HHS Public Access

Author manuscript

World J Obstet Gynecol. Author manuscript; available in PMC 2018 March 06.

Published in final edited form as:

World J Obstet Gynecol. 2016 ; 5(2): 187–196. doi:10.5317/wjog.v5.i2.187.

Gynecologic oncologists involvement on ovarian cancer standard of care receipt and survival

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Abstract

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Author contributions: Rim SH, Thomas CC and Stewart SL conceived of the study; Rim SH, Hirsch S, Thomas CC, Brewster WR, Cooney D, Thompson TD and Stewart SL wrote the paper and made substantial contributions to the conception, design, data analysis and interpretation of the data; Rim SH, Hirsch S, Thomas CC, Brewster WR and Stewart SL drafted and/or critically reviewed the manuscript for important intellectual content; all authors read and approved the final manuscript.

Institutional review board statement: The study was reviewed and approved by the Centers for Disease Control and Prevention Institutional Review Board through an expedited review process in accordance with standard procedures.

Informed consent statement: The Institutional Review Board determined that informed consent was not needed, since the analytic dataset used contained only de-identified patient information and there was no patient contact in this study.

Conflict-of-interest statement: The authors declare that they have no competing interests.

Data sharing statement: No additional data are available.

Core tip: A significant survival advantage is associated with receiving surgical standard of care (SOC), yet still some women had lower odds of receiving surgical SOC.

AIM—To examine the influence of gynecologic oncologists (GO) in the United States on surgical/chemotherapeutic standard of care (SOC), and how this translates into improved survival among women with ovarian cancer (OC).

METHODS—Surveillance, Epidemiology, and End Result (SEER)-Medicare data were used to identify 11688 OC patients (1992–2006). Only Medicare recipients with an initial surgical procedure code (n = 6714) were included. Physician specialty was identified by linking SEER-Medicare to the American Medical Association Masterfile. SOC was defined by a panel of GOs. Multivariate logistic regression was used to determine predictors of receiving surgical/chemotherapeutic SOC and proportional hazards modeling to estimate the effect of SOC treatment and physician specialty on survival.

RESULTS—About 34% received surgery from a GO and 25% received the overall SOC. One-third of women had a GO involved sometime during their care. Women receiving surgery from a GO *vs* non-GO had 2.35 times the odds of receiving the surgical SOC and 1.25 times the odds of receiving chemotherapeutic SOC ($P < 0.01$). Risk of mortality was greater among women not receiving surgical SOC compared to those who did [hazard ratio = 1.22 (95%CI: 1.12–1.33), $P < 0.01$], and also was higher among women seen by non-GOs *vs* GOs (for surgical treatment) after adjusting for covariates. Median survival time was 14 mo longer for women receiving combined SOC.

CONCLUSION—A survival advantage associated with receiving surgical SOC and overall treatment by a GO is supported. Persistent survival differences, particularly among those not receiving the SOC, require further investigation.

Keywords

Ovarian neoplasms; Gynecologic oncologist; Guidelines-based care; Surveillance; Epidemiology; and End Result Medicare

INTRODUCTION

Women in the United States with advanced stage epithelial ovarian cancer (OC) have an overall 5-year survival rate of about 30%[1]. As with many cancers, survival is closely linked with the stage of diagnosis, such that women with localized (stage I) disease have a relative 5-year survival rate of 92%; the prognosis however declines with late stage disease and metastases[2]. Without an adequate early detection strategy, ensuring that women receive appropriate, standard of care (SOC) treatment is a very important intervention that has demonstrated reduction in OC mortality[3].

National Comprehensive Cancer Control Network (NCCN) current treatment recommendations for women with epithelial OC include an evaluation prior to initiating chemotherapy along with accurate surgical staging and primary debulking surgery/cytoreduction performed by a gynecologic oncologist (GO)[3]. In most but not all cases, at least six cycles of platinum and taxane-based chemotherapy administration is recommended for advanced epithelial OCs[3]. Appropriate care not only constitutes the receipt of SOC treatment, but also quality care from an experienced GO, who is trained to both perform the surgery and administer chemotherapy[3,4]. The evidence supporting better guideline-

adherent care and outcomes among patients seen by a GO has been previously examined[5–8], and prior studies suggest only 30%–40% of women with OC are treated by a GO[5,9–11]. While NCCN cancer center patients tend to receive guideline-adherent care[12], there is potential in exploring whether differences in SOC treatment are affected across patient-level demographic and clinical subgroups.

To date, few studies have jointly considered surgical and chemotherapeutic SOC indicators in examining survival in OC patients[13–17]. In this study, we examine predictors of both SOC receipt (surgical and chemotherapeutic) and adherence to these treatments among women treated by GOs compared to non-GOs. We further quantified the survival advantage of SOC treatment receipt among OC patients.

MATERIALS AND METHODS

Data source and study population

The study included all women in the Surveillance, Epidemiology, End Results (SEER)-Medicare database[18] diagnosed with OC from January 1, 1992 to December 31, 2006 (n = 38972). We excluded women who did not have a primary epithelial OC diagnosis (n = 6175); were Medicare age-ineligible (age < 66) at date of diagnosis (n = 11716); had an invalid month of diagnosis (n = 166); had diagnoses based on autopsy or death certificate only (n = 543); had a nonepithelial ovarian malignancy (n = 3198); and were not continuously enrolled in both Medicare Part A and B or were enrolled in an Health Maintenance Organization plan during the course of treatment (n = 5486). A total of 11688 OC patients met the inclusion criteria for the study.

Definition of variables

Patient-level covariates included age, race, stage at diagnosis, marital status, year of diagnosis, geographic region of SEER registry, and cancer histology. The Charlson-Klabunde comorbidity index score was determined using Medicare claims data for 12 mo prior to and 4 mo after cancer diagnosis date, per prior studies[19,20].

We examined all procedure codes in the Medicare claims data falling within a treatment window (defined as two months prior to and one year after the diagnosis date) to determine if a patient received surgical or chemotherapeutic SOC. Since only month and year of diagnosis are reported in the SEER database, the 15th day of the month was assigned as the day of diagnosis for each patient.

SOC definitions

Per recommendation from an experienced group of GOs, consulted specifically for this project (W. Brewster, R.E. Bristow and D.K. Singh), the International Federation of Gynecologists and Obstetricians (FIGO) stage of disease categories were grouped as: I A/I B, I C/II, IIIA/III B and IIIC/IV based on similarities in current surgical and chemotherapeutic treatment regimens. FIGO stage III NOS and stage IV were grouped into stage IIIC/IV group, given that a high proportion of all stage III cases were stage IIIC.

Among the women who met the inclusion criteria (n = 11688), we examined receipt of SOC among women receiving any initial surgical care. Thus, we further excluded women who received treatment outside of the treatment window (n = 28), those who had no procedure codes of interest for any surgical care (n = 2464), and women who received neoadjuvant chemotherapy (n = 2482) (given the difficulty of cancer staging for women who are eligible for neoadjuvant chemotherapy) to examine differences in guideline-adherent treatment and survival. We also excluded all OC patients diagnosed with stage I NOS or who were unstaged at diagnosis since minimum SOC parameters are not well defined for these groups.

The GO group defined minimum surgical SOC as lymph node dissection, omentectomy and oophorectomy for all patients with FIGO stage IA/IB, IC/II or IIIA/IIIB at diagnosis, but omentectomy and oophorectomy only for women with stage IIIC/IV at diagnosis. Minimum chemotherapy SOC definition depended on: (1) stage of disease at diagnosis; (2) number of chemotherapy cycles received; and (3) type of chemotherapy agent received. For analysis, chemotherapy SOC was defined as an individual receiving the defined number of cycles (three cycles of chemotherapy for stage IC/II and six cycles for stage III/IV), with at least one multi-agent cycle (defined as one platinum based and one non-platinum based agent) using either intravenous or intraperitoneal modes of administration. One cycle of chemotherapy was equal to three weeks of treatment, given that chemotherapy is usually administered every 3–4 wk[3,21]. Patients were documented as receiving overall SOC if they received both surgical and adjuvant chemotherapeutic SOC.

The GO group recommended surgical and chemotherapy procedure codes for use in determining SOC for each FIGO stage category. Procedure codes included both International Classification of Diseases, Ninth revision, clinical modification codes and American Medical Association (AMA) Current Procedural Terminology codes.

Surgeon specialty definition

Self-reported, physician specialty information from the SEER-Medicare claims file was linked with and verified against the AMA Physician Masterfile using the unique provider identification number (UPIN) for physicians performing (or those in attendance) of an OC procedure of interest. If the operating physician UPIN was not available, but the attending physician UPIN was available, AMA specialty was assigned to the attending physician. If the UPIN for an operating and attending physician was unavailable, the self-reported physician specialty variable found in the Medicare data set was used to define specialty. When a patient received treatment from multiple physicians, care was attributed to the most specialized physician (most to least specialized: GO, gynecologist, general surgeon, and other physician). For analytic purposes, physician specialty was grouped as GO and non-GO.

Statistical analysis

We examined predictors associated with receipt of surgical and chemotherapeutic SOC. A forward selection logistic regression model was used to examine each question. Comparisons of the distribution of OC patients receiving the SOC by physician specialty was examined using the Pearson χ^2 test.

Cox proportional hazard methods were used to determine differences in survival time from date of OC diagnosis to date of death. The proportional hazards assumption was examined by testing interactions between time and each covariate in the model. The final models (Model 1 and 2) exclude women (n = 1003) who died within 4.5 mo after diagnosis (*i.e.*, women who did not live long enough to receive chemotherapy SOC). Due to a common category in the chemotherapy variables (chemotherapy SOC and chemotherapy physician specialty), we examined two different models. The first model (Model 1) examined surgery physician specialty and receipt of both SOC measurements, while the second model (Model 2) examined both surgery and chemotherapy physician specialty and receipt of surgery SOC, adjusting for patient-level and clinical factors. All final models were adjusted for covariates that had a statistically significant association from the bivariate analysis or were of importance in the literature. All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, United States).

RESULTS

Among the 11688 OC patients, 57.4% (n = 6714) received an initial surgical procedure code of interest. Table 1 shows the patient and tumor characteristics by the type of physician performing the initial surgery. The mean age of patients was mid to late-70s; most women were white, married or widowed, had no comorbidities, had FIGO stage IIIC/IV disease, and serous histology. More women received an initial surgical procedure from OB/GYNs (n = 3088) than GOs (n = 2254), general surgeons (n = 914), or other non-GO/unknown specialties (n = 419).

Among women treated by a GO, 79.2% received the surgical SOC and 52.8% received the chemotherapy SOC (Figure 1). Regardless of stage at diagnosis, women more frequently received surgical and chemotherapeutic SOC from a GO than from a non-GO.

Table 2 reports the factors associated with receipt of surgical SOC after adjusting for other covariates. Surgery performed by a GO was strongly associated with receiving surgical SOC [odds ratio (OR) for GO = 2.35; 95%CI: 2.03–2.71]. Other factors associated with greater odds of surgical SOC receipt included: More advanced stage of disease, white *vs* African-American race, younger age at diagnosis, serous *vs* adenocarcinoma not otherwise specified histologic type, being married *vs* not married, and diagnosis during the later years of the study period.

Table 2 also reports factors associated with receipt of the minimum chemotherapy SOC after adjusting for other covariates. Women who obtained chemotherapy from a GO had a higher odds of receiving chemotherapeutic SOC (OR = 1.25, 95%CI: 1.07–1.47). Other statistically significant factors for higher odds of chemotherapeutic SOC included: Less advanced stage of disease, younger age at diagnosis, histologic type (serous compared with endometrioid/mucinous/clear cell), being married compared with unmarried, living in the SEER Midwest region (compared to the SEER Northeast), and diagnosis during more recent years.

Table 3 shows the Cox regression model of time to death among the sample of OC patients who received a primary surgery procedure who did not die within 4.5 mo after diagnosis. In

Table 3 (Model 1), women who did not receive surgery SOC had increased mortality compared to women who did [hazard ratio 1.22 (95%CI: 1.12–1.33)]. Similarly, women who did not receive any chemotherapy SOC had a higher risk of earlier death compared to women who received the full contingent of chemotherapy [hazard ratio 1.29 (95%CI: 1.14–1.46)]. Increasing age, late stage disease, higher number of comorbidities, and mucinous histology compared to serous histology were all associated with increased death (Table 3, Model 1). Similar patterns were observed in Table 3, Model 2 after controlling for chemotherapy physician specialty (as opposed to chemotherapy SOC). For Model 2, women who received surgery from a GO had better survival. Although there was no significant difference in survival between chemotherapy treatment from a GO compared to non-GO, those not receiving any chemotherapy had a significantly shorter survival time (Table 3, Model 2). The median survival time for women who received the overall SOC was 52 mo compared to 38 mo for women that did not receive the overall surgical and chemotherapeutic SOC (Figure 2).

DISCUSSION

Our findings show that among OC patients receiving initial surgical treatment, only 25% of women received the overall SOC as defined by our panel of GOs. Few women (approximately one-third of women receiving a surgical procedure) had a GO involved at any point during their care. Women who obtained surgery from a GO however, were more likely to receive the surgical SOC and chemotherapeutic SOC than women who obtained treatment from a non-GO. The median survival time was 14 mo longer for women who received the overall SOC compared to women who did not receive overall SOC.

Our results are consistent with prior studies that suggest that appropriate surgical treatment in the United States is more frequently performed when a GO is the treating physician[5]. Data from a single state cancer registry study by Chan *et al*[14] showed that women with OC under the care of GOs were more likely to receive appropriate staging and chemotherapy treatments, controlling for age, stage, and grade of disease. Also similar to previous studies, our results suggest that greater utilization of GOs in the care of OC patients would be beneficial[22]. Although the level of detail in our analysis is unable to discriminate the factors underlying the low utilization, it is likely that our results reflect a complex interaction of both preference and access-relevant effects, such as the influence of a patient's choice in receipt of GO care *vs* a shortage of available GOs in some areas.

While patient treatment preferences can independently and significantly affect chemotherapy receipt[23], geographic access may also play an important role in (both chemotherapeutic or surgical) treatment receipt from a GO. For example, a previous analysis reported on the unequal distribution of GOs in the United States[24]. A recently published study suggested that OC mortality may be a function of distance to a practicing GO as counties located more than 50 miles from a gynecologic oncology practice had almost 60% increased likelihood of OC mortality than those physically closer to a practice location[25]. While earlier research efforts have indicated that treatment of OC can be improved by early referral to a GO[5,10], referral and consultation from GOs have generally been low, with only about 39% of family physicians and 51% of general internists self-reporting referrals to a GO[26]. Given that

surgery is an important determinant of outcomes for OC patients, receiving surgery/treatment from surgeons with specialized training in pelvic surgery (*i.e.*, GOs)[27], who see a high volume of cases[10,28] at high volume facilities treating more than 20 OC cases per year[28,29], might help improve outcomes.

It is important to note that there are still subgroups that require further research. Although African-American women were more likely than their white counterparts to receive their initial surgical procedure from a GO (data not shown), they had lower odds of receiving the surgical SOC and there was no difference in survival after adjusting for physician specialty, surgical SOC, and other tumor and sociodemographic characteristics. The increased risk of death among African American women noted in other studies, when controlling for receipt of chemotherapeutic SOC, suggests that there may be some important nuanced differences in the definitions of chemotherapeutic SOC[30,31], chemotherapeutic agents, and/or interaction effects between age, comorbidity, stage, and race that have not been adequately explored. Bristow *et al*[32] have previously suggested similar differences in survival between African-American and white OC patients and the complexity of examining race-based survival associations[33,34].

The findings in this study should be considered in light of several limitations: (1) our analysis was focused on fee for service Medicare; women who received treatment under managed care were not included because the managed care cases did not include codes to identify specific treatment procedures; (2) neoadjuvant chemotherapy cases, which could have later received surgical SOC, were excluded; and (3) it is a challenge to operationalize NCCN recommendations into an analytic/computer program because the recommendations are relatively complex, and some information required for the NCCN decision algorithms is not available in claims data. However, our panel of experienced GOs developed a simpler, but accurate definition of the SOC so that recommendations could be converted into analytic code. Similarly, since SOC definitions were varied for each stage at diagnosis, if claims data were not available for the full contingency of treatment procedures, it is possible that there was an underestimation of patients identified as receiving overall SOC in that subgroup. Fourth, given the limitations of Medicare data, inaccuracies or incomplete data in billing, drug, or procedure codes could have resulted in an underestimate or overestimate of the total number of surgeries and/or chemotherapy procedures performed, thus biasing the estimate. Previous studies have noted some concerns in the validation of chemotherapeutic agents within Medicare claims data[30,31]. Fifth, there is potential for misclassification of physician specialty, given the use of multiple data sources including operating physician, attending physician, and self-reported physician specialty[35]. Furthermore, in our analysis, receipt of treatment from a GO was designated as such if a GO had been seen at any point during the care. Lastly, since we assumed each cycle of treatment lasted three weeks, we calculated that it would take at least 4.5 mo for women diagnosed with stage IIIC or IV to complete the chemotherapy SOC as defined in our study. Thus, women who died within five months of the diagnosis date would not have had the opportunity to receive chemotherapy SOC. Our definition of chemotherapy SOC may have been too rigorous and potentially introduce selection or survival bias.

Our study showed that GOs more often provided the surgical and chemotherapeutic SOC. The receipt of surgical standards was associated with better survival outcomes, even after adjusting for provider specialty. As such, these two NCCN-recommendations (*i.e.*, treatment from a GO and receipt of SOC) continue to be critical points of intervention for improving survival time and reducing deaths from OC. Although it is difficult to determine when adjuvant chemotherapy is warranted based on sound clinical judgement (*i.e.*, taking into consideration the patient's comorbidities, toxicities, age, *etc.*) or patient refusal, one area that has not been carefully examined is the potential that race/ethnicity-based differences in patient and caregiver preferences may have for OC care. Future research may further explore this and the interaction effects of race, age, comorbidities on survival.

Acknowledgments

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Supported by The United States Federal Government, Centers for Disease Control and Prevention, Atlanta, GA, United States.

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COMMENTS

Background

Ovarian cancer (OC) is the deadliest gynecologic cancer among women. Standard treatment for OC consists of extensive surgery and chemotherapy. Gynecologic oncologists (GOs) more often adhere to standard treatment guidelines among OC patients, resulting in longer patient survival.

Research frontiers

Low survival rates from OC may be related to lack of GO involvement in surgery or chemotherapy and/or lack of standard treatment receipt. Research measuring receipt of standard of care and its effect on survival can help reveal areas for intervention to improve OC mortality.

Innovations and breakthroughs

These results among over 6000 OC patients aged 65 and older indicate that a low proportion received standard treatment. Not having seen a GO, African American race, and being older (80+) were associated with not receiving standard treatment. Women who received standard treatment survived over one year longer than those who did not receive standard treatment.

Applications

Ensuring appropriate referral of OC patients to GOs for treatment will likely increase survival rates from OC. Education of primary care providers and/or health systems changes that promote referral would be beneficial to increase referral rates. Research is needed into patient factors and other potential reasons underlying lack of referral.

Terminology

GOs are subspecialists trained to administer both surgical and chemotherapeutic treatment to OC patients.

Peer-review

The authors investigated the influence of GO in the United States on surgical/chemotherapeutic SOC, and how this translates into improved survival among women with OC. The authors claimed that a survival advantage is associated with receiving surgical SOC and overall treatment by a GO. This manuscript provides useful information to the medical students, clinicians, and researchers in this field.

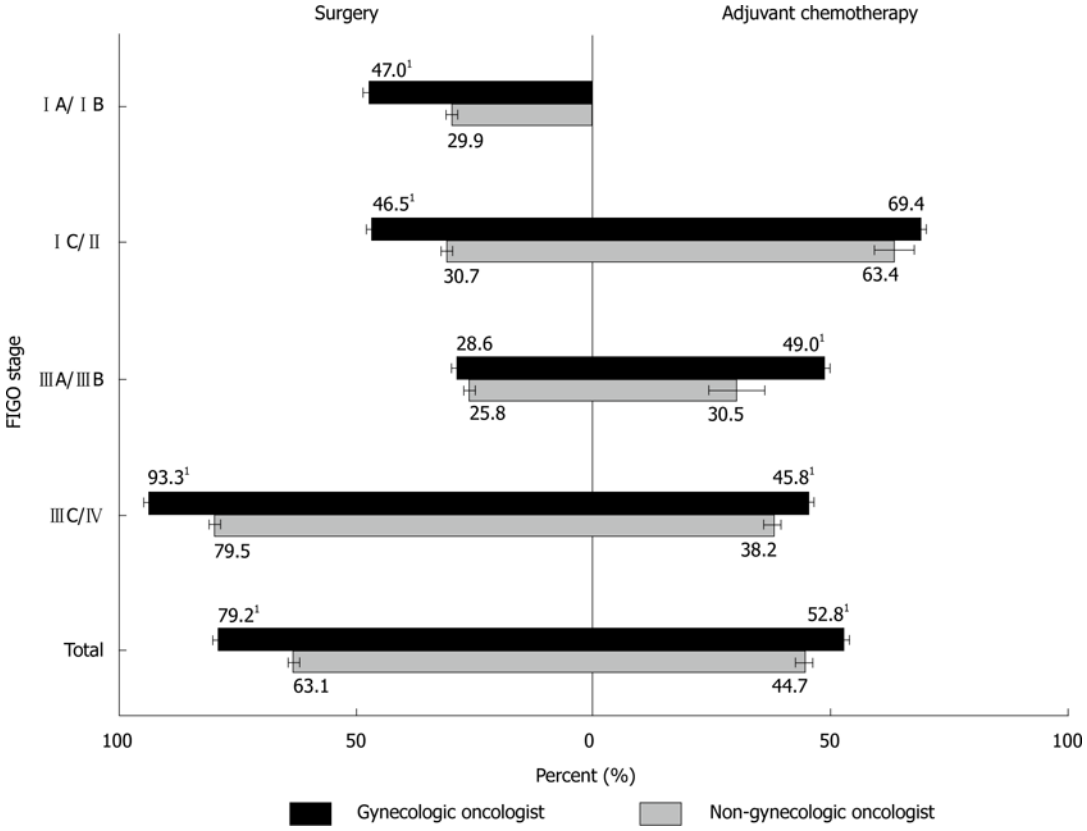

Figure 1. Surgical standard of care (*n* = 4434) and adjuvant chemotherapy standard of care (*n* = 2595) receipt by physician specialty and International Federation of Gynecologists and Obstetricians stage

(1) Surgery SOC treatment was based on ovarian cancer patients receiving surgery prior to chemotherapy (*n* = 6714); (2) Stages 1, not otherwise specified and Unknown/unstaged were removed from analysis; (3) Surgeon specialty and chemotherapy specialty was categorized according to the most specialized care received during the course of the treatment window; (4) Women who received surgery SOC by a surgeon specialty who could not be identified are not shown (*n* = 17); (5) There were 177 women who received a chemotherapy procedure code of interest but for whom physician specialty could not be identified and 1238 women who did not receive a chemotherapy procedure code of interest.[1] Denote that the estimate is statistically significantly higher for GO compared to Non-GO. SOC: Standard of care; GO: Gynecologic oncologist.

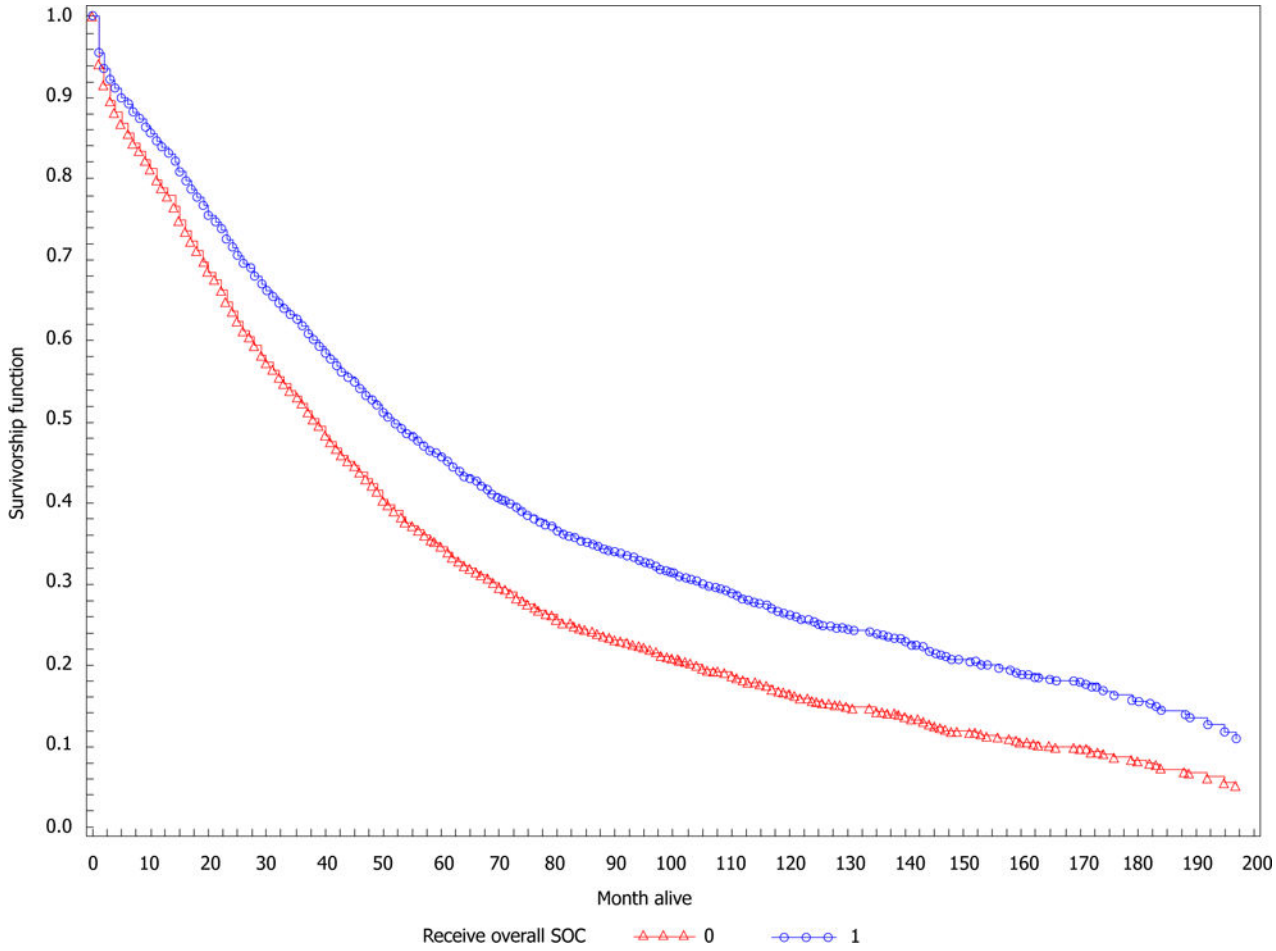

Figure 2. Ovarian cancer survivor curves[1] by receipt of overall standard of care[2] (*n* = 1678)

[1]All covariates held at the reference level noted in Table 3; [2]0 = Did not receive overall standard of care; 1 = Did receive overall SOC. SOC: Standard of care.

Table 1

Characteristics of ovarian cancer patients who received any initial surgical procedure by physician specialty (*n* = 6714)

Characteristic	Surgeon specialty[1]			
	GO	Non-GO		
		OBGYN	General surgeon	Other[2]
No. of patients	2254	3088	914	419
Mean age at diagnosis (stddev)	74.6 (5.9)	74.8 (6.1)	77.0 (6.8)	75.5 (6.2)
Race *n* (%)				
White	1995 (88.5)	2844 (92.1)	827 (90.5)	379 (90.5)
African American	121 (5.4)	104 (3.4)	49 (5.4)	26 (6.2)
Hispanic	35 (1.6)	31 (1.0)	*3*	*3*
Asian	53 (2.4)	66 (2.1)	*3*	*3*
Other[4]	47 (2.1)	37 (1.2)	*3*	*3*
Marital status				
Married	1052 (46.7)	1424 (46.1)	327 (35.8)	170 (40.6)
Single	159 (7.1)	221 (7.2)	53 (5.8)	31 (7.4)
Divorced	148 (6.6)	166 (5.4)	58 (6.3)	29 (6.9)
Widowed	799 (35.4)	1168 (37.8)	458 (50.1)	176 (42.0)
Separated/unknown	96 (4.2)	109 (3.5)	*3*	*3*
Charlson-Klabunde comorbidity score				
0	1521 (67.5)	2133 (69.1)	605 (66.2)	266 (63.5)
1	498 (22.1)	644 (20.9)	188 (20.6)	93 (22.2)
2	175 (7.8)	189 (6.1)	78 (8.5)	38 (9.1)
3	45 (2.0)	80 (2.6)	29 (3.2)	*3*
4 or more	*3*	42 (1.4)	*3*	*3*
FIGO treatment stage				
IA/IB	200 (8.9)	383 (12.4)	66 (7.2)	43 (10.3)
IC/II	276 (12.2)	516 (16.7)	90 (9.8)	40 (9.5)
IIIA/IIIB	119 (5.3)	179 (5.8)	59 (6.5)	*3*
IIIC/IV	1580 (70.1)	1898 (61.5)	660 (72.2)	308 (73.5)
Unstaged/NOS	79 (3.5)	112 (3.7)	39 (4.2)	*3*
Histology				
Serous	1460 (64.8)	1897 (61.4)	554 (60.6)	254 (60.6)
Endometrioid	238 (10.6)	381 (12.3)	73 (8.0)	46 (11.0)
Mucinous	129 (5.7)	235 (7.6)	79 (8.6)	25 (6.0)
Clear cell	84 (3.7)	127 (4.1)	*3*	*3*
Adenocarcinoma	275 (12.2)	344 (11.1)	175 (19.1)	66 (15.8)
Other[5]	68 (3.1)	104 (3.3)	20 (2.2)	*3*

[1] Surgeon specialty was categorized according to the most specialized care received during the course of the treatment window

[2]39 women received a surgery procedure code during the treatment window (defined as a period of two months prior and one year after a patient's diagnosis date in which procedures were performed) but surgeon specialty could not be identified

[3]Denotes cell size suppression of less than 20

[4]Other race includes designation of "Other" or Native American

[5]Other histology includes Transitional. GO: Gynecologic oncologists; FIGO: International Federation of Gynecologists and Obstetricians; NOS: Not otherwise specified.

Table 2

Predictors of receipt of minimum surgical and chemotherapeutic standard of care[1]

	Surgical standard of care[2]		Chemotherapeutic standard of care[2]	
	Odds ratio (95%CI)	***P* value**	**Odds ratio (95%CI)**	***P* value**
Physician specialty[3]				
Gynecologic oncologist	2.35 (2.03–2.71)	< 0.01	1.25 (1.07–1.47)	0.006
Non-gynecologic oncologist	1.00		1.00	
Age at diagnosis				
66–69	1.00		1.00	
70–74	0.80 (0.67–0.96)	0.017	0.93 (0.78–1.09)	0.393
75–79	0.83 (0.69–1.0)	0.053	0.79 (0.66–0.94)	0.008
80–84	0.58 (0.47–0.71)	< 0.01	0.61 (0.48–75)	< 0.001
⩾ 85	0.40 (0.31–0.51)	< 0.01	0.31 (0.21–0.48)	< 0.001
Race[4]				
White	1.00			
African American	0.67 (0.50–0.91)	0.01	–	
Other	0.83 (0.62–1.10)	0.208	–	
Treatment stage[5]				
IA/IB	0.08 (0.07–0.10)	< 0.01	NA	NA
IC/II	0.08 (0.07–0.10)	< 0.01	3.46 (2.86–4.18)	< 0.001
IIIA/IIIB	0.05 (0.04–0.07)	< 0.01	0.83 (0.64–1.09)	0.182
IIIC/IV	1.00		1.00	
Charlson-Klabunde comorbidity score				
0	1.00		1.00	
1	0.84 (0.72–0.98)	0.029	0.84 (0.71–0.99)	0.029
2	0.81 (0.63–1.02)	0.084	0.78 (0.60–1.03)	0.078
3	0.65 (0.44–0.97)	0.039	0.49 (0.31–0.80)	0.005
4 or more	1.09 (0.60–1.97)	0.771	0.63 (0.29–1.37)	0.247
Histology				
Serous	1.00		1.00	
Endometrioid	1.10 (0.90–1.35)	0.356	0.70 (0.56–0.89)	0.003
Mucinous	0.95 (0.74–1.35)	0.67	0.49 (0.34–0.70)	< 0.001
Clear cell	1.29 (0.93–1.78)	0.13	0.62 (0.41–0.93)	0.026
Transitional	0.70 (0.27–1.79)	0.454	0.76 (0.30–1.97)	0.572
Adenocarcinoma (NOS)	0.44 (0.37–0.54)	< 0.001	1.04 (0.86–1.27)	0.695
Other	1.05 (0.70–1.56)	0.813	0.74 (0.47–1.13)	0.168
Marital status				
Married	1.00		1.00	
Not married	0.83 (0.72–0.95)	0.007	0.75 (0.66–0.86)	< 0.001
Unknown	1.03 (0.69–1.52)	0.87	0.73 (0.48–1.09)	0.127
Year of diagnosis				

	Surgical standard of care[2]		Chemotherapeutic standard of care[2]	
	Odds ratio (95%CI)	***P* value**	**Odds ratio (95%CI)**	***P* value**
1993–1997	0.62 (0.52–0.73)	< 0.01	0.28 (0.23–0.33)	< 0.001
1998–2002	0.79 (0.68–0.92)	0.003	1.09 (0.94–1.26)	0.261
2003–2006	1.00		1.00	
SEER region[4]				
Northeast	–		1.00	
Midwest	–		0.76 (0.62–0.93)	0.009
South	–		1.09 (0.88–1.37)	0.424
West	–		0.93 (0.78–1.10)	0.391

[1] Minimum SOC treatment was based on patients receiving surgery prior to chemotherapy ($n = 6714$)

[2] Surgery SOC ($n = 4434$) and chemotherapy SOC ($n = 2595$)

[3] Physician specialty was categorized according to the most specialized care received during the course of the treatment window; there were 39 and 177 cases where physician specialty could not be identified for surgery or chemotherapy procedures, respectively (results for this group not shown)

[4] Race was not entered into the chemotherapy SOC model based on forward selection entry criteria ($P \leq 0.10$); Region was not entered into the surgery SOC model based on forward selection entry criteria ($P \leq 0.10$)

[5] Stage I NOS, Stage IA/IB (for chemotherapy SOC) and unknown/unstaged were removed from the analysis since current guidelines recommend early stage patients not receive chemotherapy treatment. NOS: Not otherwise specified; SOC: Standard of care; SEER: Surveillance, Epidemiology, and End Result; NA: Not applicable.

Table 3

Cox proportional hazard model of time-to-death among ovarian cancer patients

Predictor	Model 1[1]		Model 2[1]	
	Hazard ratio (95%CI)	*P* value	Hazard ratio (95%CI)	*P* value
Received surgery SOC[2]				
Yes	1.00		1.00	
No	1.22 (1.12–1.33)	< 0.01	1.21 (1.11–1.31)	< 0.01
Received chemotherapy SOC[2]			*4*	
Yes	1.00		*4*	
No, but received some chemotherapy	0.95 (0.89–1.02)	0.18	*4*	
Received no chemotherapy	1.29 (1.14–1.46)	< 0.01	*4*	
Age at diagnosis				
66–69	1.00		1.00	
70–74	1.07 (0.98–1.17)	0.13	1.05 (0.97–1.15)	0.24
75–79	1.23 (1.12–1.34)	< 0.01	1.21 (1.10–1.32)	< 0.01
80–84	1.52 (1.37–1.69)	< 0.01	1.48 (1.33–1.65)	< 0.01
⩾ 85	1.96 (1.70–2.26)	< 0.01	1.92 (1.67–2.21)	< 0.01
Race				
White	1.00		1.00	
African American	1.11 (0.95–1.29)	0.18	1.13 (0.97–1.32)	0.12
Other	0.90 (0.78–1.05)	0.17	0.88 (0.75–1.02)	0.09
Year of diagnosis				
1993–1997	1.27 (1.17–1.38)	< 0.01	1.24 (1.14–1.35)	< 0.01
1998–2002	1.18 (1.09–1.27)	< 0.01	1.17 (1.08–1.27)	< 0.01
2003–2006	1.00		1.00	
Treatment stage				
IA/IB	0.20 (0.18–0.23)	< 0.01	0.17 (0.15–0.20)	< 0.01
IC/II	0.35 (0.32–0.40)	< 0.01	0.36 (0.32–0.40)	< 0.01
IIIA/IIIB	0.61 (0.53–0.71)	< 0.01	0.62 (0.54–0.71)	< 0.01
IIIC/IV	1.00		1.00	
Charlson-Klabunde comorbidity score				
0	1.00		1.00	
1	1.28 (1.18–1.38)	< 0.01	1.26 (1.17–1.36)	< 0.01
2	1.38 (1.22–1.56)	< 0.01	1.37 (1.21–1.55)	< 0.01
3	1.64 (1.34–2.00)	< 0.01	1.64 (1.34–2.01)	< 0.01
⩾ 4	2.33 (1.73–3.15)	< 0.01	2.27 (1.67–3.09)	< 0.01
Histology				
Serous	1.00		1.00	
Endometrioid	0.76 (0.68–0.85)	< 0.01	0.75 (0.68–0.84)	< 0.01
Mucinous	1.22 (1.06–1.41)	< 0.01	1.22 (1.06–1.41)	< 0.01
Clear cell	0.83 (0.69–1.00)	0.05	0.83 (0.69–1.00)	0.05
Transitional	0.79 (0.47–1.31)	0.36	0.79 (0.48–1.32)	0.37

Predictor	Model 1[1]		Model 2[1]	
	Hazard ratio (95%CI)	*P* value	Hazard ratio (95%CI)	*P* value
Adenocarcinoma (NOS)	1.07 (0.98–1.18)	0.14	1.07 (0.97–1.17)	0.2
Other	1.02 (0.82–1.28)	0.85	1.02 (0.82–1.28)	0.85
Marital status				
Married	1.00		1.00	
Not Married	1.07 (1.00–1.14)	0.05	1.07 (1.00–1.14)	0.05
Unknown	1.00 (0.82–1.23)	0.97	0.99 (0.80–1.21)	0.89
Surgeon specialty[3]				
Non-GO	1.00		1.00	
GO	0.90 (0.84–0.96)	< 0.01	0.90 (0.84–0.97)	< 0.01
Chemotherapy specialty[3]				
Non-GO	[4]		1.00	
GO	[4]		0.98 (0.89–1.08)	0.68
Did not receive chemotherapy	[4]		1.33 (1.19–1.47)	< 0.01

[1]Model 1 and Model 2: Includes OC patients who did not have an unknown FIGO stage at diagnosis, and survived at least 4.5 mo after diagnosis;

[2]Minimum SOC procedure codes for surgery

[3]Missing surgeon and physician specialty excluded from analysis

[4]Excluded from the model based inclusion criteria. Chemotherapy SOC and chemotherapy physician specialty cannot be included in the same model because the common level of “did not receive chemotherapy” would introduce a singularity and prevent model convergence. OC: Ovarian cancer; SOC: Standard of care; GO: Gynecologic oncologist; FIGO: International Federation of Gynecologists and Obstetricians; NOS: Not otherwise specified.