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Exploring the Impact of Income and Race on Survival for Women with Advanced Ovarian Cancer undergoing Primary Debulking Surgery at a High-Volume Center

Renee A. Cowan^a, Jill Tseng^a, Narisha Ali^a, Helen Dearie^a, Vijayashree Murthy^a, Renee L. Gennarelli^b, Alexia Iasonos^b, Nadeem R. Abu-Rustum^{a,c}, Dennis S. Chi^{a,c}, Kara C. Long Roche^{a,c}, Carol L. Brown^{a,c}

^aDepartment of Surgery, Memorial Sloan Kettering Cancer Center;

^bDepartment of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center;

^cDepartment of Surgery, Weill Cornell Medical College

Abstract

Objective: To evaluate patients with advanced ovarian cancer (OC) undergoing primary debulking surgery (PDS) at a high-volume center (HVC), to determine whether sociodemographic disparities in PDS outcome and overall survival (OS) were present.

Methods: All patients with stages IIIB-IV high-grade OC undergoing PDS at our institution from 1/2001–12/2013 were identified. Patients self-identified race/ethnicity as Non-Hispanic White (NHW), Non-Hispanic Black (NHB), Asian (A), or Hispanic (H). Income level for the entire cohort was estimated using the census-reported income level for each patient's zip code as a proxy for SES. Main outcome measures were PDS outcome and median OS. Cox proportional hazards model was used to examine differences in OS by racial/ethnic and income category, controlling for selected clinical factors.

Results: 963 patients were identified for analysis: 855 NHW; 43 A, 34 H, 28 NHB, and 3 unknown. PDS outcome was not significantly different among NHB and H as compared to NHW. Compared to NHW, Asians were more likely to have >1cm residual (AOR 2.32, 95%CI 1.1–4.9, $p=0.03$). Median income for the entire cohort was \$85,814 (range \$10,926–\$231,667). After adjusting for significant prognostic factors, there were no significant differences in PDS outcome between income groups ($p=0.7281$). Median OS was 55.1mos (95%CI 51.8–58.5) with no significant differences in OS between the income ($p=0.628$) or racial/ethnic ($p=0.615$) groups.

Corresponding Author: Renee A. Cowan, MD, Gynecology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA, cowanr@mskcc.org.

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Conclusion: Statistically significant socio-demographic disparities in PDS and survival outcomes were not observed among women with advanced OC treated at this HVC. Increased efforts are needed to centralize care to and increase the diversity of pts treated at HVCs.

INTRODUCTION

Ovarian cancer is a complex heterogeneous disease affecting a diverse group of women. Each year in the United States over 22,000 women are diagnosed with ovarian cancer [1]. Most of these patients present at advanced stages and eventually succumb to their disease [2]. Appropriate management requires combined surgical and systemic medical treatment, ideally provided by a skilled team of clinicians specializing in gynecologic oncology. National and international studies have demonstrated that clinicians who treat a high volume (≥ 20 cases per year) of ovarian cancer patients provide superior healthcare quality and survival outcomes [3–8]. This is likely due to their increased experience and adherence to national guidelines [9, 10].

There are very clear disparities in the distribution of and access to high-volume providers and higher-volume or specialized hospitals. Some researchers suggest that 65–80% of centers handle less than 10 cases of advanced ovarian cancer per year [5, 11]. Patients treated in low-volume centers are more likely to be of lower socioeconomic status (SES), to belong to racial/ethnic minority groups, and to have Medicare or Medicaid insurance; and they are more likely to present with Stage IV disease [5, 12]. In fact, SES has been identified as the most consistent predictor of where a patient receives her care [13]. Population-based studies report that women with lower household incomes are less likely to be treated at a high-volume center (HVC), and are less likely to receive guideline-adherent care. Thus, these patients are also less likely to receive optimal surgical management, and they have lower rates of overall survival (OS) [14–16].

It has been hypothesized that equitable access to HVCs and high-volume providers would mitigate socioeconomic and racial/ethnic disparities in outcome for women with ovarian cancer [17, 18]. In the past decade there have been numerous studies demonstrating the value of high-volume cancer care, not just in ovarian cancer, but also in other diseases that require a complex treatment strategy such as lung, pancreatic, and colorectal cancers [19–22]. The objective of this study was to evaluate patients with advanced ovarian cancer who underwent primary debulking surgery (PDS) at an HVC, to determine whether socioeconomic and racial/ethnic disparities persist in surgical outcome and survival.

METHODS

Study population

This is a retrospective single-institution study of a cohort of patients with International Federation of Gynecology and Obstetrics (FIGO) stages IIIB-to-IV epithelial ovarian, fallopian tube, or peritoneal cancer. Patients were identified using an institutional surgical database. The study population consisted of women ≥ 18 years of age, diagnosed with primary invasive advanced-stage epithelial ovarian cancer, who underwent PDS from January 1, 2001 to December 31, 2013. After obtaining IRB exemption, we collected the

demographic, clinical, pathologic, and outcome data for all women in the study cohort. Patients who received neoadjuvant chemotherapy were excluded. Patients were also excluded if they had non-epithelial or borderline tumors, or non-ovarian pathology.

Data Analysis

Data on patient demographics, tumor characteristics, operative findings, outcomes of PDS, progression-free survival (PFS), and OS were collected. Patients self-identified as Non-Hispanic White (NHW), Non-Hispanic Black (NHB), Asian (A), or Hispanic (H). Patients were excluded from the racial portion of the analysis if their race/ethnicity was not documented anywhere in the medical record. The median household income was determined by using the census-reported income level of each patient's zip code. The median household income per zip code was based on the 2010–2014 American Community Survey (ACS) 5-year estimates, and was used as a proxy for SES [23]. Patients were categorized by census-based income categories, which we refer to as SES groups. The median household incomes were as follows: Group 1, < \$50,000; Group 2, \$50–99,999; Group 3, \$100–149,999; and Group 4, ≥ \$150,000. The main outcome measures were PDS outcome (optimal versus sub-optimal) and median OS. PDS outcome was determined by the amount of residual disease, as recorded on the operative report. Optimal outcome was defined as residual disease ≤ 1 cm. Suboptimal outcome was defined as residual disease > 1 cm. OS was defined as time elapsed (in months) from the date of PDS to the date of last follow-up, or death. Follow-up data were collected until August 2016. The Cox proportional hazards model was used to examine differences in OS by income category, when controlling for selected clinical factors. The Kaplan-Meier method was used to generate survival curves [24].

RESULTS

Patient and Surgery Characteristics

Nine hundred and sixty patients meeting the inclusion criteria for the racial portion of the analysis were identified. Nine hundred and sixty-three patients met the inclusion criteria for the income based portion of the analysis. 855 (89%) identified as non-Hispanic White women; 43 (4%) as Asian (A); 34 (4%) as Hispanic (H), and 28 (3%) as non-Hispanic Black (NHB). The 3 patients that had an unknown race were excluded from the racial analysis cohort. The median age at time of diagnosis was 62 years (range 19–95) for both cohorts. Asian women were significantly younger than other racial/ethnic groups with a median age of 53 ($p < 0.0001$).

Twelve percent had a known BRCA 1/2 mutation. Eighty-nine percent had high-grade serous histologies. The majority had carcinomatosis (81%) and/or bulky upper abdominal disease (60%) at the time of PDS. There were statistically significant differences between the racial groups in BRCA status, BMI, and income. These are detailed in Table 1. There were statistically significant differences between the income groups in ASA level and race/ethnicity, detailed in Table 2.

Examining Race

At time of PDS, 82% of patients in the cohort were left with 1cm or less residual disease, resulting in an optimal debulking outcome. After controlling for age, BMI, income, BRCA status, ASA status, tumor grade, presence of carcinomatosis and upper abdominal disease, PDS outcome was not significantly different among NHB and H as compared to NHW. As compared to NHW, Asians were more likely to have >1cm residual (adjusted OR 2.32, 95% CI 1.1–4.9, $p=0.03$). Median OS was 55.1 mos (95% CI: 51.8–58.5) for this cohort. On both univariate and multivariate analysis, there was no significant difference in OS between racial or ethnic groups (adjusted $p=0.615$), detailed in Table 3. See Figure 1 for a Kaplan Meier OS plot.

Examining Income

The median income for the entire cohort was \$85,814 (range \$10,926–\$231,667). Figure 2 shows the frequency distribution of median household incomes based on the patients' zip codes. Patient distribution across income groups was not symmetrical; a majority was categorized as Group 2, (\$50,000–\$99,999), and few patients were from zip codes in the lowest (Group 1) or highest (Group 4) income groups. There were 129 patients (13.4%) from zip codes with median income in Group 1, 496 (51.1%) in Group 2, 283 (29.4%) in Group 3, and 55 (5.7%) in Group 4. There was no significant difference in age, stage, grade, or tumor burden between income groups. The data was also analyzed using median income quartiles, which demonstrated no difference.

The median OS for this cohort was also 55.1 months (95% CI, 51.8–58.5). On univariate analysis, there was no significant difference in OS with respect to SES group. After controlling for age, race, BMI, BRCA status, ASA status, tumor grade, presence of carcinomatosis or upper abdominal disease, and PDS outcome, there was no significant difference in OS between the four income groups (adjusted $p=0.603$) (detailed in Table 3). A Kaplan-Meier OS plot is shown in Figure 3.

DISCUSSION

It has been demonstrated that ovarian cancer patients from socioeconomically disadvantaged groups and from racial and ethnic minorities have comparatively lower rates of optimal resection at the time of PDS, and higher mortality rates [14, 25]. Some hypothesize that this is due to a lack of guideline-adherent care and/or lack of access to expert, high-volume centers [9, 13, 14, 25]. The objective of this study was to determine if surgical outcomes and survival differences were present in a large, socio-demographically diverse cohort of ovarian cancer patients treated at a single high-volume institution. The current study suggests that, in ovarian cancer patients treated at an HVC by expert providers, survival is similar regardless of race or income. Optimal surgical outcomes were similar between NHW, NHB, and H groups as well.

It is possible that differences in outcomes are due, in part, to the fact that patients in certain racial groups and those with lower SES may have worse tumor or disease characteristics. Peterson et al sought to determine the association between SES and tumor characteristics by

examining the stage, grade, debulking status, and neighborhood SES of over 500 confirmed cases of epithelial ovarian cancer derived from over 80% of the hospitals in Cook County, Illinois [26]. Though 83% of their cohort was White, they found that lower SES or “neighborhood disadvantage” was associated with later stage at diagnosis, higher-grade tumors, and suboptimal debulking. However, they were unable to correlate these factors with survival data. While all of these characteristics are associated with decreased survival, the study did not address differences in hospital or provider utilization, which would likely mitigate those negative factors. In this study, we explored differences in carcinomatosis and bulky upper abdominal disease as surrogates for more aggressive tumor biology and found no difference between racial/ethnic and income groups.

In our cohort, Asian women were younger, but after controlling for this and other clinical factors had higher rates of > 1cm residual disease at conclusion of PDS. Despite this, we did not find a significant difference in survival between Asian women and women from the other racial/ethnic groups, perhaps secondary to our small sample size. On the other hand, other studies with larger cohorts of Asian women diagnosed with ovarian cancer have noted longer survivals [27]. In 2015, Fuh et al published results from a study of the Surveillance, Epidemiology, and End Results (SEER) program which compared 48,328 White women to 3,932 Asian women diagnosed with all stages of epithelial ovarian cancer over a 21 year period [28]. Similarly, they found that Asian patients were younger than White patients. Additionally, they determined that Asian women maintained a survival advantage after adjusting for age, stage, histology, and extent of surgical treatment. They postulated that these findings could be secondary to the Asian patients representing a healthier migrant population with more socioeconomic advantage or that sicker immigrant patients may return to their native country after severe illness [28]. Some researchers have hypothesized that some Asian women expression variants of certain genes that may metabolize chemotherapeutic agents in a way that makes them more susceptible to cure [29]. We are unable to test either hypothesis from our data; however, further research is needed to explore the validity of these differences and the reasons why they may exist. Tumor biology may play a role, though in our cohort we did not detect a statistically significant survival advantage in this population. The clinical trials, salvage therapies, and radical tertiary surgical approaches that are available at HVCs may compensate for the tumor biology possessed by various racial/ethnic groups.

In two comparative studies of large population based databases Bristow characterized the association between various socio-demographic variables, access to high-volume providers, receipt of guideline adherent care and survival outcomes [13, 14]. In the 2014 investigation of the California Cancer Registry, they studied almost 12,000 women with advanced ovarian cancer and found an independent inverse association between SES and ethnicity and utilization of HVC care; patients of lower SES, those with Medicaid insurance, and those from Hispanic or Asian ethnic backgrounds were more likely to undergo treatment by lower-volume providers at lower-volume centers. Additionally, they found that patients who were treated by high-volume providers at a high-volume hospital had the longest OS, whereas patients treated at a low-volume hospital by low-volume providers had the poorest OS [13]. In the 2015 exploration of the SEER-Medicare database, they studied over 10,000 women with advanced ovarian cancer and found that Black race and low SES were independently

associated with receiving non-guideline adherent care [14]. Deviation from guideline-mediated treatment was associated with an increased risk of disease-related mortality. This suggests that expert guideline-adherent treatment mitigates the survival disparity for disadvantaged groups.

The current study has several limitations. First, due to its retrospective nature, it lacks details on individual patient's SES, such as income or education level; nevertheless, median household income based on documented zip code is an acceptable way of representing an individual's SES and the features of their environment [23]. Second, the median household income in New York City is \$53,373, which is lower than the median household income for the entire study cohort [30]. It is possible that this cohort is not completely representative of women in the lower SES groups; however, almost one-quarter of the patients were at or below this level. Moreover, historical epidemiologic data has suggested that women of higher SES backgrounds have an increased incidence of ovarian cancer compared to those in lower SES groups; this could contribute to the fact that our cohort had higher SES than that of the general NYC population [31]. Additionally, this study population was overwhelmingly composed of NHW women, with NHB, Asian, and Hispanic women comprising only 19% of the cohort. This imbalance not only highlights the disparity that exists for ethnic minorities utilizing high-volume ovarian cancer care, but may also affect the ability to identify statistically significant differences. We did not have large enough samples of NHB, Asian, and Hispanic patients to definitively conclude that no survival differences exist. However, ovarian cancer disproportionately affects NHW women; many population-based retrospective studies reflect similar demographic compositions, and have yielded clinically meaningful results [14, 16, 32–35]. Retrospective cohort studies such as this one serve as a means of generating hypotheses that can then be tested. Additional studies may require over-sampling of NHB, Hispanic, and Asian women to further explore these differences. Another option may include combining data from more than one HVC to obtain a larger sample of minority patients. Finally, it is possible that there was a selection bias by studying patients who were treated with primary debulking surgery followed by adjuvant chemotherapy. At this time, we are unable to report on concurrent patients who were treated with primary chemotherapy; however, there is no reason to believe that survival differences would be present between the racial/ethnic or income groups, as patients within each group were treated with the same neoadjuvant chemotherapeutic approach by the same disease management team.

Despite these limitations, we were able to account for clinical characteristics that could have confounded the outcomes. All of the patients in this cohort were treated by a fellowship-trained, board-certified, expert gynecologic oncologist. Additionally, our institution's disease management team ensured that patients received NCCN guideline-adherent care, including the appropriate surgery and chemotherapy.

These findings support the conclusions of others who have proposed centralization of ovarian cancer care to expert centers. When patients are treated at an institution that has a high rate of optimal debulking and high OS rates, each patient utilizing care at that institution has a higher likelihood of obtaining those same outcomes regardless of their clinical or demographic risk factors. The racial and socioeconomic disparities in ovarian

cancer surgical outcomes and survival can be decreased, and possibly eliminated, by pipelining patients to HVCs staffed by high-volume providers who are appropriately equipped for dealing with the complexities of this disease. There should be national efforts to 1) educate patients and their providers regarding the benefits of expert care, and 2) reduce system-related barriers to ensure equitable utilization of HVCs by all women diagnosed with advanced ovarian cancer.

Further research should focus on confirming these findings at other HVCs, and developing methods to identify and eliminate the barriers that women from racial/ethnic minorities, and those of lower SES, from seeking the care of high-volume, expert providers. Furthermore, partnerships should be established between HVCs and lower-volume hospitals in the community, to support patients whose circumstances prevent them from being treated at a high-volume center.

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HIGHLIGHTS:

- Racial disparities in OS in treatment of advanced OC were not observed at this HVC
- SES disparities in PDS/OS in treatment of advanced OC were not observed at this HVC
- Greater efforts are needed to centralize care/increase diversity for OC pts at HVCs

Figure 1:
Kaplan-Meier Curves by Race

Figure 2:
Frequency Distribution of Median Household Incomes

Figure 3:
Kaplan-Meier Curves by Income (1=<\$50,000, 4=>\$150,000)

Table 1.

Patient and Tumor Characteristics by Racial/Ethnic Group

	Non-Hispanic White (n=855)	Non-Hispanic Black (n=28)	Asian (n=43)	Hispanic (n=34)	p-value
Median Age (range)	62 (19–95)	70 (32–83)	53 (30–79)	59 (44–80)	<.0001
Median Household Income (range)	\$87,946 (10,926–231,667)	\$55,557 (27,197–162,674)	\$82,011 (32,983–169,583)	\$58,943 (26,764–168,868)	<.0001
BRCA Status					0.0077
Negative	268 (31)	9 (32)	12 (28)	7 (21)	
BRCA 1 Positive	64 (8)	1 (4)	9 (21)	4 (12)	
BRCA 2 Positive	34 (4)	0 (0)	4 (9)	1 (3)	
Status Unknown	489 (57)	18 (64)	18 (42)	22 (65)	
ASA					0.408
1–2	458 (54)	11 (39)	25 (58)	17 (50)	
3–4	390 (46)	17 (61)	18 (42)	17 (50)	
BMI (range)	26 (16–59)	27 (18–40)	23 (17–39)	27 (19–43)	0.007
Pre-Op Albumin (range)	4.1 (2.0–5.1)	4.2 (2.3–4.6)	4.1 (2.9–4.8)	4.0 (3.0–4.6)	0.59
Primary Site of Disease					0.701
Ovary	649 (76)	19 (68)	34 (79)	24 (73)	
Fallopian Tube	130 (15)	6 (21)	7 (16)	4 (12)	
Peritoneum	74 (9)	3 (11)	2 (5)	5 (15)	
Tumor Histology					0.052
High grade serous	764 (89)	27 (96)	35 (81)	28 (82)	
Carcinosarcoma	25 (3)	1 (4)	0 (0)	2 (6)	
Clear cell	9 (1)	0 (0)	3 (7)	0 (0)	
Other	57 (7)	0 (0)	5 (12)	4 (12)	
Carcinomatosis					0.343
Yes	688 (81)	26 (93)	36 (86)	27 (79)	
No	166 (19)	2 (7)	6 (14)	7 (21)	
Bulky Upper Abdominal Disease					0.219
Yes	508 (59)	22 (79)	25 (58)	19 (56)	
No	347 (41)	6 (21)	18 (42)	15 (44)	
Residual Disease					0.056
0cm	360 (42)	8 (29)	20 (47)	15 (44)	
0–1cm	339 (40)	9 (32)	11 (26)	14 (41)	
>1cm	156 (18)	11 (39)	12 (28)	5 (15)	

Table 2.

Patient and Tumor Characteristics by Median Income Grouping Category (n=963)

	<\$50,000 (n=129)	\$50–99,999 (n=496)	\$100–149,999 (n=283)	\$150,000 (n=55)	p-value
Median Age (range)	65 (29–95)	61 (25–88)	62 (30–81)	64 (19–84)	0.4305
BRCA Status					0.122
Negative	32 (25)	160 (32)	86 (30)	20 (36)	
BRCA 1 Positive	8 (6)	41 (8)	26 (9)	3 (5)	
BRCA 2 Positive	1 (1)	22 (4)	14 (5)	2 (4)	
Status Unknown	88 (68)	273 (55)	157 (55)	30 (55)	
ASA					0.0226
1–2	59 (46)	261 (53)	167 (60)	24 (44)	
3–4	69 (54)	232 (47)	112 (40)	31 (56)	
Primary Site of Disease					0.9731
Ovary	102 (79)	374 (75)	212 (75)	43 (78)	
Fallopian Tube	19 (15)	75 (15)	46 (16)	8 (15)	
Peritoneum	8 (6)	47 (9)	25 (9)	4 (7)	
Tumor Histology					0.4165
High grade serous	113 (88)	444 (90)	250 (88)	49 (89)	
Carcinosarcoma	2 (2)	14 (3)	9 (3)	3 (5)	
Clear cell	1 (1)	3 (1)	7 (2)	1 (2)	
Other	13 (10)	35 (7)	17 (6)	2 (4)	
PDS Outcome					0.7281
Optimal	100 (78)	399 (80)	231 (82)	46 (84)	
Sub-optimal	29 (22)	97 (20)	52 (18)	9 (16)	
Race/Ethnicity					0.0002
Non-Hispanic White	100 (78)	441 (89)	263 (93)	51 (93)	
Non-Hispanic Black	13 (10)	12 (2)	1 (<1)	2 (4)	
Asian	6 (5)	23 (5)	13 (5)	1 (2)	
Hispanic	9 (7)	18 (4)	6 (2)	2 (2)	

Table 3.

Median (A) and Adjusted (B) Overall Survival By Race and Income

Table 3A: Median Overall Survival			Table 3B: Adjusted Overall Survival*		
	Median (mos)	95% CI	HR	95%CI	p-value
Race					0.615
NHW	55.25	(51.84–58.49)	REF	---	
NHB	40	(19.54–78.82)	0.795	(0.50–1.27)	
Asian	80.79	(50.89–114.59)	1.21	(0.78–1.89)	
Hispanic	38.1	(24.95–94.72)	1.1	(0.68–1.76)	
Income					0.603
\$150,000	63.57	(42.36–107.64)	REF	---	
\$100,000–\$149,999	54.33	(47.87–58.49)	1.3	(0.87–1.92)	
\$50,000–\$99,999	57.74	(51.77–65.34)	1.2	(0.82–1.77)	
<\$50,000	48.62	(40.39–59.77)	1.18	(0.77–1.81)	

* From adjusted Cox models