Gynecologic Oncology 132 (2014) 403–410

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

High-volume ovarian cancer care: Survival impact and disparities in access for advanced-stage disease☆

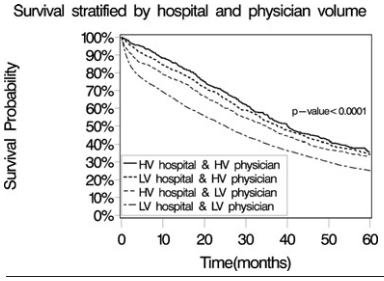
Robert E. Bristow [a,*], Jenny Chang [b], Argyrios Ziogas [b], Leslie M. Randall [a], Hoda Anton-Culver [b]

[a] Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of California, Irvine-Medical Center, Orange, CA, USA
[b] Department of Epidemiology, University of California, Irvine, CA, USA

HIGHLIGHTS

- Among patients with advanced-stage ovarian cancer, the provider combination of HVH/HVP is an independent predictor of improved disease-specific survival.
- Access to high-volume ovarian cancer providers is limited.
- Barriers are more pronounced for patients with low socioeconomic status, Medicaid insurance, and racial minorities.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 15 November 2013
Accepted 13 December 2013
Available online 20 December 2013

Keywords:
Ovarian cancer
Disparities
Access to care

ABSTRACT

Objective. To characterize the impact of hospital and physician ovarian cancer case volume on survival for advanced-stage disease and investigate socio-demographic variables associated with access to high-volume providers.

Methods. Consecutive patients with stage IIIC/IV epithelial ovarian cancer (1/1/96–12/31/06) were identified from the California Cancer Registry. Disease-specific survival analysis was performed using Cox-proportional hazards model. Multivariate logistic regression analyses were used to evaluate for differences in access to high-volume hospitals (HVH) (≥20 cases/year), high-volume physicians (HVP) (≥10 cases/year), and cross-tabulations of high- or low-volume hospital (LVH) and physician (LVP) according to socio-demographic variables.

Results. A total of 11,865 patients were identified. The median ovarian cancer-specific survival for all patients was 28.2 months, and on multivariate analysis the HVH/HVP provider combination (HR = 1.00) was associated with superior ovarian cancer-specific survival compared to LVH/LVP (HR = 1.31, 95%CI = 1.16–1.49). Overall, 2119 patients (17.9%) were cared for at HVHs, and 1791 patients (15.1%) were treated by HVPs. Only 4.3% of patients received care from HVH/HVP, while 53.1% of patients were treated by LVH/LVP. Both race and socio-demographic characteristics were independently associated with an increased likelihood of being cared for by the LVH/LVP combination and included: Hispanic race (OR = 1.72, 95%CI = 1.22–2.42), Asian/Pacific Islander race (OR = 1.57, 95%CI = 1.07–2.32), Medicaid insurance (OR = 2.51, 95%CI = 1.46–4.30), and low socio-economic status (OR = 2.84, 95%CI = 1.90–4.23).

Conclusions. Among patients with advanced-stage ovarian cancer, the provider combination of HVH/HVP is an independent predictor of improved disease-specific survival. Access to high-volume ovarian cancer providers is limited, and barriers are more pronounced for patients with low socioeconomic status, Medicaid insurance, and racial minorities.

☆ This study was funded in part by the Queen of Hearts Foundation.

* Corresponding author at: Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, University of California, Irvine School of Medicine, 101 The City Drive, Building 56, Room 260, Orange, CA 92868, USA. Fax: +1 714 4546 7754.
E-mail address: rbristow@uci.edu (R.E. Bristow).

0090-8258/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ygyno.2013.12.017

Introduction

The United States accounts for approximately 10% of the world ovarian cancer burden, with an estimated 22,240 new cases being diagnosed in 2013 and 14,030 disease-related deaths [1,2]. The National Institutes of Health, National Cancer Institute, American College of Obstetricians and Gynecologists, Society of Gynecologic Oncology, and the National Comprehensive Cancer Network (NCCN) have recommended that women with suspected ovarian cancer should be afforded an evaluation and surgical intervention by a qualified gynecologic oncologist, and the Society of Surgical Oncology practice guidelines add that "…optimal treatment of this disease requires the skillful and appropriate integration of cancer surgery and chemotherapy, and is best carried out in centers in which a coordinated and experienced multidisciplinary team is available" [3–6].

Inadequate access to high-volume providers for disease processes with a demonstrated positive volume–outcome relationship has contributed to widespread racial disparities in cancer care in the United States [7]. For ovarian cancer, the extent to which racial and socioeconomically based differences in access to high-volume providers contribute to disparities in treatment and survival has not been well characterized [8]. The primary objective of the current study was, therefore, to investigate the impact of socio-demographic variables, including race, payer status, and socioeconomic status (SES), on access to high-volume ovarian cancer hospitals and physicians in the most clinically challenging patient population —those with stage IIIC/IV disease. As a secondary objective, we aimed to characterize the combined impact of both hospital and physician case volume on ovarian cancer-specific survival.

Methods

The study design was a retrospective population-based study of invasive epithelial ovarian cancer reported to California Cancer Registry (CCR) and received exempt status by the Institutional Review Board of the University of California, Irvine (HS#2011-8317). CCR case reporting is estimated to be 99% for the entire state of California, with follow-up completion rates exceeding 95% [9]. International Classification of Disease Codes for Oncology (ICD-O) based on World Health Organization's criteria was used for tumor location and histology. Cases were identified using ovarian Surveillance, Epidemiology, and End Results (SEER) primary site code (C569).

The initial study population included women who were age 18 years or older at the time of diagnosis of a first or only invasive epithelial ovarian cancer. A total of 21,044 incident ovarian cancer cases were identified during the time period between January 1, 1996 and December 31, 2006, with follow-up extending through January 2008. Sequential exclusion of 101 borderline tumors, 151 germ cell tumors, 14 sex cord tumors, 246 cases that had missing ICD-O-2 morphology code, 742 cases that were prepared from autopsy or death certificate only, 168 with unknown surgery and/or chemotherapy information, 1242 with incomplete clinical information and 53 with incomplete hospital information, left 18,327 cases of all stages. The final number of cases included in this study was 11,865, who were diagnosed with International Federation of Gynecology and Obstetrics (FIGO) stage IIIC or stage IV disease.

The main outcome variables were annual ovarian cancer hospital volume, annual ovarian cancer physician volume, and the combination of hospital and physician volume categories. Hospital volume was calculated based on the average annual number of all ovarian cancer cases (stages I–IV) that were admitted in that hospital. Hospitals with ≥20 cases per year were classified as high-volume (HVH), and hospitals with <20 cases per year were considered low-volume (LVH). Physician volume was derived from the average annual number of all cases (Stages I–IV) from each patient's physician (surgeon, medical oncologist or attending physician, whichever had higher volume). Physicians with ≥10 cases per year were categorized as high-volume (HVP), and those with <10 cases per year were considered low-volume (LVP) [10–13]. A case was considered as HVP if any of a patient's treating physicians was high volume. Physician volume was categorized as unknown if the case had no specific physician information.

Explanatory variables included patient and tumor characteristics. Race/ethnicity was categorized into four groups: White, Black, Hispanic, and Asian/Pacific Islander. Insurance type/payer status was grouped into 4 categories: Private insurance (Managed care, HMO, PPO or other private insurance), Medicaid, Medicare, or Other insurance type (military, county-funded, uninsured, and self pay). Socioeconomic Status (SES) was classified according to increasing quintile of Yost score: lowest (SES-1), low-middle (SES-2), middle (SES-3), high-middle (SES-4) and highest (SES-5) [9]. The Yost score is an index of SES level based on a principal components analysis of census variables at the Census block-level and includes education, household income, proportion below 200% poverty level, house value, rent, percent employed, and percent with blue-collar employment [14]. Age at diagnosis was used either as a continuous variable or categorical variable with four groups: younger than 45 years, 45 to 54 years, 55 to 69 years, and 70 years or older. Tumor characteristics such as FIGO stage, grade, histology and size of the tumor were also included as explanatory variables.

Descriptive statistics were compiled, and differences of characteristics among outcome variable groups were analyzed with χ^2 test or Fisher's Exact test for categorical variables. After examining proportional odds assumption and model fit, multinomial logistic regression models were used to perform multivariate analyses for outcomes that had more than two categories. The high-volume provider group was set up as the referent in the model for each outcome variable. Binary logistic regression was performed for dichotomous outcomes. Odds ratios (OR) and their 95% confidence intervals (95%CI) were calculated. Disease-specific survival analysis was performed using the Kaplan–Meier estimate of survival probability. After verifying the proportionality assumption, a Cox-proportional hazards model was fitted to evaluate the independent effect on survival of demographic variables, disease-related characteristics, and provider volume predictor combinations. Possible interaction terms of main effects were tested, and statistically insignificant factors were removed from the final model using forward selection. Adjusted hazard ratios (HR) and 95%CIs were generated. All statistical analyses were performed using SAS 9.2.

Results

Population characteristics

The median age at diagnosis was 65.0 years (range = 18–104 years), and 7272 patients (61.3%) had Stage IIIC disease, while 38.7% had Stage IV disease (Table 1). White patients accounted for 71.7% of cases, followed in frequency by Hispanics (15.3%), Asian/Pacific Islanders (8.3%), and Blacks (4.7%). Private insurance was the most common payer category (47.7%), and 32.5% of patients had Medicare.

A total of 400 hospitals provided care to advanced-stage ovarian cancer patients during the 11-year study period. Of the 11,865 cases, 11,845 had a recorded county of residence. Twelve hospitals (0.03%) were categorized as HVH and accounted for 2119 cases (17.9%). The 388 LVHs accounted for 9726 cases (82.1%). Among all patients, HVP accounted for 15.1% of cases (1791 patients), and 61.9% of patients (n = 7341) were cared for by LVPs. In 23.0% (n = 2733) of cases the physician was unknown. Just 4.3% of patients were cared for by the combination of a HVP at a HVH, while the combination of LVP/LVH accounted for 53.1% of cases.

Survival analysis —effect of provider volume combinations

The median ovarian cancer-specific survival for all patients was 28.2 months. On univariate analysis, hospital and physician ovarian cancer volume combinations were significantly associated with median

Table 1
Study population characteristics.

Characteristic	n	Percentage
Total	11,865	100.0
Age		
<45 years	1043	8.8
45–54 years	2083	17.6
55–69 years	4214	35.5
≥70 years	4525	38.1
Race		
White	8509	71.7
Hispanic	1813	15.3
Asian/Pacific Islander	982	8.3
Black	561	4.7
Insurance		
Private[a]	5660	47.7
Medicare	3853	32.5
Medicaid	986	8.3
Other[b]	1366	11.5
Socioeconomic status (SES)		
Lowest (SES-1)	1545	13.0
Low-middle (SES-2)	2156	18.2
Middle (SES-3)	2508	21.1
High-middle (SES-4)	2769	23.3
Highest (SES-5)	2887	24.3
Stage		
IIIC	7272	61.3
IV	4593	38.7
Tumor grade		
Grade I	348	2.9
Grade II	1573	13.3
Grade III	5028	42.4
Grade IV	1249	10.5
Not specified	3667	30.9
Histology		
Serous	5789	48.8
Mucinous	419	3.5
Endometrioid	644	5.4
Clear cell	322	2.7
Adenocarcinoma NOS[c]	1988	16.8
Other	2703	22.8
Hospital type		
ACOS[d] approved	3960	33.4
Not-ACOS[d] approved	4809	40.5
Unknown	3096	26.1
Hospital volume		
High (HVH, ≥20 cases/year)	2119	17.9
Low (LVH, <20 cases/year)	9746	82.1
Physician volume		
High (HVP, ≥10 cases/year)	1791	15.1
Low (LVP, <10 cases/year)	7341	61.9
Unknown	2733	23.0
Hospital and physician volume		
HVH/HVP	515	4.3
HVH/LVP	1038	8.8
LVH/HVP	1276	10.8
LVH/LVP	6303	53.1
HVH/unknown physician volume	566	4.8
LVH/unknown physician volume[d]	2167	18.3

[a] Private insurance: managed care, HMO, PPO or other private insurance.
[b] Other insurance: military, county-funded, uninsured, and self pay.
[c] NOS: not otherwise specified.
[d] American College of Surgeons cancer program.

ovarian cancer-specific survival: HVH/HVP = 40.2 months (95%CI = 35.6–45.5 months), HVH/LVP = 34.9 months (95%CI = 31.6–37.4 months), LVH/HVP = 37.6 months (95%CI = 34.8–41.0 months), and LVH/LVP = 25.1 months (95%CI = 23.9–26.0 months) ($p < 0.0001$) (Fig. 1). Across racial and socioeconomic strata, the LVH/LVP provider combination demonstrated the lowest ovarian cancer-specific survival compared to other provider combinations for Whites ($p < 0.001$), Blacks ($p = 0.048$), Hispanics ($p = 0.001$), Asian/Pacific Islanders ($p = 0.002$), SES-1 ($p < 0.001$), SES-2 ($p = 0.001$), SES-3 ($p < 0.001$), SES-4 ($p < 0.001$), and SES-5 ($p < 0.001$). Cox proportional hazards model for disease-specific survival revealed that, after controlling for other variables and removing non-significant factors in a stepwise fashion, the HVH/HVP combination (HR = 1.00) was associated with superior ovarian cancer-specific survival compared to LVH/LVP (HR = 1.31, 95%CI = 1.16–1.49) (Table 2). HVH/HVP survival was also superior to the combinations of HVH/LVP and LVH/HVP, although these differences did not reach statistical significance. Increasing age, stage IV disease, and atypical histological subtype were also significantly associated with survival.

Access according to hospital case volume

HVH care was more common among Black patients (23.0%) compared to Whites (17.9%), Hispanics (15.4%), and Asian/Pacific Islanders (18.9%, $p = 0.004$). Increasing SES was related to the frequency of HVH care in a linear fashion, increasing from 13.5% for SES-1 to 23.4% for SES-5 ($p < 0.001$). The binary logistic regression model for the probability of LVH care (compared to HVH care) revealed a statistically significant and independent inverse association between SES and the probability of care at a LVH. Compared to the highest SES category, SES-5 (referent), the odds of LVH care increased in a linear fashion from 1.34 (95%CI = 1.17–1.52) for SES-4 to 1.90 (95%CI = 1.58–2.28) for SES-1 (Table 3). Patients with Medicare (OR = 1.38, 95%CI = 1.22–1.57), Other insurance (OR = 1.30, 95%CI = 1.11–1.53), and stage IV disease (OR = 1.32, 95%CI = 1.19–1.46) were significantly more likely to receive care at a LVH. In contrast, Black race was associated with a statistically significant decreased likelihood of care at a LVH.

Access according to physician case volume

White patients had access to HVPs in 16.4% of cases, compared to 10.7% for Blacks, 11.8% for Hispanics, and 12.3% for Asian/Pacific Islanders ($p < 0.001$). Increasing SES was related to the frequency of HVP care in a linear fashion, increasing from 12.2% for SES-1 to 20.0% for SES-5 ($p < 0.001$). Multinomial logistic regression analysis of the probability of LVP care revealed that Black patients (OR = 1.35, 95%CI = 1.01–1.81), Hispanics (OR = 1.37, 95%CI = 1.15–1.63), and Asian/Pacific Islanders (OR = 1.43, 95%CI = 1.15–1.1.76) were at increased risk for LVP care compared to Whites (Table 4). Similar to hospital volume, SES was inversely related to the odds of LVP care. Compared to the highest SES category, SES-5 (referent), the odds of

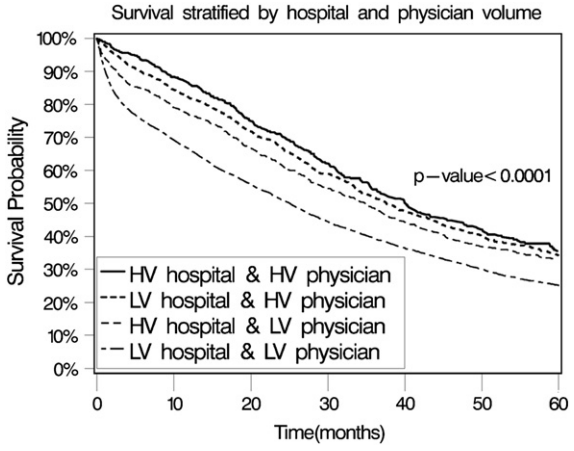


Fig. 1. Ovarian cancer-specific survival stratified by hospital and physician volume: HV-hospital/HV-physician n = 515, HV-hospital/LV-physician n = 1038, LV-hospital/HV-physician n = 1276, LV-hospital/LV-physician n = 6303 ($p < 0.0001$).

Table 2
Cox proportional hazards model for disease-specific survival.

Characteristic	Hazard ratio	95%CI[a]
Age[b]	1.03	1.02–1.03
Stage		
IIIC	1.00	
IV	1.51	1.44–1.58
Tumor grade		
Grade I	1.00	
Grade II	1.32	1.11–1.56
Grade III	1.44	1.23–1.70
Grade IV	1.50	1.26–1.79
Not specified	2.00	1.69–2.36
Histology		
Serous	1.00	
Mucinous	1.63	1.43–1.84
Endometrioid	0.92	0.82–1.03
Clear cell	1.46	1.27–1.69
Adenocarcinoma NOS[c]	1.47	1.38–1.57
Other	1.31	1.23–1.39
Tumor size		
<5 cm	1.00	
5–10 cm	0.97	0.89–1.06
>10 cm	0.90	0.82–0.99
Unknown	1.08	1.00–1.17
Hospital and physician volume		
HVH[d]/HVP[e]	1.00	
HVH[d]/LVP[f]	1.14	0.98–1.31
LVH[g]/HVP[e]	1.08	0.94–1.25
LVH[g]/LVP[f]	1.31	1.16–1.49
HVH[d]/Unknown physician volume	1.05	0.89–1.23
LVH[g]/Unknown physician volume	1.25	1.09–1.43

[a] Confidence interval.
[b] Continuous variable.
[c] NOS: not otherwise specified.
[d] HVH: high-volume hospital.
[e] HVP: high-volume physician.
[f] LVP: low-volume physician.
[g] LVH: low-volume hospital.

Table 3
Binary logistic regression model for the probability of low-volume hospital care (compared to high-volume hospital care).

Characteristic	OR[a]	95%CI[b]
Age[c]	1.01	1.00–1.01
Race		
White	1.00	
Hispanic	1.03	0.88–1.20
Asian/Pacific Islander	0.96	0.81–1.14
Black	0.59	0.48–0.73
Insurance		
Private[d]	1.00	
Medicare	1.38	1.22–1.57
Medicaid	1.14	0.95–1.38
Other[e]	1.30	1.11–1.53
Socioeconomic status (SES)		
Lowest (SES-1)	1.90	1.58–2.28
Low-middle (SES-2)	1.71	1.47–1.99
Middle (SES-3)	1.48	1.29–1.70
High-middle (SES-4)	1.34	1.17–1.52
Highest (SES-5)	1.00	
Stage		
IIIC	1.00	
IV	1.32	1.19–1.98
Tumor grade		
Grade I	1.00	
Grade II	1.48	1.11–1.98
Grade III	1.23	0.94–1.61
Grade IV	0.77	0.57–1.02
Not specified	1.37	1.03–1.82
Histology		
Serous	1.00	
Mucinous	1.24	0.94–1.63
Endometrioid	1.30	1.05–1.63
Clear cell	0.96	0.73–1.27
Adenocarcinoma NOS[f]	1.68	1.42–1.98
Other	1.18	1.04–1.34
Tumor size		
<5 cm	1.00	
5–10 cm	0.77	0.64–0.93
>10 cm	0.75	0.62–0.91
Unknown	0.81	0.69–0.96

[a] Odds ratio.
[b] Confidence interval.
[c] Continuous variable.
[d] Private insurance: managed care, HMO, PPO or other private insurance.
[e] Other insurance: military, county-funded, uninsured, and self pay.
[f] NOS: not otherwise specified.

LVP care was increased by 31% to 53% for patients with lower SES. Medicare payer status and stage IV disease were also independently associated with a higher likelihood of treatment by a LVP.

Access according to hospital/physician volume combinations

Access to HVH/HVP by race ranged from a high of 5.0% for Whites to a low of 2.3% for Hispanics ($p < 0.001$). By payer status, access to HVH/HVP was highest for patients with Private insurance (5.6%) and lowest for those with Medicaid (1.5%, $p < 0.001$). SES was inversely related to access to HVH/HVP in a linear fashion ranging from 2.1% for SES-1 to 7.1% for SES-5 ($p < 0.001$). The multinomial logistic regression model for the probability of non-HVH/HVP care revealed that both Hispanic race (OR = 1.72, 95%CI = 1.22–2.42) and Asian/Pacific Islander race (OR = 1.57, 95%CI = 1.07–2.32) were associated with a higher likelihood of care by the LVH/LVP combination (Table 5). Compared to patients with the highest SES (SES-5), those in lower SES strata were at increased risk of being treated by LVH/LVP, with the highest risk being for those with the lowest SES (SES-1, OR = 2.84, 95%CI = 1.90–4.23). Patients with Medicaid and Other payer status were at a more than 2-fold increased odds of receiving care by LVH/LVP, while stage IV disease was associated with a 36% increased likelihood of LVH/LVP care.

Conclusions

Eliminating health disparities and improving the health of all socio-demographic groups have become national priorities [15–17]. For women with ovarian cancer, racial and ethnic minority populations, the economically disadvantaged, and those with safety-net insurance have worse survival outcomes and are more likely to receive less than the standard of care [18,19]. For example, data from the National Center for Health Statistics and the National Cancer Institute indicate that from 1975 to 2004, the 5-year survival rate for White women with ovarian cancer increased from 37% to 45%, while the 5-year survival rate for Black women actually decreased from 43% to 38% during the same time period [20]. Disparities in access to advances in ovarian cancer treatment are thought to account for much of the widening survival gap along socio-demographic lines [21]. This type of health care disparity can be reframed as a fundamental issue of health care quality, such that high-quality care should be accessible to all segments of the population regardless of skin color, culture, or socioeconomic station.

The body of health services research on volume–outcome relationships for cancer care convincingly indicates that the absolute benefit from care at high-volume centers exceeds the benefit from breakthrough treatments and merits efforts to concentrate the initial care for all forms of cancer [22]. Disparities in access to high-volume health care providers and hospitals have been described according to race, ethnicity, and socio-demographic characteristics for several types of cancer (breast, colorectal, gastric, lung, pancreatic) as well as cardiovascular disease and orthopedic conditions [23,24]. For ovarian cancer, a consistent volume–outcome relationship has been well documented by multiple population-based and single-institution studies showing superior treatment and survival outcomes associated with the surgical expertise and multidisciplinary resources afforded by high-volume surgeons and

Table 4
Multinomial logistic regression analysis of the probability of low-volume physician care and probability of unknown physician volume (compared to high-volume physician care).

Characteristic	Low-volume physician		Unknown physician volume	
	OR[a]	95%CI[b]	OR[a]	95%CI[b]
Age[c]	1.01	1.01–1.02	1.01	1.01–1.02
Race				
White	1.00		1.00	
Hispanic	1.37	1.15–1.63	1.33	1.10–1.62
Asian/Pacific Islander	1.43	1.15–1.76	1.53	1.21–1.93
Black	1.35	1.01–1.81	1.36	0.98–1.88
Insurance				
Private[d]	1.00		1.00	
Medicare	1.27	1.10–1.46	0.70	0.59–0.82
Medicaid	1.21	0.97–1.51	1.19	0.93–1.52
Other[e]	1.14	0.96–1.36	1.06	0.87–1.30
Socioeconomic status (SES)				
Lowest (SES-1)	1.46	1.19–1.78	1.33	1.06–1.67
Low-middle (SES-2)	1.53	1.29–1.81	1.45	1.20–1.76
Middle (SES-3)	1.50	1.29–1.76	1.48	1.24–1.77
High-middle (SES-4)	1.31	1.13–1.51	1.28	1.08–1.51
Highest (SES-5)	1.00		1.00	
Stage				
IIIC	1.00		1.00	
IV	1.24	1.10–1.40	1.32	1.16–1.51
Tumor grade				
Grade I	1.00		1.00	
Grade II	1.09	0.80–1.49	0.88	0.61–1.27
Grade III	0.97	0.72–1.31	0.95	0.67–1.35
Grade IV	0.81	0.59–1.12	0.79	0.55–1.16
Not specified	2.44	1.76–3.39	2.22	1.53–3.22
Histology				
Serous	1.00		1.00	
Mucinous	1.60	1.15–2.23	1.42	0.98–2.06
Endometrioid	1.07	0.86–1.32	0.78	0.60–1.02
Clear cell	1.02	0.74–1.41	0.97	0.67–1.40
Adenocarcinoma NOS[f]	2.30	1.86–2.84	2.18	1.73–2.74
Other	1.18	1.02–1.37	1.01	0.85–1.19
Tumor size				
<5 cm	1.00		1.00	
5–10 cm	0.80	0.66–0.97	0.76	0.61–0.94
>10 cm	0.79	0.65–0.95	0.75	0.59–0.94
Unknown	1.21	1.01–1.44	1.23	1.01–1.50

[a] Odds ratio.
[b] Confidence interval.
[c] Continuous variable.
[d] Private insurance: managed care, HMO, PPO or other private insurance.
[e] Other insurance: military, county-funded, uninsured, and self pay.
[f] NOS: not otherwise specified.

high-volume hospitals [10–13,25–31]. Disparities in ovarian cancer survival associated with race and SES are, therefore, thought to be largely due to unequal access to care and administration of non-standard treatment regimens, although a genetic susceptibility and higher frequency of modifiable risk factors cannot be excluded as causative factors [32]. In a review of the global literature, Chornokur et al. concluded that unequal access to care is primarily a consequence of lower SES and lack of private health insurance among minority populations [32]. Indeed, single institution and cooperative group trial studies have shown that when access to specialty providers at high-volume centers is provided equally and all patients receive comparable treatment, racial disparities in ovarian cancer survival are largely mitigated [33–35].

While the "unequal access" hypothesis is widely held, there is surprisingly limited data on the extent to which race, SES, and payer status independently contribute to inequalities in access to high-volume ovarian cancer physicians and hospitals [13,18]. One of the few studies specifically examining access to high-volume ovarian cancer surgeons was a retrospective cohort study of CCR data 1991–2002 reported by Aranda et al. in 2008 [8]. This study encompassed 13,186 patients with all stages of disease but excluded over 50% of the original study population (28,060 patients) because of unknown surgeon identifier or unknown stage of disease and was only limited to patients that underwent initial surgery. This study found that Black race, Hispanic race, Medicare insurance, and Medicaid insurance were associated with a lower likelihood of being operated on by a HVS. Additional data from McGuire et al. suggest that even within a large managed care organization there may be nuanced differences in access to expert care according to race [36]. Importantly, no previous studies on disparities in access to care have conducted correlative survival analysis with treatment by high-volume providers. To address these knowledge gaps, the current study aimed to characterize the impact of hospital and physician ovarian cancer case volume on survival for advanced-stage disease and concurrently investigate socio-demographic variables associated with access to high-volume providers.

Given the strong volume–outcome relationship for ovarian cancer, the current findings that just 17.9% of ovarian cancer patients were cared for at HVHs and that only 15.1% were treated by HVPs is disconcerting but also underscores a considerable opportunity to improve survival outcomes through more effective concentration of services. To both analyze predictors of access to high-volume care as well as quantify the effect of various provider-setting combinations on ovarian cancer-specific survival, the current study employed a novel cross-tabulation of both hospital and physician volumes. After controlling for other factors, the provider combination of HVP/HVH was associated

Table 5
Multinomial logistic regression model for the probability of non-high-volume hospital/high-volume physician care (HVH = high-volume hospital, LVH = low-volume hospital, HVP = high-volume physician, LVP = low-volume physician).

Characteristic	HVH/LVP		LVH/HVP		LVH/LVP		HVH/Unknown		LVH/Unknown	
	OR[a]	95%CI[b]	OR[a]	95%CI[b]	OR[a]	95%CI[b]	OR[a]	95%CI[b]	OR[a]	95%CI[b]
Age[c]	1.01	1.00–1.02	1.01	1.00–1.02	1.02	1.01–1.03	1.02	1.01–1.03	1.02	1.01–1.03
Race										
White	1.00		1.00		1.00		1.00		1.00	
Hispanic	1.63	1.11–2.39	1.33	0.92–1.94	1.72	1.22–2.42	2.03	1.35–3.07	1.57	1.10–2.25
Asian/Pacific Islander	1.75	1.14–2.69	1.19	0.77–1.83	1.57	1.07–2.32	1.94	1.21–3.11	1.66	1.11–2.49
Black	1.70	0.99–2.91	0.75	0.42–1.32	0.99	0.60–1.62	1.92	1.08–3.44	0.91	0.54–1.53
Insurance										
Private[d]	1.00		1.00		1.00		1.00		1.00	
Medicare	1.00	0.75–1.31	0.82	0.63–1.08	1.12	0.89–1.42	0.25	0.17–0.35	0.73	0.57–0.94
Medicaid	3.21	1.81–5.70	2.59	1.47–4.59	2.51	1.46–4.30	1.79	0.96–3.31	2.83	1.63–4.91
Other[e]	2.36	1.55–3.60	2.50	1.67–3.77	2.34	1.59–3.43	1.71	1.08–2.70	2.34	1.57–3.48
Socioeconomic status (SES)										
Lowest (SES-1)	1.35	0.86–2.12	2.09	1.35–3.23	2.84	1.90–4.23	1.89	1.15–3.10	2.45	1.61–3.72
Low-middle (SES-2)	1.01	0.72–1.42	1.24	0.90–1.72	1.96	1.47–2.60	1.23	0.83–1.80	1.82	1.34–2.46
Middle (SES-3)	1.78	1.29–2.47	1.96	1.43–2.69	2.61	1.96–3.47	2.21	1.54–3.18	2.47	1.82–3.35
High-middle (SES-4) 1.31	1.16	0.88–1.54	1.24	0.95–1.63	1.60	1.26–2.03	1.27	0.92–1.75	1.55	1.20–2.00
Highest (SES-5)	1.00		1.00		1.00		1.00		1.00	
Stage										
IIIC	1.00		1.00		1.00		1.00		1.00	
IV	1.01	0.79–1.28	1.06	0.84–1.34	1.36	1.10–1.67	1.05	0.80–1.37	1.48	1.19–1.84
Tumor grade										
Grade I	1.00		1.00		1.00		1.00		1.00	
Grade II	1.13	0.61–2.12	1.54	0.85–2.80	1.58	0.93–2.70	0.88	0.44–1.77	1.34	0.75–2.39
Grade III	0.93	0.52–1.66	1.23	0.71–2.14	1.16	0.71–1.91	0.96	0.51–1.81	1.16	0.68–1.98
Grade IV	0.88	0.48–1.61	0.71	0.40–1.28	0.60	0.36–1.01	0.58	0.29–1.16	0.66	0.37–1.16
Not specified	2.44	1.29–4.61	1.18	0.63–2.20	2.81	1.62–4.88	1.69	0.84–3.41	2.77	1.53–5.00
Histology										
Serous	1.00		1.00		1.00		1.00		1.00	
Mucinous	1.76	0.85–3.63	1.34	0.65–2.78	2.04	1.05–3.96	1.54	0.70–3.39	1.85	0.93–3.68
Endometrioid	1.21	0.74–1.96	1.44	0.92–2.25	1.45	0.96–2.20	0.85	0.48–1.52	1.10	0.70–1.72
Clear cell	1.68	0.88–3.21	1.40	0.73–2.67	1.22	0.67–2.20	0.92	0.42–2.03	1.35	0.72–2.51
Adenocarcinoma NOS[f]	1.61	1.04–2.50	1.10	0.70–1.73	2.61	1.76–3.87	1.48	0.92–2.37	2.59	1.73–3.89
Other	0.99	0.75–1.32	0.96	0.73–1.26	1.18	0.92–1.50	0.81	0.58–1.12	1.03	0.79–1.33
Tumor size										
<5 cm	1.00		1.00		1.00		1.00		1.00	
5–10 cm	0.72	0.49–1.07	0.72	0.50–1.03	0.61	0.44–0.85	0.74	0.46–1.20	0.56	0.40–0.81
>10 cm	0.99	0.66–1.50	1.00	0.68–1.47	0.74	0.52–1.06	1.10	0.67–1.81	0.68	0.47–0.99
Unknown	0.91	0.63–1.31	0.72	0.51–1.02	0.95	0.69–1.30	1.68	1.09–2.59	0.8	5 0.61–1.18

[a] Odds ratio.
[b] Confidence interval.
[c] Continuous variable.
[d] Private insurance: managed care, HMO, PPO or other private insurance.
[e] Other insurance: military, county-funded, uninsured, and self pay.
[f] NOS: not otherwise specified.

with an independent and statistically significant 31% improvement in ovarian cancer-specific survival compared to the LVP/LVH pairing. Unfortunately, access to this optimum high-volume provider combination was extremely limited, with only 4.3% of patients receiving care from HVH/HVP and 53.1% of patients being treated by LVH/LVP. Non-White race was a consistent predictor of reduced access to HVPs both overall and even when care was administered at a HVH. Paradoxically, Black patients were significantly more likely to receive care at a HVH but less likely to be treated by a HVP, a finding that has been noted in other studies [13,18]. The reasons for this apparent contradiction are unclear.

Previous investigators have shown that SES indicators such as education level, employment status, and income are predictive of access to subspecialty care by a gynecologic oncologist. In an early study of CCR data (1994–1996) Chan and coworkers analyzed 1491 ovarian cancer patients and found that bivariate measures of neighborhood affluence and education level were associated with access to a gynecologic oncologist [37]. Similarly, Mercado et al. reported combined data from the CCR and statewide cancer registries from New York, Florida, and Washington State on 31,897 patients with advanced-stage disease between 1991 and 2004 and found that increasing poverty level predicted reduced access to a gynecologic oncologist [38]. Data specifically examining access to high-volume care, however, is more limited. In the study by Aranda et al., the only SES parameter investigated was the proportion of the Census block living at <200% poverty level and this was not predictive of access to a high-volume ovarian cancer surgeon [8]. In contrast, the current data show that decreasing composite index of SES was highly correlated with reduced access to HVPs and HVHs as individual variables. Accordingly, the combined analysis cross-tabulating volume-based access to both hospital and physicians revealed that, compared to the highest SES group (SES-5), the lower four quintile SES groups (SES-1 through SES-4) were all significant and independent predictors of care by the LVP/LVH combination. The striking consistency of the relationship between low SES and more limited access to high-volume care suggests that the collective predictive value represented by the composite Yost score may mitigate the volatility of individual Census block-level measures.

Insurance status also emerged as an important determinant of volume-based care. Patients with Medicare were less likely to have access to both a HVH and a HVP. Interestingly, Medicaid insurance was not associated with either HVP or HVH care individually but was a strong and independent predictor of non-HVP/HVH care in the combined analysis. Other insurance (military, county-funded, uninsured, and self pay) was also a significant and independent predictor of non-

HVP/HVH care. Aranda et al. found that both Medicare and Medicaid insurance were associated with statistically significantly reduced access to a high-volume surgeon [8]. The type of health insurance can be considered both a health system factor and an individual-level measure of SES and has been linked to expenditure on cancer treatment, reinforcing the current finding that payer status appears to influence access to appropriate care [39].

The association between higher tumor grade and atypical histological subtypes with an increased likelihood of low-volume provider care is not readily explained by the variables available in this population-based dataset. It is possible that these associations could be related to extent of initial disease, and therefore linked to patient medical condition and performance status, both of which could affect the likelihood of referral. Neither of these variables is captured by the CCR. It is also possible that the differences in gynecologic pathology experience and expertise exist between low- and high-volume hospitals, which could have introduced a level of variation in the consistency of pathologic diagnosis.

Strengths of the current study include the large study population size, the proven reliability of the California Cancer Registry, and examination of a contemporary time period during which no major treatment paradigm shifts occurred. There are also several limitations that must be considered when interpreting these data. First, this was a retrospective study design using a population-based data set and is subject to the inherent potential for reporting and selection bias that accompanies such methodology. Second, and perhaps most importantly, we were unable to control for potentially important unreported variables that could influence both survival outcome as well as referral patterns. Such variables include the presence of medical comorbidities, the extent of initial disease, and amount of residual tumor. A third potential limitation is that we intentionally did not adjust for adherence or non-adherence to NCCN treatment guidelines, as we have previously shown a strong positive association between high provider volume and adherence to standard of care practices [31]. Controlling for treatment-related variables intrinsically associated with HVHs and HVS, such as variation in surgical practices and chemotherapy use, could potentially mask or mitigate a positive volume–outcome (survival) effect [40]. Fourth, we were unable to examine the potential effect of physician specialty, as the California Cancer Registry does not capture this information routinely. Finally, as this was a retrospective observational study, we were unable to account for the effects of patient preference or ability/willingness to travel in selection of healthcare providers and treatment delivery settings.

Despite these limitations, the current data offer several observations that potentially account for disparities in ovarian cancer treatment and survival according to race and socio-demographic characteristics. High physician and hospital annual case volume are associated with improved ovarian cancer survival, and access to high-volume care is unfortunately limited. While race, payer status, and SES are associated with access to high-volume care, SES appears to be the dominant or at least the more consistent predictor. Additional research is needed to further define the underlying reasons for disparities in access to expert care, adjust for variation due to differences in medical comorbidities and performance status, and identify opportunities to improve access to high-volume providers for all women but specifically racial/ethnic minorities, women of low SES, those with safety-net insurance, and the uninsured.

Conflict of interest statement

No author has a conflict of interest to disclose.

Acknowledgment

Dr. Robert E. Bristow was supported in part by the Queen of Hearts Foundation.

References

[1] Siegel R, Naishadham D, Jemal A. Cancer statistics 2013. CA Cancer J Clin 2013;63:11–30.
[2] Globocan. (IARC) Section of Cancer Information (9/10/2013). globocan.iarc.fr/factsheet.asp; 2008.
[3] Seltzer V, Batson JL, Drukker BH, et al. National Institutes of Health Consensus Development Conference Statement. Ovarian cancer: screening, treatment, and follow-up. Gynecol Oncol 1994;55:S4–S14.
[4] The role of the obstetrician–gynecologist in the early detection of epithelial ovarian cancer. Committee Opinion No. 477. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:742–6.
[5] Morgan RJ, Alvarez RD, Armstrong DK, Burger RA, Chen LM, Copeland L, et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): ovarian cancer including fallopian tube cancer and primary peritoneal cancer. Version 2.2013. National Comprehensive Cancer Network, Inc.; 2013.
[6] Hoskins W, Rice L, Rubin S. Ovarian cancer surgical practice guidelines. Oncology 1997;11:896–904.
[7] Parsons HM, Habermann EB, Stain SC, Vickers SM, Al-Refaie WB. What happens to racial and ethnic minorities after cancer surgery at American College of Surgeons National Surgical Quality Improvement Program hospitals? J Am Coll Surg 2012;214:539–49.
[8] Aranda MA, McGory M, Sekeris E, Maggard M, Ko C, Zingmond DS. Do racial/ethnic disparities exist in the utilization of high-volume surgeons for women with ovarian cancer? Gynecol Oncol 2008;111:166–72.
[9] Parikh-Patel A, Allen M, Wright WE. Validation of self-reported cancers in the California Teachers Study. Am J Epidemiol 2003;157:539–45.
[10] Goff BA, Matthews BJ, Wynn M, Muntz HG, Lishner DM, Baldwin LM. Ovarian cancer: patterns of surgical care across the United States. Gynecol Oncol 2006;103:383–90.
[11] Goff BA, Matthews BJ, Larson EH, Andrilla CH, Wynn M, Lishner DM, et al. Predictors of comprehensive surgical treatment in patients with ovarian cancer. Cancer 2007;109:2031-20.
[12] Bristow RE, Zahurak ML, Diaz-Montes TP, Giuntoli RL, Armstrong DK. Impact of surgeon and hospital ovarian cancer surgical case volume on in-hospital mortality and related short-term outcomes. Gynecol Oncol 2009;115:334–8.
[13] Bristow RE, Palis BE, Chi DS, Cliby WA. The National Cancer Database on advanced-stage epithelial ovarian cancer: impact of hospital surgical case volume on overall survival and surgical treatment paradigm. Gynecol Oncol 2010;118:262–7.
[14] Yost K, Perkins C, Cohen R, Morris C, Wright W. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. Cancer Causes Control 2001;12:703–11.
[15] Institute of Medicine. The unequal burden of cancer. Washington, DC: National Academy Press; 1999.
[16] Institute of Medicine. Unequal treatment: confronting racial and ethnic disparities in healthcare. Washington, DC: National Academy Press; 2003.
[17] Freeman HP. Poverty, culture, and social injustice: determinants of cancer disparities. CA Cancer J Clin 2004;54:72–7.
[18] Bristow RE, Zahurak ML, Ibeanu OA. Racial disparities in ovarian cancer surgical care: a population-based analysis. Gynecol Oncol 2011;121:364–8.
[19] Bristow RE, Powell MA, Al-Hammadi N, Chen L, Miller JP, Roland PY, et al. Disparities in ovarian cancer care quality and survival according to race and socioeconomic status. J Natl Cancer Inst 2013;105:823–32.
[20] Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics. CA Cancer J Clin 2009;59:225–49.
[21] Terplan M, Schluterman N, Mcnamara EJ, Tracy JK, Temkin SM. Have racial disparities in ovarian cancer increased over time? An analysis of SEER data. Gynecol Oncol 2012;125:19–24.
[22] Hillner BE, Smith TJ, Desch CE. Hospital and physician volume of specialization and outcomes in cancer treatment: importance in quality cancer care. J Clin Oncol 2000;18:2327–40.
[23] Liu JH, Zingmond DS, McGory ML, SooHoo NF, Ettner SL, Brook RH, et al. Disparities in the utilization of high-volume hospitals for complex surgery. JAMA 2006;296:1973–80.
[24] Epstein AJ, Gray BH, Schlesinger M. Racial and ethnic differences in the use of high-volume hospitals and surgeons. Arch Surg 2010;145:179–86.
[25] Kumpulainen S, Grenman S, Kyyronen P, Pukkula E, Sankila R. Evidence of benefit from centralized treatment of ovarian cancer: a nationwide population-based survival analysis in Finland. Int J Cancer 2002;102:541–4.
[26] Tingulstad S, Skjeldestad FE, Hagen B. The effect of centralization of primary surgery on survival in ovarian cancer patients. Obstet Gynecol 2003;102:499–505.
[27] Marth C, Hieble S, Oberainger W, Winter R, Leodolter S, Sevelda P. Influence of department volume on survival for ovarian cancer: results from a prospective quality assurance program of the Austrian Association of Gynecologic Oncology. Int J Gynecol Cancer 2009;19:94–102.
[28] Ioka A, Tsukuma H, Ajiki W, Oshima A. Influence of hospital procedure volume on ovarian cancer survival in Japan, a country with a low incidence of ovarian cancer. Cancer Sci 2004;95:233–7.
[29] Wimberger P, Lehmann N, Kimmig R, Burges A, Meier W, DuBois A. Prognostic factors for complete debulking in advanced ovarian cancer and its impact on survival. An exploratory analysis of a prospectively randomized phase III study of the Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group (AGO-OVAR). Gynecol Oncol 2007;106:69–74.
[30] Wright JD, Herzog TJ, Siddiq Z, Arend R, Neugut AI, Burke WM, et al. Failure to rescue as a source of variation in hospital mortality for ovarian cancer. J Clin Oncol 2012;30:3976–82.
[31] Bristow RE, Chang J, Ziogas A, Anton-Culver H. Adherence to treatment guidelines for ovarian cancer as a measure of quality care. Obstet Gynecol 2013;121:1226–34.
[32] Chornokur G, Amankwah EK, Schildkraut JM, Phelan CM. Global ovarian cancer health disparities. Gynecol Oncol 2013;129:258–64.

[33] Bristow RE, Ueda S, Gerardi MA, Ajiboye OB, Ibeanu OA. Analysis of racial disparities in stage IIIC epithelial ovarian cancer care and outcomes in a tertiary gynecologic oncology referral center. Gynecol Oncol 2011;122:319–23.
[34] Farley JH, Tian C, Rose GS, Brown CL, Birrer M, Maxwell GL. Race does not impact outcomes for advanced ovarian cancer patients treated with cisplatin/paclitaxel. Cancer 2009;115:4210–7.
[35] Terplan M, Temkin S, Tergas A, Lengyel E. Does equal treatment yield equal outcomes? The impact of race on survival in epithelial ovarian cancer. Gynecol Oncol 2008;111:173–8.
[36] McGuire V, Herrinton L, Whittemore AS. Race, epithelial ovarian cancer survival, and membership in a large health maintenance organization. Epidemiology 2002;13:231–4.
[37] Chan JK, Kapp DS, Shin JY, Husain A, Teng NN, Berek JS, et al. Influence of the gynecologic oncologist on the survival of ovarian cancer. Obstet Gynecol 2007;109:1342–50.
[38] Mercado C, Zingmond D, Karlan BY, Sekaris E, Gross J, Maggard-Gibons M, et al. Quality of care in advanced ovarian cancer: the importance of provider specialty. Gynecol Oncol 2010;117:18–22.
[39] Thorpe KE, Howard D. Health insurance and spending among cancer patients. Health Aff 2003;W3(Suppl.):189–98.
[40] Schrag D, Earle C, Fu X, Panageas KS, Yabroff KR, Bristow RE, et al. Associations between hospital and surgeon procedure volumes and patient outcomes after ovarian cancer resection. J Natl Cancer Inst 2006;98:163–71.