Outcomes of Women With High-Grade and Low-Grade Advanced-Stage Serous Epithelial Ovarian Cancer

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Abstract

Objective—To compare outcomes of women with advanced stage low-grade serous ovarian cancer and high-grade serous ovarian cancer, and identify factors associated with survival among patients with advanced stage low-grade serous ovarian cancer.

Methods—A retrospective study of patients diagnosed with grade 1 or 3, advanced-stage (stage IIIC and IV) serous ovarian cancer between 2003 and 2011 was undertaken using the National Cancer Database, a large administrative database. The effect of grade on survival was analyzed using the Kaplan-Meier method. Factors predictive of outcome were compared using the Cox proportional hazards model. Among women with low-grade serous ovarian cancer, propensity score matching was used to compare all-cause mortality among similar women who underwent chemotherapy and lymph node dissection and those who did not.

Results—A total of 16,854 (95.7%) patients with high-grade serous ovarian cancer and 755 (4.3%) patients with low-grade serous ovarian cancer were identified. Median overall survival was 40.7 months among high-grade patients and 90.8 months among women with low-grade tumors (p<0.001). Among patients with low-grade serous ovarian cancer in the propensity-score matched cohort, the median overall survival was 88.2 months among the 140 patients who received chemotherapy and 95.9 months among the 140 that did not received chemotherapy (p=0.7). Conversely, in the lymph node dissection propensity-matched cohort, median overall survival was 106.5 months among the 202 patients who underwent lymph node dissection and 58 months among the 202 who did not (p<0.001).

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Conclusions—When compared to high-grade serous ovarian cancer, low-grade serous ovarian cancer is associated with improved survival. In patients with advanced-stage low-grade serous ovarian cancer, lymphadenectomy but not adjuvant chemotherapy was associated with improved survival.

Precis

In advanced serous ovarian cancer, low-grade tumors have a better prognosis than high-grade, and in low-grade tumors, lymphadenectomy, but not chemotherapy, is associated with improved survival.

Introduction

Serous epithelial ovarian tumors are the most common sub-type of ovarian cancer. Numerous studies have supported a two–tier grading system for serous ovarian carcinoma based on histology: low-grade and high-grade.(1–3) Low-grade serous ovarian carcinomas are rare, accounting for only 5–10% of all epithelial ovarian cancers.(4) Low-grade serous ovarian tumors typically demonstrate KRAS or BRAF mutations (5–8), while high-grade serous ovarian tumors are often genetically unstable and express p53 mutations.(9–11)

High-grade serous ovarian tumors usually present at advanced stages and are frequently responsive to first-line platinum-based chemotherapy.(12) However, women with high-grade serous ovarian cancer experience frequent recurrences and decreased survival as compared to patients with low-grade tumors.(13) While low-grade serous ovarian tumors tend to follow a more indolent course, chemotherapy is less effective in this population.(14–16) However, these patients often receive adjuvant chemotherapy. According to a single-institution study, 55% of patients with low-grade serous ovarian cancer received adjuvant therapy.(15) There is a lack of high-quality data to guide clinician and patient decision-making regarding treatment. A PubMed and Medline search of articles published in English from January 1, 1980 – August 31, 2016 using the term "low-grade serous ovarian cancer" confirmed that there are no randomized controlled trials comprised exclusively of women with low-grade serous ovarian cancer, and retrospective studies are limited by small numbers of patients. The objective of this study was to use a large national cancer database to compare outcomes of women with advanced stage low-grade serous ovarian cancer and high-grade serous ovarian cancer, and identify factors associated with survival among patients with advanced stage low-grade serous ovarian cancer.

Materials and Methods

This is a retrospective study using the National Cancer Database is a clinical oncology database sourced from over 1,500 hospitals, capturing approximately 70% of newly diagnosed cancer cases across the United States. The National Cancer Database was used to identify women 18 years and older diagnosed with advanced stage (IIIC and IV) serous ovarian carcinoma from January 1, 2003 until December 31, 2011. Patients with grade 1 (low-grade) and grade 3 (high- grade) tumors were included. Patients with grade 2 tumors were excluded. There is substantial variation in classification of grade 2 tumors (17), and we sought to define the high-grade and low-grade populations as accurately as possible in the

absence of central pathology review. Patients were excluded if they were diagnosed with other primary cancers (n=5,201), if they had missing data on lymph node dissection or chemotherapy utilization or received chemotherapy or radiation prior to surgery (n=6,435). We also excluded patients who were treated outside of the facility where they were diagnosed with ovarian cancer (n=308) as well as patients with stage I-IIIB or unknown stage (n=9,573). Patients with unknown survival (n=1), race (n=201), or facility type (n=30) were also excluded. This study was exempt from our Institutional Review Board because all information from the National Cancer Database is deidentified.

Participant User Files were used to abstract demographic, socioeconomic and clinical variables and descriptive statistics were calculated. Adjuvant therapy (chemotherapy or radiation) was defined as any additional therapy received within the first 6 months of primary surgery. Staging was determined in accordance to the 1988 International Federation of Gynecology and Obstetrics (FIGO) staging system.(18) Registry location was divided into geographic area of residence at the time of diagnosis: central, eastern and western. Year of diagnosis was classified as 2003–2005, 2006–2008, 2009–2011. Median household income from zip code of residence was categorized into quartiles and used as a proxy for socioeconomic status. Census data and the American Community Survey also contributed to socioeconomic classifications depending on the date of diagnosis and death. The treating facility was categorized according to the Commission on Cancer Accreditation program as a Community Cancer Program, Comprehensive Community Cancer Program, Academic/ Research Program, or other. Insurance status was categorized as uninsured, private insurance, Medicare, or another type of government insurance (military or Medicaid). Educational attainment for each patient's area of residence was estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from the 2012 American Community Survey data thereby providing a measure of the proportion of adults in the patient's zip code who did not graduate from high school. The Charlson/Deyo co-morbidity index was used to report comorbidities among the patients. The Charlson/Deyo Comorbidity Index includes comorbidities likely to impact survival among hospitalized cancer patients; a score of zero means none of the comorbidities were present (19). Subjects were assigned a score of 0, 1, or >1. Survival time was measured from the date of diagnosis until death from any cause, censoring, or last follow-up, as verified by the National Cancer Database program vital status determination. Given the cohort of patients diagnosed from 1/1/2003 through 12/31/2011 and available follow-up data through 1/1/2014, in those patients who survived we had a minimum of 2 years of follow-up data in this study.

Standard univariate analyses were performed and the distribution of demographic, clinical, and treatment characteristics were compared using chi-square tests. A student t test was used to assess the significance of differences in the mean values of continuous variables. The association of grade with overall survival was assessed using the Kaplan-Meier method and the log-rank test. Cox proportional hazards models were used to calculate adjusted group Hazard Ratios, and their 95% confidence intervals (CI) were utilized to assess the importance of histology as an independent predictor of survival after adjusting for the following prognostic factors: age, race, socioeconomic status, facility type, stage, surgery, lymph node dissection, co-morbidity index, period of diagnosis, education, insurance, hospital volume, treatment, and registry location.

Patients with low-grade serous ovarian cancer were then analyzed separately to assess the impact of chemotherapy and lymph node dissection on overall survival. Propensity score matching was undertaken to create a cohort in which subjects who did and did not receive chemotherapy were balanced on covariates that could affect the decision to administer chemotherapy and thereby con found the association between use of chemotherapy and survival.(20) We included factors that the clinician would have known at the time of treatment decision-making which were available in the National Cancer Database (e.g. age, race, stage, lymph node status, etc). We fit logistic regression models to estimate the probability of receiving chemotherapy; independent variables included age, period of diagnosis, race–ethnicity, treating facility type, insurance status, income, geographic region, rural–urban status, education level, tumor size, stage and lymph node dissection. We then matched each woman who received chemotherapy with a woman who did not who had the same propensity to undergo chemotherapy using a caliper of 0.2.(21) We plotted survival functions for women who underwent chemotherapy and those who did not in the propensity score matched cohort using the Kaplan Meier method, and compared these using the log rank test. We then calculated the relative hazard of overall mortality associated with receipt of chemotherapy using a univariate Cox proportional hazard model. We employed a similar approach to assess the impact of lymph node dissection on overall survival. Propensity score for receipt of lymphadenectomy was calculated in a logistic regression model using all aforementioned independent variable, with lymph node dissection used as the dependent variable. Since information regarding chemotherapy utilization was unknown by the surgeon when choosing to perform or omit lymphadenectomy, this variable was not used to calculate propensity score. To estimate the association of lymphadenectomy and overall survival independent of chemotherapy use, we used a multivariable Cox proportional hazard model with chemotherapy as a covariate.

All statistical tests were 2 sided and differences were considered statistically significant at p < 0.05 and when hazard ratio confidence intervals did not include or cross 1.00. R version 3.0.3 was used for all statistical analyses.

Results

A total of 17,609 patients with grade 1 and 3 advanced stage serous ovarian cancer were identified. Of these, 755 (4.3%) were diagnosed with low-grade serous ovarian cancer while 16,854 (95.7%) had high-grade serous ovarian cancer. Table 1 illustrates the demographic differences between these two groups. High-grade serous ovarian cancer patients were older at diagnosis compared to women with low-grade serous ovarian cancer (62.3 years versus 53.6 years; p<0.001). Patients with high-grade serous ovarian cancer had higher rates of stage IV disease (26.1% versus 17.2%; p<0.001) and lower rate of lymph node dissection (55.6% versus 67.4%; p<0.001). The majority of women were white in both groups (90.1% versus 92.1%; p=0.1). Comorbidities scores were similar among high-grade serous ovarian cancer patients and low-grade serous ovarian cancer patients, with the majority of women presenting with a score of 0 (83.3% versus 83.4%, p= 0.3). Women with high-grade serous ovarian cancer had higher rates of chemotherapy delivery (83.5% versus 80.6%; p=0.01).

The median overall survival for women with high-grade serous ovarian cancer was 40.7 months (95%CI=40.08–41.5) and 90.8 months (95%CI=78.7–106.3) in women with low-grade serous ovarian cancer (p<0.001) When patients with stage IIIC and stage IV disease were evaluated separately, the median overall survival among women with stage IIIC high-grade serous ovarian cancer was 43.8 months (95%CI 42.9–44.8) compared to 98.1 months (95%CI=88.02.3–111.6) in low-grade serous ovarian cancer (p<0.001) (Figure 1). Among patients with stage IV disease, the median overall survival in high-grade serous ovarian cancer was 32.5 months (95%CI=31.2–33.8) and 55.2 months (95%CI=40.8–84.5) in low-grade serous ovarian cancer patients (p<0.001) (Figure 2).

Over the entire study period, and after adjusting for age, race, socioeconomic status, facility type, stage, surgery, lymph node dissection, chemotherapy, co-morbidity index, period of diagnosis, education, hospital volume, and registry location, high-grade serous ovarian cancer was associated with worse overall survival (Hazard Ratio 2.13; 95%CI=1.89–2.40) (Table 2).

Patients with low-grade serous ovarian cancer were analyzed separately. In a multivariable model, patients with income in the 4th quartile and other government insurance were more likely to receive chemotherapy. Women located in the west geographic location and classified as "other" race were less likely to receive chemotherapy. With regards to lymph node dissection, women age 80 and older, with stage IV disease and tumor size <3cm were less likely to undergo dissection. Women with private insurance were more likely to undergo lymph node dissection than women with other types of insurance (Table 3).

Propensity score matching between patients with low-grade serous ovarian cancer yielded 140 patients who received chemotherapy and 140 patients who did not. (Table 4). After propensity score matching, all characteristics were balanced in the two groups. The median follow up time was 72.9 months (66.4–78.1) and there were 56 deaths among patients who received chemotherapy and 52 among those who did not. The median overall survival in the chemotherapy administration propensity-matched cohort was 88.2 months (95%CI=68.6-not reached) for the women who underwent chemotherapy and 95.9 months (95%CI=73.7-not reached) in those who did not (p=.0.7). In a Cox regression model that included the propensity-matched cohorts, chemotherapy delivery was not associated with risk of death (HR 0.96, 95%CI=0.66–1.4).

Propensity score matching for lymph node dissection yielded 202 patients who underwent lymphadenectomy and 202 patients who did not. All variables were also well balanced between the groups (Table 5). The median follow-up was 72.7 months (66.7–75.2) and there were 65 deaths among patients who underwent lymphadenectomy and 102 among those who did not. The median overall survival in the lymph node dissection propensity-matched cohort was 106.5 months (95%CI=103.5-not reached) for the women who underwent lymph node dissection and 58 months (95%CI=46.7–87.2) in those who did not (p<0.001). In a Cox regression model that included the lymph node dissection propensity-matched cohorts, lymph node dissection was associated with improved survival after adjustment for chemotherapy (Hazard Ratio 0.54, 95%CI=0.39–0.74).

Discussion

Low-grade serous ovarian cancer is a rare histological subtype of ovarian cancer lacking specific data to inform prognosis and appropriate treatment strategies. In this investigation we used a large national cancer database to compare the presenting characteristics and outcomes of women with advanced stage low-grade serous ovarian cancer and high-grade serous ovarian cancer, as well as identify factors associated with survival among patients with low-grade serous ovarian cancer. The current study suggests that there are several distinct clinical characteristics between women with low-grade serous ovarian cancer and high-grade serous ovarian cancer, such as a younger age at diagnosis and a significantly longer median overall survival in patients with low-grade serous ovarian cancer. When patients with low-grade serous ovarian cancer were separately analyzed, we found that chemotherapy was not associated with improved survival; conversely, lymph node dissection was associated with improved survival in this population.

Our finding of a more favorable outcome and younger age at presentation in women with low-grade serous ovarian cancer compared to high-grade serous ovarian cancer parallels the results of prior studies. In a retrospective study using the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database, Plaxe (13) reported that in women with metastatic disease median overall survival was 85 months in low-grade serous patients and 36 months among the high-grade serous group. Other single institution studies demonstrate similar results.(15,22) These findings support that low-grade serous ovarian tumors represent a distinct entity, and their presentation should rank high in the differential diagnoses list of younger women presenting with metastatic epithelial ovarian cancer.

Currently, many patients with stage II–IV low-grade serous ovarian cancer undergo cytoreductive surgery followed by platinum-based chemotherapy.(23) However, prior studies have shown that low-grade serous ovarian cancers are less sensitive to conventional chemotherapy compared to high-grade serous ovarian tumors. Schmeler et al. (16) identified 25 women who received neoadjuvant chemotherapy, however, only one patient (4%) demonstrated a complete response to treatment. A separate analysis of 39 women diagnosed with low-grade serous ovarian cancer who underwent a suboptimal debulking showed an objective response in only 10 patients (23.1%), compared to 90.1% in the control cohort of high-grade serous ovarian cancer (p<0.001).(24) In a recent study of patients with low-grade primary peritoneal cancer, of the 48 patients that received chemotherapy 66.7% of patients were noted to have persistent or progressive disease.(25) Furthermore, Gershenson et al.(14) found a response rate of less than 4% among women with recurrent low-grade serous ovarian cancer. Our results also suggest that chemotherapy offers limited benefit in the adjuvant treatment of women with low-grade serous ovarian cancer. In the current analysis, we found that chemotherapy administration was not associated with improved survival in the propensity score-matched cohort of women with low-grade serous ovarian cancer. While this is compelling and argues against chemotherapy as adjuvant treatment for low-grade serous ovarian cancer patients, there may be clinically relevant factors that may be associated with a worse prognosis (such as residual disease) that are not available in the National Cancer Database data and which drove the decision to give these patients chemotherapy. Additionally, it is important to note that only a small number of patients with low-grade

serous ovarian cancer (N=140) who did not received chemotherapy were included in the propensity score analysis, and this might limit our findings.

Emerging data suggests that other agents may be active in low-grade serous ovarian cancer. In a single-institution retrospective study of stage II –IV low-grade serous ovarian cancer patients who underwent cytoreductive surgery and platinum-based chemotherapy, 114 patients underwent surveillance and 66 patients received hormonal maintenance with letrazole, anastrazole or leuprolide. Patients on hormonal maintenance had a significantly improved median progression free survival (52.0 months versus 29.9 months) and decreased risk of recurrence (Hazard Ratio=0.21; 95% CI .10–0.43) when compared to women on surveillance alone (26). A small number of patients in our cohort received hormonal treatment, and we were not able to perform a separate analysis of these patients. Another single-institution series reported median progression-free survival of 48 months for 12 low-grade serous ovarian cancer patients receiving bevacizumab. (27) While further trials are needed to identify what, if any, chemotherapy or hormonal regimen is beneficial, clinicians should consider discussing with patients the lack of evidence for adjuvant chemotherapy. setting.

The role of lymphadenectomy in advanced ovarian cancer remains controversial. (28–29) Interestingly, we found that among the lymph node dissection propensity-matched cohort, lack of lymph node dissection was associated with increased risk of death. Based on results of our literature search, this association between lymphadenectomy and survival for low-grade serous ovarian cancer patients has not been previously reported. However, it is possible that lymph node dissection upstaged some women with no evidence of macroscopic disease, who may have had a survival advantage based on their initial low tumor volume rather than the lymph node dissection. Unfortunately, the information regarding the specifics of lymphadenectomy was not available in our data. Prior studies have shown that women with retroperitoneal lymph node metastasis as the only site of extra-ovarian involvement have a better prognosis compared to patients with macroscopic peritoneal metastases.(30) The patients in this study were staged according to the FIGO criteria prior to the most recent updated criteria in 2014. Therefore there may be patients classified as IIIC due to isolated lymph node metastases in our study, which by the 2014 FIGO staging system would be stage IIIA1. It is possible that the benefit of lymphadenectomy for some of these patients was diagnostic and not therapeutic, however, we attempted to reduce potential bias by including initial tumor size in the propensity score analysis and restricting the analysis to women with stage IIIC and IV disease. Additionally, healthier patients have a baseline better prognosis and these women are also more likely to have a lymph node dissection. In order to reduce this selection bias, we included comorbidity index score in the propensity score analysis.

Although our analysis benefits from a large study population and its ability to adjust for patients' demographic characteristics, socioeconomic status, comorbidities and adjuvant treatment, there are several limitations that must be considered when interpreting the findings. The retrospective nature of this study creates inherent bias due to non-randomized allocation to treatment groups, as well as other limitations including reliance on database information from a wide variety of institutions, absence of central pathology review, as well as lack of information regarding specific surgical and treatment factors and missing data

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points for some patients. Clinically important factors such as gross residual disease and chemotherapy regimens are not available in this database for this cohort of patients. These factors likely have a significant impact on the clinical course of both high-grade and low-grade serous ovarian cancer and deserve further investigation.. However, given the rarity of low-grade serous ovarian cancer, large-scale prospective trials are very challenging to conduct and large database analyses can provide valuable insights in an otherwise difficult to study disease.
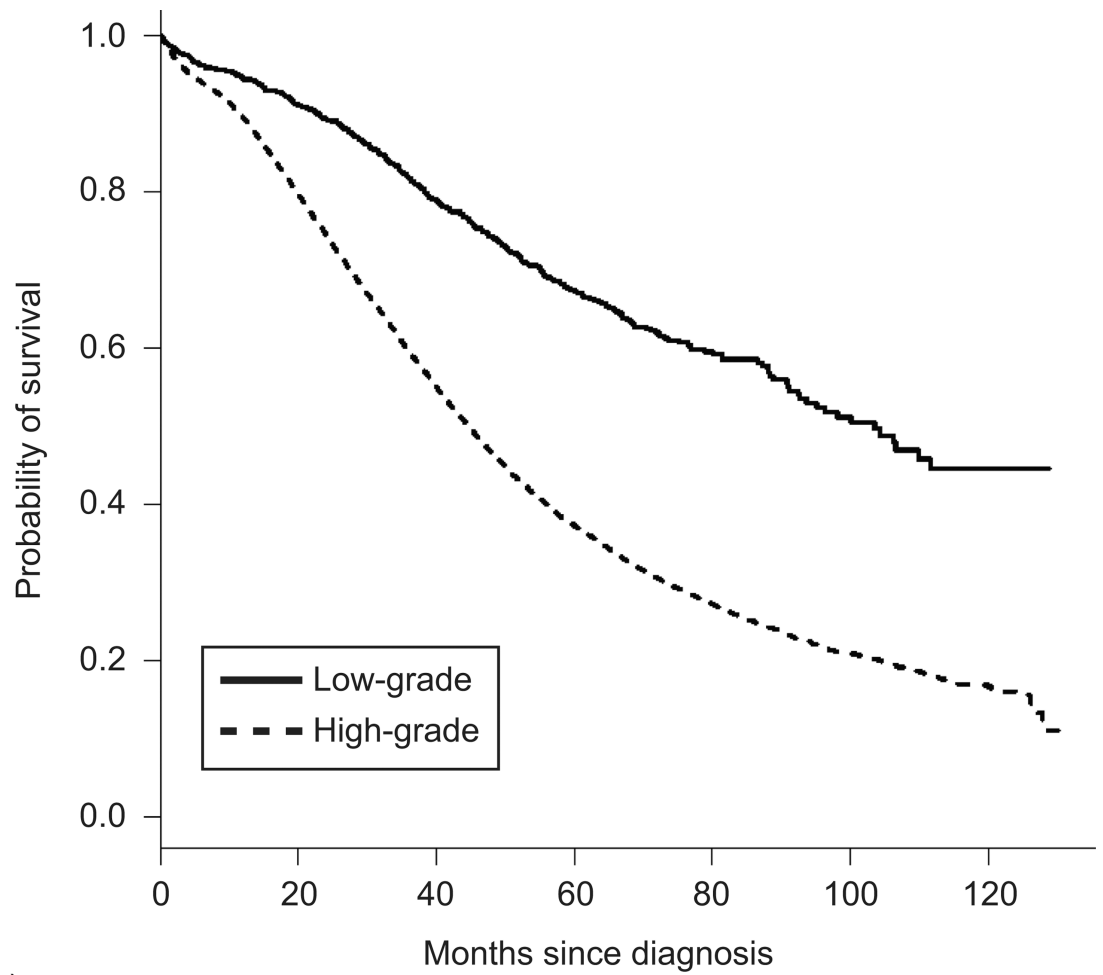
Acknowledgments

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Figure 1.
Mortality for women diagnosed with stage IIIC low-grade and high-grade serous ovarian carcinoma.
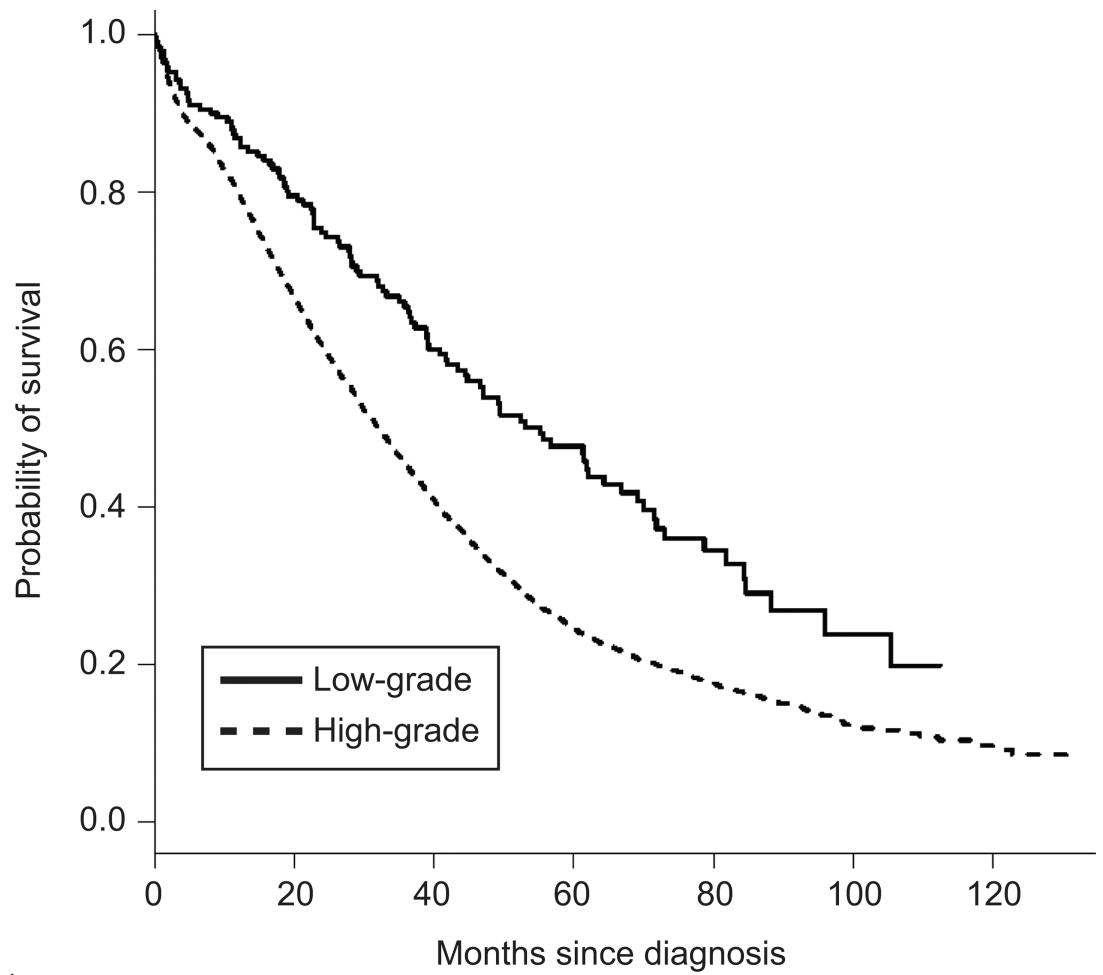
Number at risk (n)							
Low-grade	625	531	359	222	114	43	9
High-grade	12,454	9,182	4,977	2,421	1,011	368	68

Figure 2.
Mortality for women diagnosed with stage IV low-grade and high-grade serous ovarian carcinoma.

Table 1

Demographic and clinical characteristics of the study population.

Characteristic	Low-Grade Tumor	High-Grade Tumor	P
N(%)	755 (4.29)	16,854 (95.71)	
Mean Age [Years (standard deviation)]	53.6 (±15.34)	62.3 (±11.66)	<0.001
Race [N (%)]			0.1
White	695 (92.1)	15,186 (90.1)	
African-American	43 (5.7)	1,108 (6.6)	
Other	17 (2.3)	560 (3.3)	
Year of diagnosis [N (%)]			0.03
2003–2005	268 (35.5)	5,349 (31.7)	
2006–2008	264 (35.0)	5,864 (34.8)	
2009–2011	223 (29.5)	5,641 (33.5)	
Region [N (%)]			<0.001
Northeast	128 (17.0)	3,023 (17.9)	
Midwest	201 (26.6)	4,397 (26.1)	
South	333 (44.1)	6,507 (38.6)	
West	93 (12.3)	2,927 (17.4)	
Charlson/Deyo Score [N (%)]			0.3
0	630 (83.4)	14,032 (83.3)	
1	109 (14.4)	2,320 (13.8)	
2	16 (2.1)	502 (3.0)	
Stage [N (%)]			<0.001
IIIC	625 (82.8)	12,454 (73.9)	
IV	130 (17.2)	4,400 (26.1)	
Lymph Node Dissection [N (%)]	509 (67.4)	9,379 (55.6)	<0.001
Adjuvant Treatment [N (%)]			0.01
None	146 (19.3)	2,776 (16.5)	
Chemotherapy	603 (80.6)	14,026 (83.5)	
Radiation	1 (0.1)	5 (0.0)	
Chemo-radiation	5 (0.7)	47 (0.3)	

Table 2

Effect of various factors on mortality in patients with advanced stage (IIIC and IV) papillary serous ovarian cancer.

Age (Years)	Adjusted Hazard Ratio (95% Confidence Interval)
<60	Ref.
60–69	1.12 (1.07–1.18)
70–79	1.40 (1.31–1.50)
80	2.14 (1.97–2.33)
Time Period	
2003–2005	Ref.
2006–2008	0.90 (0.86–0.94)
2009–2011	0.90 (0.85–0.95)
Race	
White	Ref.
African-American	1.12 (1.03–1.21)
Other	0.89 (0.79–1.00)
Charlson/Deyo Score	
0	Ref.
1	1.18 (1.12–1.25)
2	1.42 (1.28–1.58)
Histology Type	
Low-Grade	Ref.
High-Grade	2.13 (1.89–2.40)
Lymph Node Dissection	
No	Ref.
Yes	0.73 (0.70–0.76)
Stage	
IIIC	Ref.
IV	1.35 (1.29–1.41)
Adjuvant Treatment	
None	Ref.
Chemotherapy	0.57 (0.54–0.60)
Radiotherapy	0.52 (0.17–1.62)
Chemo-radiotherapy	0.74 (0.54–1.03)

[*]Also included in the model: insurance, income level, education, registry location, facility type, hospital volume

Table 3

Adjusted associations between patients' socio-demographic and disease characteristics and use of chemotherapy and lymph node dissection in women with low-grade serous ovarian cancer

Age (Years)	Chemotherapy [Adjusted HR (95% Confidence Interval)]	Lymph Node dissection [Adjusted HR (95% Confidence Interval)]
< 60	Ref.	Ref.
60–69	1.17 (0.66–2.09)	0.68 (0.43–1.08)
70–79	0.67 (0.30–1.49)	0.54 (0.27–1.05)
80	0.47 (0.17–1.27)	0.40 (0.16–0.99)
Time Period		
2003–2005	Ref.	Ref.
2006–2008	1.18 (0.75–1.85)	1.63 (1.10–2.40)
2009–2011	1.67 (1.00–2.77)	1.18 (0.79–1.78)
Race		
White	Ref.	Ref.
Black	0.52 (0.24–1.12)	1.08 (0.53–2.24)
Other	0.29 (0.09–0.87)	1.27 (0.39–4.14)
Registry Location		
Northeast	Ref.	Ref.
Midwest	1.37 (0.69–2.71)	1.36 (0.81–2.26)
South	0.67 (0.37–1.23)	1.26 (0.78–2.03)
West	0.33 (0.16–0.68)	1.45 (0.77–2.72)
Facility Type		
Academic	Ref.	Ref.
Community	0.72 (0.29–1.81)	1.22 (0.53–2.81)
Comprehensive	0.91 (0.60–1.37)	0.84 (0.59–1.18)
Insurance		
None	Ref.	Ref.
Private	1.57 (0.73–3.39)	2.13 (1.11–4.11)
Medicare	1.24 (0.47–3.25)	1.57 (0.70–3.52)
Other Government	3.21 (1.10–9.35)	1.34 (0.59–3.04)
Unknown	1.27 (0.31–5.15)	1.02 (0.32–3.28)
Income		
1st Quartile	Ref.	Ref.
2nd Quartile	1.70 (0.90–3.21)	1.21 (0.70–2.08)
3rd Quartile	1.39 (0.76–2.56)	1.28 (0.74–2.20)
4th Quartile	2.06 (1.06–3.98)	1.38 (0.79–2.42)
Unknown	1.09 (0.24–4.87)	2.22 (0.54–9.10)
Charlson/Deyo Score		
0	Ref.	Ref.

Age (Years)	Chemotherapy [Adjusted HR (95% Confidence Interval)]	Lymph Node dissection [Adjusted HR (95% Confidence Interval)]
1	0.98 (0.56–1.71)	1.28 (0.80–2.06)
2	0.51 (0.16–1.67)	0.95 (0.32–2.83)
Tumor Size		
<1cm	Ref.	Ref.
<2cm	0.32 (0.06–1.86)	0.22 (0.04–1.28)
<3cm	0.77 (0.12–5.01)	0.10 (0.02–0.62)
<4cm	4.83 (0.36–64.11)	0.33 (0.05–2.15)
<5cm	0.26 (0.04–1.52)	0.30 (0.05–1.82)
>5cm	0.71 (0.14–3.44)	0.25 (0.05–1.26)
Unknown	0.63 (0.13–3.14)	0.19 (0.04–0.97)
Stage		
IIIC	Ref.	Ref.
IV	0.64 (0.39–1.03)	0.35 (0.23–0.53)

*Also included in the model urban vs. rural setting and education level not shown.

Table 4

Demographic and clinical characteristics of women with low-grade serous ovarian cancer after propensity score matching for utilization of chemotherapy.

	Chemotherapy	No Chemotherapy	P
N	140	140	
Mean Age [Years (SD)]	57.68 (15.71)	55.99 (15.90)	0.9
Race [N (%)]			0.6
White	115 (84.6)	120 (88.22)	
African-America	16 (11.8)	11 (8.1)	
Other	5 (3.7)	5 (3.7)	
Period of Diagnosis [N (%)]			0.8
2003–2005	57 (41.9)	52 (38.2)	
2006–2008	49 (36.0)	50 (36.8)	
2009–2011	30 (22.1)	34 (25.0)	
Facility Type [N (%)]			0.7
Academic	55 (40.4)	59 (43.4)	
Community	10 (7.4)	7 (5.1)	
Comprehensive	71 (52.2)	70 (51.5)	
Urban vs. Rural [N (%)]			0.8
Urban	120 (88.2)	123 (90.4)	
Rural	2 (1.5)	2 (1.5)	
Unknown	14 (10.3)	11 (8.1)	
Registry Location [N (%)]			0.9
Northeast	23 (16.9)	20 (14.7)	
Midwest	25 (18.4)	24 (17.6)	
South	68 (50.0)	68 (50.0)	
West	20 (14.7)	24 (17.6)	
Income [N (%)]			1.0
1st Quartile	26 (19.1)	25 (18.4)	
2nd Quartile	32 (23.5)	33 (24.3)	
3rd Quartile	42 (30.9)	41 (30.1)	
4th Quartile	30 (22.1)	30 (22.1)	
Unknown	6 (4.4)	7 (5.1)	
Insurance [N (%)]			0.7
None	10 (7.4)	9 (6.6)	
Private	66 (48.5)	75 (55.1)	
Medicare	41 (30.1)	40 (29.4)	
Other Government	14 (10.3)	8 (5.9)	
Unknown	5 (3.7)	4 (2.9)	

	Chemotherapy	No Chemotherapy	P
Charlson/Deyo Score [N (%)]			0.9
0	107 (78.7)	110 (80.9)	
1	23 (16.9)	21 (15.4)	
2	6 (4.4)	5 (3.67	
Education Level [N (%)]			0.9
<7%	23 (16.9)	22 (16.2)	
7–13%	39 (28.7)	44 (32.4)	
13–21%	42 (30.9)	37 (27.2)	
>21%	26 (19.1)	26 (19.1)	
Unknown	6 (4.4)	7 (5.1)	
Stage [N (%)]			0.5
IIIC	110 (80.9)	104 (76.5)	
IV	26 (19.1)	32 (23.5)	
Tumor size [N (%)]			1.0
<1cm	3 (2.2)	2 (1.5)	
<2cm	9 (6.6)	7 (5.1)	
<3cm	5 (3.7)	5 (3.7)	
<4cm	1 (0.7)	1 (0.7)	
<5cm	9 (6.6)	8 (5.9)	
>5cm	58 (42.6)	65 (47.8)	
Unknown	51 (37.5)	48 (35.3)	

*
SD: Standard Deviation.

Table 5

Demographic and clinical characteristics of women with LGCS after propensity score matching for utilization of lymph node dissection.

	Lymph Node Dissection	No Lymph Node Dissection	P
N	202	202	
Mean Age (Years, SD)	54.08 (15.14)	55.54 (14.83)	0.3
Race [N (%)]			0.6
White	185 (91.6)	187 (92.6)	
African-America	10 (5.0)	11 (5.4)	
Other	7 (3.5)	4 (2.0)	
Period of Diagnosis [N (%)]			0.3
2003–2005	87 (43.1)	81 (40.1)	
2006–2008	54 (26.7)	68 (33.7)	
2009–2011	61 (30.2)	53 (26.2)	
Facility Type [N (%)]			0.8
Academic	91 (45.0)	96 (47.5)	
Community	10 (5.0)	9 (4.5)	
Comprehensive	101 (50.0)	97 (48.0)	
Urban vs. Rural [N (%)]			0.8
Urban	188 (93.1)	188 (93.1)	
Rural	2 (1.0)	3 (1.5)	
Unknown	12 (5.9)	11 (5.4)	
Registry Location [N (%)]			0.9
Northeast	40 (19.8)	37 (18.3)	
Midwest	46 (22.8)	50 (24.8)	
South	93 (46.0)	89 (44.1)	
West	23 (11.4)	26 (12.9)	
Income [N (%)]			0.9
1st Quartile	26 (12.9)	25 (12.4)	
2nd Quartile	53 (26.2)	56 (27.7)	
3rd Quartile	58 (28.7)	59 (29.2)	
4th Quartile	59 (29.2)	55 (27.2)	
Unknown	6 (3.0)	7 (3.5)	
Insurance [N (%)]			0.9
None	17 (8.4)	15 (7.4%)	
Private	111 (55.0)	111 (55.0%)	
Medicare	50 (24.8)	54 (26.7%)	
Other Government	16 (7.9)	17 (8.4%)	
Unknown	8 (4.0)	5 (2.5%)	

	Lymph Node Dissection	**No Lymph Node Dissection**	**P**
Charlson/Deyo Score [N (%)]			0.7
0	167 (82.7)	168 (83.2)	
1	31 (15.3)	28 (13.9)	
2	4 (2.0)	6 (3.0)	
Education Level [N (%)]			0.7
<7%	48 (23.8)	46 (22.8)	
7–13%	75 (37.1)	65 (32.2)	
13–21%	48 (23.8)	53 (26.2)	
>21%	25 (12.4)	31 (15.3)	
Unknown	6 (3.0)	7 (3.5)	
Stage [N (%)]	171 (84.7)	165 (81.7)	
IIIC	31 (15.3)	37 (18.3)	
IV			
Tumor size [N (%)]			0.7
<1cm	4 (2.0)	2 (1.0)	
<2cm	9 (4.5)	9 (4.5)	
<3cm	10 (5.0)	6 (3.0)	
<4cm	5 (2.5)	4 (2.0)	
<5cm	12 (5.9)	8 (4.0)	
> 5cm	95 (47.0)	98 (48.5)	

[*]SD: Standard Deviation.