic characteristics of the patients were not significantly different in the after matching cohort (P<0.05).

Univariate Kaplan-Meier analysis of DFS and OS

Figure 1 shows the Kaplan-Meier survival curves of the effect of lymphadenectomy in DFS and OS. In the before PSM cohort, the Kaplan-Meier analysis showed that lymphadenectomy had a significant protective effect on DFS (P <0.001) and OS (P<0.001), the results are shown in **Figure 1A** and**1B** . In the after matching cohort, there were no significant difference between lymphadenectomy and no lymphadenectomy groups in both DFS (P =0.058) and OS (P =0.067), the results are shown in**Figure 1C** and **1D** .

Univariate and multivariate Cox proportional hazard analysis for DFS and OS

Univariate and multivariate Cox proportional hazard regression analysis were performed on the after matching cohort. Univariate Cox proportional hazard regression analysis showed that age [?]50 years (P =0.011), pathological stage I or II (P =0.010), residual tumor lesions <1 cm (P =0.004) were associated with longer DFS. Age [?]50 years (P =0.032) and residual tumor lesions <1 cm (P =0.010) were associated with longer OS, while positive ascites cytology (P =0.029) was associated with poor OS. In the multivariate Cox proportional hazards regression analysis, age >50 years (HR, 2.35; 95% CI, 1.21-4.56; P =0.012) and FIGO stage III or IV (HR, 4.97; 95% CI, 1.16-21.38; P =0.031) were independent prognostic risk factors of DFS, while residual tumor lesions <1 cm (HR, 0.51; 95% CI, 0.26-0.98; P =0.044) was independent prognostic

protection factor of DFS. Patients with residual tumor lesions <1 cm (HR, 0.33; 95% CI, 0.15-0.76;P =0.009) had a better OS, while age >50 years (HR, 2.68; 95% CI, 1.10-6.55; P =0.031) was associated with shorter OS. The above results are shown in **Table 2** and **Table 3** .

Subgroup analysis stratified by the FIGO staging

Finally, we conducted a subgroup analysis stratified by the FIGO staging and performed PSM for patients in stage I and II, stage III and IV respectively. The basic clinical characteristics of patients before and after PSM are shown in **Table S1** and **Table S2** . In the before PSM cohort, there were statistically differences in CA-125 level (P =0.092) and adjuvant therapy (P =0.008) in the stage I and II, while there were statistically differences in age (P =0.006) and operation method (P =0.049) in stage III and IV. Patients in each group were matched by PSM in a 1:1 ratio. A total of 22 women in the stage I and II groups were selected for the matching cohort, and 11 (50.0%) patients underwent lymphadenectomy and 11 (50.0%) did not. A total of 66 women in the stage III and IV groups were selected for the matched cohort, and 30 (45.5%) patients underwent lymphadenectomy and 36 (54.5%) did not. There was no statistical significance in the basic characteristics of patients in the postoperative cohort (P >0.05).

Figure 2 and **Figure 3** show the Kaplan-Meier survival curves of the effect of lymphadenectomy in each subgroup in DFS and OS, respectively. In the before PSM cohort, the Kaplan-Meier analysis showed that lymphadenectomy had a significant protective effect on DFS (P =0.036) and OS (P =0.018) in FIGO stage III and IV. It also showed that there existed a protective effect on OS (P =0.011) in FIGO stage I and II, but no significant difference in DFS (P =0.296). The results are shown in **Figure 2A** ,**2B** , **3A** and **3B** respectively. In the after matching cohort, there were no significant difference both in DFS (P =0.470) and OS (P =0.226) between the two groups in FIGO stage I and II. It showed similar results in DFS (P =0.168) and OS (P =0.197) in FIGO stage III and IV. The results are shown in**Figure 2C** , **2D** , **3C** and **3D**respectively.

Discussion

Main findings:

We performed a multicenter retrospective study to evaluate the effect of lymphadenectomy on prognosis in LGSOC patients. After a rigorous matching of the clinical characteristics of the patients, we found no significant survival benefit from lymphadenectomy. In the subgroup analysis of the FIGO staging, there were also no significant benefits from lymphadenectomy in both early and advance LGSOC patients. The prognosis of LGSOC patients was mainly related to the age, FIGO stage and effective cytoreductive surgery.

Strengths and limitations:

In our study, the median DFS time and OS time are concordant with published studies.[2,15,18] Among women who had undergone lymphadenectomy, we recorded 27.7% (28/101) lymph node metastases, which may be related to the fact that most of the cases were advanced patients. The number of patients who did not undergo lymphadenectomy in early LGSOC patients is small, so there is interference in the results of subgroup analysis. The main shortcomings of this study are the nature of retrospective study. Some patients with advanced ovarian cancer died after surgery due to intestinal obstruction or other complications, and some patients lost follow-up due to long time. We did not discuss the preoperative lymph node status indicated by imaging studies and intraoperative exploration. The influence of the range of lymphadenectomy on the prognosis has not been further analyzed. Finally, there is no discussion of postoperative complications related to lymphadenectomy.

The strength of our study lies in the large samples from 4 medical centers to ensure the authenticity and reliability of data analysis, which is rare at present. In order to make the research results more credible, we used PSM to balance the basic clinical characteristics of patients to further fit prospective clinical trials and explore the impact of lymphadenectomy on the survival-related prognosis of patients. At the end of the article, a subgroup analysis was performed to explore the clinical benefits of lymphadenectomy in patients of different FIGO stages.

Interpretation:

Compared with HGSOC, LGSOC is relatively rare in clinical practice and lacks corresponding diagnosis and treatment evidence. The LGSOC is characterized by slow growth pattern and insensitivity to chemotherapy.[9] Therefore, the initial cytoreductive surgery is more significant in LGSOC than HGSOC.[28]Data from Gynecologic Oncology Group (GOG) 182 on 189 patients with LGSOC showed that patients with residual lesions greater than 1 cm after initial cytoreductive surgery had significantly shorter DFS (14.1 months*vs* 33.2 months, P <0.001) and OS (42.0 months*vs* 96.9 months, P <0.001) than those with less residual lesions.[29] Most scholars believed that in the initial cytoreductive surgery for LGSOC patients, it was ideal to remove all macroscopic tumor lesions as much as possible.[9,12,13,17] In our study, similar results were found that effective tumor reduction was closely associated with longer DFS (P =0.044) and OS (P =0.009). However, whether lymphadenectomy was included in cytoreductive surgery as an initial surgical treatment plan to improve the survival outcome of LGSOC patients was still inconclusive. Therefore, we conducted this multicenter clinical retrospective study to further evaluate the effect of lymphadenectomy on the prognosis of LGSOC patients with different FIGO stages.

Our study found that lymphadenectomy had no obvious survival benefit for patients with LGSOC, which is the same as the results of some previous studies. In the related studies of ovarian cancer, lymphadenectomy also seemed not to bring significant benefits to patients. A prospective randomized trial of the removal of enlarged lymph nodes and systematic lymphadenectomy in advanced ovarian cancer showed that there was a difference in DFS, but there was no statistical difference in OS.[25] Our study did not discuss whether there were enlarged lymph nodes that were explored before or during surgery, which may have selection bias. A randomized study of systematic lymphadenectomy and sampling in early ovarian cancer showed that systematic lymphadenectomy contributed to staging, with no survival benefit.[26] A randomized trial of lymphadenectomy in patients with advanced epithelial ovarian cancer, the LION study, enrolled 647 patients, and showed that if there are no obvious enlarged lymph nodes before and during surgery, there is no survival benefit from lymphadenectomy.[24] These studies were prospective randomized clinical trials with high authenticity and reliability, but the majority of patients had HGSOC and only a few patients had LGSOC.

Gockley et al. used the National Cancer Database to analyze 404 patients who were matched by lymphadenectomy and showed that lack of lymphadenectomy is associated with an increased risk of death. The authors also used PSM to balance differences in basic characteristics of patients, but due to data limitations, there is no disease recurrence related assessment.[30] Simon et al. retrospectively analyzed the effect of lymphadenectomy on PFS and OS in 126 LGSOC patients, and showed no significant improvement in prognosis, and subgroup analysis showed the same results.[19] The above studies are shown in **Table S3** . On the basis of previous research, we included 147 patients from four centers, used PSM to balance the clinical characteristics of the patients, and finally carried out the subgroup analysis stratified by FIGO staging, which made the statistical analysis more rigorous, and more accurately evaluates the role of lymphadenectomy in the prognosis of patients with LGSOC.

Ovarian cancer seriously affects women's survival. In patients with low-grade serous ovarian cancer, it is ideal to remove all macroscopic tumor lesions, but whether systematic lymphadenectomy provides a survival benefit remains controversial. In this study, we demonstrate that lymphadenectomy has no significant survival benefit in LGSOC. We included 147 patients, and there have been few studies with such large data in previous studies. These results may influence surgical decisions. Clinicians and patients may refuse lymphadenectomy in order to avoid more postoperative complications. Of course, prospective multicenter studies are needed to confirm this, although this may be difficult to achieve due to the small number of LGSOC.

Conclusions

Finally, LGSOC is a rare ovarian malignant tumor. Despite great efforts in the past few decades, there is still a lack of precise guidance on surgical diagnosis and treatment. In conclusion, our results indicate that

lymphadenectomy seems not provide a significant clinical benefit to LGSOC patients. These results may influence surgical decisions about how to treat LGSOC. We recommend that all LGSOC patients undergo a detailed preoperative evaluation, accurately formulate the surgical treatment plan, and improve the prognosis of patients.

Disclosure of interests

All authors declare no conflict of interest.

Contribution to authorship

KS, RC, ZC, and BK made substantial contributions to the conception and design, acquisition of data, and critical revision of the manuscript. RC and ZC made contributions to the interpreting of data and drafting of manuscript. GC, QY, YS, TQ, LL, and CS made substantial contributions to patient selection and clinical data. LS, JL, XZ, JL, PL, LS, XP, and LZ made substantial contributions to acquisition of data. All authors read and approved the final manuscript.

Details of ethics approval

This retrospective study was approved by the Ethical Committee of Qilu Hospital of Shandong University (protocol number KYLL-202011-158-1) and obtained a waiver for informed consent. Before the analysis, the privacy of each patient was maintained.

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Figure legends:

Figure 1 The Kaplan-Meier curves in the before and after PSM cohorts.

(A, B) In the before matching cohort, Kaplan-Meier survival analysis revealed that lymphadenectomy had a protective effect on the DFS and OS of patients.

(C, D) After matching of the clinical characteristics of the patients, we found no significant survival benefit from lymphadenectomy.

DFS, disease-free survival; OS, overall survival.

Figure 2 The Kaplan-Meier curves of patients with FIGO I and II in the before and after PSM cohorts.

(A, B) In the before matching cohort, Kaplan-Meier survival analysis revealed that lymphadenectomy had a protective effect on the OS of patients.

(C, D) After matching, we found no significant survival benefit from lymphadenectomy.

DFS, disease-free survival; OS, overall survival.

Figure 3 The Kaplan-Meier curves of patients with FIGO III and IV in the before and after PSM cohorts.

(A, B) In the before matching cohort, Kaplan-Meier survival analysis revealed that lymphadenectomy had a protective effect on the DFS and OS of patients.

(C, D) After matching, we found no significant survival benefit from lymphadenectomy.

DFS, disease-free survival; OS, overall survival.

Table 1 Characteristics of patients in the before and after PSM cohorts

	Before Matching (n=147)	**Before Matching (n=147)**	**Before Matching (n=147)**	**After Matching (n=86)**	**After Matching (n=86)**	**After Matching (n=86)**
Characteristic	**Pelvic lymphadenectomy (n=101)**	**No pelvic lymphadenectomy (n=46)**	***P* value**	**Pelvic lymphadenectomy (n=40)**	**No pelvic lymphadenectomy (n=46)**	***P* value**
Age, year			0.024			0.173
[?]50	68 (67.3)	22 (47.8)		25 (62.5)	22 (47.8)	
>50	33 (32.7)	24 (52.2)		15 (37.5)	24 (52.2)	
FIGO (2014)			0.007			0.466
I and II	48 (47.5)	11 (23.9)		7 (17.5)	11 (23.9)	
III and IV	53 (52.5)	35 (76.1)		33 (82.5)	35 (76.1)	
CA-125, U/mL			0.023			0.502
[?]35	25 (24.8)	4 (8.7)		2 (5.0)	4 (8.7)	

	Before Matching (n=147)	Before Matching (n=147)	Before Matching (n=147)	After Matching (n=86)	After Matching (n=86)	After Matching (n=86)
>35	76 (75.2)	42 (91.3)		38 (95.0)	42 (91.3)	
Operation method			0.088			0.429
Laparotomy	78(77.2)	41 (89.1)		36 (90.0)	41 (89.1)	
Laparoscopy	23 (22.8)	5 (10.9)		4 (10.0)	5 (10.9)	
Tumor size, cm			0.918			0.545
[?]9	58 (57.4)	26 (56.5)		20 (50.0)	26 (56.5)	
>9	43 (42.6)	20 (43.5)		20 (50.0)	20 (43.5)	
Pathological consistency			0.475			0.080
Consistent	63 (62.4)	27 (58.7)		25 (62.5)	27 (58.7)	
Not consistent	22 (21.8)	8 (17.4)		12 (30.0)	8 (17.4)	
Without	16 (15.8)	11 (23.9)		3 (7.5)	11 (23.9)	
Debulking surgery			0.164			0.468
Optimal ([?]1 cm)	77 (76.2)	30 (65.2)		29 (72.5)	30 (65.2)	
Suboptimal (>1 cm)	24 (23.8)	16 (34.8)		11 (27.5)	16 (34.8)	
Ascites cytology			0.231			0.697
Positive	14 (13.9)	11 (23.9)		7 (17.5)	11 (23.9)	
Negative	37 (36.6)	12 (26.1)		13 (32.5)	12(26.1)	
Without	50 (49.5)	23 (50.0)		20 (50.0)	23 (50.0)	
Adjuvant therapy			0.081			0.260
None	11 (10.9)	10 (21.7)		5 (12.5)	10 (21.7)	
Chemotherapy	90 (89.1)	36 (78.3)		35 (87.5)	36 (78.3)	

Values are presented as n (%).

PSM, propensity score matching; FIGO, International Federation of Gynecology and Obstetrics; CA-125, carbohydrate antigen 125.

Table 2 Univariable Cox proportional hazards regression analysis for DFS and OS in the after PSM cohort.

	DFS	DFS	OS	OS
Characteristic	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P* value**
Age, year		0.011		0.032?¿?
50	Reference		Reference	
>50	2.27 (1.22-4.58)		2.65 (1.09-6.44)	
FIGO (2014)		0.010		0.128
I and II	Reference		Reference	

	DFS	**DFS**	**OS**	**OS**
III and IV	6.56 (1.57-27.27)		3.10 (0.72-13.26)	
CA-125, U/mL		0.982		0.836?¿?
35	Reference		Reference	
>35	0.98 (0.24-4.12)		1.24 (0.17-9.20)	
Operation method		0.166		0.318
Laparotomy	Reference		Reference	
Laparoscopy	0.25 (0.03-1.79)		0.04 (0.00-20.84)	
Tumor size, cm		0.252		0.621?¿?
9	Reference		Reference	
>9	1.46 (0.76-2.79)		0.81 (0.35-1.88)	
Rapid pathology		0.496		0.517
Consistent	0.90 (0.36-2.23)	0.816	1.23 (0.35-4.30)	0.746
Not consistent	Reference		Reference	
Without	1.44 (0.50-4.14)	0.494	2.01(0.50-8.16)	0.327
Debulking surgery		0.004		0.010
Optimal ([?]1 cm)	0.38 (0.20-0.73)		0.34 (0.15-0.77)	
Suboptimal (>1 cm)	Reference		Reference	
Ascites cytology		0.240		0.087
Positive	2.20 (0.88-5.47)	0.091	5.69 (1.20-26.98)	0.029
Negative	Reference		Reference	
Without	1.60 (0.70-3.67)	0.262	4.51 (1.02-19.98)	0.048
Adjuvant therapy		0.086		0.271
None	Reference		Reference	
Chemotherapy	2.82 (0.87-9.18)		2.26 (0.53-9.64)	

PSM, propensity score matching; DFS, disease-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics, CA-125, cancer antigen 125.

Table 3 Multivariate Cox proportional hazards regression analysis for DFS and OS in the after PSM cohort.

	DFS	**DFS**	**OS**	**OS**
Characteristic	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P* value**
Age (Year)		0.012		0..031?¿?
50	Reference		Reference	
>50	2.35 (1.21-4.56)		2.68(1.10-6.55)	
FIGO (2014)		0.031		
I and II	Reference			
III and IV	4.97 (1.16-21.38)			
Debulking surgery		0.044		0.009
Optimal ([?]1 cm)	0.51(0.26-0.98)		0.33 (0.15-0.76)	
Suboptimal (>1 cm)	Reference		Reference	

PSM, propensity score matching; DFS, disease-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics.

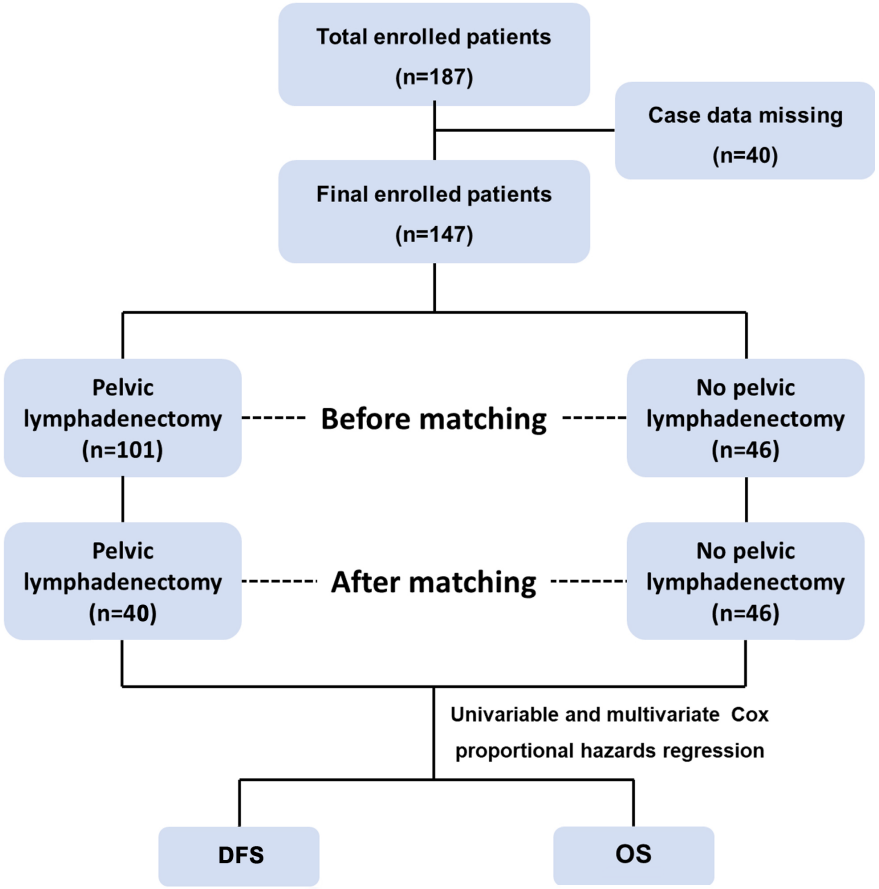
Supplemental Material

The supplemental material includes:

Figure S1

Table S1 - Table S3

Figure S1: The workflow of this study.



DFS, disease-free survival; OS, overall survival.

Table S1 Characteristics of patients in the before and after PSM cohorts (FIGO I and II)

	Before Matching (n=59)	Before Matching (n=59)	Before Matching (n=59)	After Matching (n=19)	After Matching (n=19)	After Matching (n=19)
Characteristic	**Pelvic lymphadenectomy (n=48)**	**No pelvic lymphadenectomy (n=11)**	***P* value**	**Pelvic lymphadenectomy (n=11)**	**No pelvic lymphadenectomy (n=11)**	***P* value**
Age, year			1.000			1.000
[?]50	31 (64.6)	7 (63.6)		7 (63.6)	7 (63.6)	

	Before Matching (n=59)	Before Matching (n=59)	Before Matching (n=59)	After Matching (n=19)	After Matching (n=19)	After Matching (n=19)
>50	17 (35.4)	4 (36.4)		4 (36.4)	4 (36.4)	
FIGO (2014)			1.000			1.000
I	39 (81.3)	9 (81.8)		9 (81.8)	9 (81.8)	
II	9 (18.8)	2 (18.2)		2 (18.2)	2 (18.2)	
CA-125, U/mL			0.092			0.149
[?]35	20 (41.7)	1 (9.1)		5 (45.5)	1 (9.1)	
>35	28 (58.3)	10 (90.9)		6 (54.5)	10 (90.9)	
Operation method			0.326			1.000
Laparotomy	36 (75.0)	6 (54.5)		7 (63.6)	6 (54.5)	
Laparoscopy	12 (25.0)	5 (45.5)		4 (36.4)	5 (45.5)	
Tumor size, cm			0.772			1.000
[?]9	30 (62.5)	8 (72.7)		8 (72.7)	8 (72.7)	
>9	18 (37.5)	3 (27.3)		3 (27.3)	3 (27.3)	
Fast pathology			0.802			0.896
Consistent	33 (68.8)	7 (63.6)		6 (54.5)	7 (63.6)	
Not consistent	9 (18.8)	3 (27.3)		4 (36.4)	3 (27.3)	
Without	6 (12.5)	1 (9.1)		1 (9.1)	1 (9.1)	
Debulking surgery			0.572			1.000
Optimal ([?]1 cm)	45 (93.8)	10 (90.9)		11 (100.0)	10 (90.9)	
Suboptimal (>1 cm)	3 (6.3)	1 (9.1)		0 (0.0)	1 (9.1)	
Ascites cytology			0.747			0.420
Positive	7 (14.6)	2 (18.2)		1 (9.1)	2 (18.2)	
Negative	22 (45.8)	6 (54.5)		4 (36.4)	6 (54.5)	
Without	19 (39.6)	3 (27.3)		6 (54.5)	3 (27.3)	
Adjuvant therapy			0.008			1.000
None	9 (18.8)	7 (63.6)		7 (63.6)	7 (63.6)	
Chemotherapy	39 (81.3)	4 (36.4)		4 (36.4)	4 (36.4)	

Values are presented as n (%).

PSM, propensity score matching; FIGO, International Federation of Gynecology and Obstetrics; CA-125, carbohydrate antigen 125.

Table S2 Characteristics of patients in the before and after PSM cohorts (FIGO III and IV)

	Before Matching (n=87)	Before Matching (n=87)	Before Matching (n=87)	After Matching (n=58)	After Matching (n=58)	After Matching (n=58)
Characteristic	**Pelvic lymphadenectomy (n=53)**	**No pelvic lymphadenectomy (n=36)**	***P* value**	**Pelvic lymphadenectomy (n=30)**	**No pelvic lymphadenectomy (n=36)**	***P* value**
Age, year			0.006			0.498
[?]50	37 (71.2)	15 (41.7)		15 (50.0)	15 (41.7)	
>50	15 (28.8)	21 (58.3)		15 (50.0)	21 (58.3)	
FIGO (2014)			1.000			1.000
I	47 (90.4)	33 (91.7)		27 (90.0)	33 (91.7)	
II	5 (9.6)	3 (8.3)		3 (10.0)	3 (8.3)	
CA-125, U/mL			0.711			0.681
[?]35	4 (7.7)	4 (11.1)		2 (6.7)	4 (11.1)	
>35	48 (92.3)	32 (88.9)		28 (93.3)	32 (88.9)	
Operation method			0.049			1.000
Laparotomy	42 (80.8)	35 (97.2)		29 (96.7)	35 (97.2)	
Laparoscopy	10 (19.2)	1 (2.8)		1 (3.3)	1 (2.8)	
Tumor size, cm			0.937			0.300
[?]9	27 (51.9)	19 (52.8)		12 (40.0)	19 (52.8)	
>9	25 (48.1)	17 (47.2)		18 (60.0)	17 (47.2)	
Fast pathology			0.569			0.750
Consistent	30 (57.7)	20 (55.6)		19 (63.3)	20 (55.6)	
Not consistent	12 (23.1)	6 (16.7)		5 (16.7)	6 (16.7)	
Without	10 (19.2)	10 (27.8)		6 (20.0)	10 (27.8)	
Debulking surgery			0.904			0.679
Optimal ([?]1 cm)	31 (59.6)	21 (58.3)		19 (63.3)	21 (58.3)	
Suboptimal (>1 cm)	21 (40.4)	15 (41.7)		11 (36.7)	15 (41.7)	
Ascites cytology			0.237			0.457
Positive	7 (13.5)	9 (25.0)		4 (13.3)	9 (25.0)	
Negative	15 (28.8)	6 (16.7)		7 (23.3)	6 (16.7)	
Without	30 (57.7)	21 (58.3)		19 (63.3)	21 (58.3)	
Adjuvant therapy			0.396			1.000
None	2 (3.8)	3 (8.3)		2 (6.7)	3 (8.3)	

	Before Matching (n=87)	Before Matching (n=87)	Before Matching (n=87)	After Matching (n=58)	After Matching (n=58)	After Matching (n=58)
Chemotherapy	50 (96.2)	33 (91.7)		28 (93.3)	33 (91.7)	

Values are presented as n (%).

PSM, propensity score matching; FIGO, International Federation of Gynecology and Obstetrics; CA-125, carbohydrate antigen

Table S3 Studies about prognosis of lymph node dissection in patients with OC/LGSOC.

Author	V Simon, 2020[19]	V Simon, 2020[19]	**Allison Gockley, 2017[30]**	**Allison Gockley, 2017[30]**	**Philipp Harter, 2019[24]**	**Philipp Harter, 2019[24]**	**Pierluigi Benedetti Panici, 2005[25]**	**Pierluigi Benedetti Panici, 2005[25]**	**A Maggioni, 2006[26]**	**A Maggioni, 2006[26]**	**Our research (Before PSM)**	**Our research (Before PSM)**	**Our research (After PSM)**
Grouping	LND-	LND+	LND-	LND+	LND-	LND+	bulky nodes+	LND+	LN sampling	LND+	LND-	LND+	LND
Year	58	51	55.54	54.08	60	60	56	53	52	51-138	50.83	46.4	50.83
No.patients	31	91	202	202	324	323	211	216	130		46	101	46
Histological types	LGSOC	LGSOC	LGSOC	LGSOC	AOC	AOC	AOC	AOC	OC	OC	LGSOC	LGSOC	LGS
FIGO criteria	FIGO	FIGO	FIGO 2014	FIGO 2014	FIGO	FIGO	FIGO	FIGO	FIGO	FIGO	FIGO 2014	FIGO 2014	FIGO 2014
FIGO stage													
I	6 (20.7)	11 (12.2)	-	-	17 (5.2)	15 (4.6)	-	-	90 (69.2)	102 (73.9)	9 (19.6)	39 (38.6)	9 (19.6
II			-	-	52 (16.0)	41 (12.7)	-	-	39 (30.0)	33 (23.9)	2 (4.3)	9 (8.9)	2 (4.3)
III	23 (79.3)	79 (87.8)	171 (84.7)	165 (81.7)	24 (75.3)	261 (80.8)	199 (94.3)	207 (95.8)	-	-	32 (69.6)	48 (47.5)	32 (69.6
IV			31 (15.3)	37 (18.3)	11 (3.4)	6 (1.9)	12 (5.7)	9 (4.2)	-	-	3 (6.5)	5 (5.0)	3 (6.5)
LN status													
pN+	-	58.2%	-	-	-	55.7%	42%	70%	5%	15%	-	27.7%	-
pN-	-	41.8%	-	-	-	44.3%	58%	30%	95%	85%	-	72.3%	-
Follow-up (months)	27.5	27.5	72.7	72.7	72	72	68.4	68.4	87.8	87.8	31.4	42	31.4
Median DFS/PFS (months)	41	41	-	-	25.5	25.5	22.4	29.4	-	-	32	106	32

Author	V Simon, 2020[19]	V Simon, 2020[19]	Allison Gockley, 2017[30]	Allison Gockley, 2017[30]	Philipp Harter, 2019[24]	Philipp Harter, 2019[24]	Pierluigi Benedetti Panici, 2005[25]	Pierluigi Benedetti Panici, 2005[25]	A Maggioni, 2006[26]	A Maggioni, 2006[26]	Our research (Before PSM)	Our research (Before PSM)	Our research (After PSM)
5-year DFS /PFS	41% (31.2–54.1%)	41% (31.2–54.1%)	-	-	-	-	21.6%	31.2%	71.3%	78.3%	33.2%	64.0%	33.2%
Median OS (months)	130	130	58	106.5	69.2	65.5	56.3	58.7	-	-	90	-	90
5-year OS	77% (68.3–87.1%)	77% (68.3–87.1%)	-	-	-	-	47%	48.5%	81.3%	84.2%	57.6%	86.9%	57.6%

Values are presented as n(%) or median (range).

PSM, propensity score matching; LND, lymph node dissection; LN, lymph node; LGSOC, low grade serous ovarian cancer; AOC, advanced ovarian cancer; OC, ovarian cancer; FIGO, International Federation of Gynecology and Obstetrics; pN, pathological lymph node status; PFS, progression-free survival; DFS, disease-free survival; OS, Overall survival.