Published in final edited form as:

Gynecol Oncol. 2008 November ; 111(2): 173–178. doi:10.1016/j.ygyno.2008.08.013.

Does equal treatment yield equal outcomes? The impact of race on survival in epithelial ovarian cancer

Mishka Terplan, MD, MPH, Sarah Temkin, MD, Ana Tergas, MD, and Ernst Lengyel, MD, PhD
Department of Obstetrics and Gynecology, The University of Chicago

Abstract

Objective—To determine if race impacts the survival of patients with epithelial ovarian cancer in a large academic medical center.

Methods—Demographic and clinical-pathologic information from patients treated at the University of Chicago from 1992–2007 was analyzed. Continuous variables were analyzed with *t* tests and categorical variables with chi square tests. Survival curves were evaluated using Kaplan-Meier methods and Cox proportional hazard models were constructed for both overall and disease free survival.

Results—209 women with epithelial ovarian cancer were included in the study, 163 (78%) white and 46 (22%) African American. The baseline demographic characteristics and clinico-pathologic factors such as disease stage, grading, CA-125 levels, rates of optimal debulking (<1 cm residual tumor), platinum sensitivity and American Society of Anesthesiologists score (ASA) were similar between the groups. The median overall survival for African American women was similar: 37.2 months (95% Confidence Interval (CI): 22.5, 52.9) while it was 34.1 months (95% CI: 27.4, 42.6) for white women.

Conclusions—There is no evidence of a racial disparity in either treatment or survival for ovarian cancer patients treated at a large academic center. Given that large epidemiologic studies suggested a difference in survival between African American and white women, other sources of disparities must be sought.

INTRODUCTION

Health disparities were first brought to the national attention in 1985 when Margaret Heckler (the then secretary of Health and Human Services) included disparity data in her annual report card on the health status of Americans. She described the existence of disparities as, “a sad and significant fact... An affront both to our ideals and to the ongoing genius of American medicine”. Since then the elimination of racial disparities in cancer burden has been identified as a national priority by the National Cancer Institute, the American Cancer Society and the Institute of Medicine and is one of the major goals of *Healthy People 2010* (1–3).

Corresponding author: Mishka Terplan MD, MPH, The University of Chicago, Department of Obstetrics and Gynecology, 5841 S Maryland Ave, MC 2050, Chicago, IL 60637. Phone: 773-834-7033, E-mail: mterplan@babies.bsd.uchicago.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of Interest statement:

The authors declare that there are no conflicts of interest.

Despite these goals, for every cancer case captured in the SEER (Surveillance Epidemiology and End Results) database, African Americans have worse survival. With an estimated 22,430 new cases and an expected 15,280 deaths in 2007, ovarian cancer is the second most common gynecologic cancer in the US and the leading cause of female reproductive cancer mortality (1;3). The 5 year survival from ovarian cancer increased between 1975 and 2002 in white women from 36 to 45%, but during that same time interval it fell for African American women from 43 to 39% (4). The age-adjusted mortality rate for ovarian cancer is higher for white women (5), but 2 and 5 year survival rates are worse for African Americans (4;6). This raises the question of how much African Americans have benefited from advances in ovarian cancer treatment such as cytoreductive surgery and platinum based chemotherapy (both developed in the 1980s). African American women are diagnosed at later stages than white women (7–9) and are less likely to undergo surgery in general (10), site-specific/recommended surgery (7; 9) or lymphadenectomy with staging (8) in particular. African American women are also less likely to receive standard chemotherapy (11–13), or both surgery and chemotherapy (14).

The purpose of the current study was to study epithelial ovarian cancer survival between white and African American women among a group of women who all had equal access to medical care within a single institution. We hypothesized that equal treatment would yield equal outcomes.

METHODS

Clinical Data

We conducted a retrospective cohort study of women treated for ovarian cancer from 1992–2007 at the University of Chicago. All patients who had undergone primary treatment for Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) stage I to IV epithelial ovarian, fallopian, or peritoneal cancer were selected for the study. Treatment consisted of either primary tumor debulking followed by platinum based chemotherapy or neo-adjuvant chemotherapy followed by surgery for those patients with advanced disease or co-morbidities, or in cases when the attending surgeon thought the cancer was unresectable. All surgical procedures were performed by one of five Gynecologic Oncologists at the University of Chicago and all pathology was verified by a single gynecologic pathologist at the University of Chicago. Optimal debulking was defined by a residual tumor size of less than 1 cm at the completion of surgery. The clinical information was stored in a Microsoft Access database (Version 2003-SP2) as previously reported (15;16)

The database contains socio-demographic variables such as race, insurance status and age, as well as clinico-pathologic factors such as family history of cancer, stage at presentation and data regarding clinical course such as type of surgery, chemotherapy regimen, presence of residual disease, pre- and postoperative CA-125 levels and platinum sensitivity. Histopathologic data was entered according to the World Health Organization classification of ovarian cancer. Age was calculated as age at the time of diagnosis. Racial categorization was made by the physician upon the initial assessment. Recurrence was defined as a tripling in the value of CA-125 and/or a new tumor as detected by radiological or clinical exam.

Follow-up information was gathered by reviewing the hospital and outpatient clinic charts, data from the Illinois Cancer Registry, the U.S. Social Security Index, and by contacting physicians involved in the patient's care. Follow-up information was updated every 6 months through October 2007. The University of Chicago accepts all patients regardless of insurance status and place of residence however it does not accept uninsured patients. Although all patients with a diagnosis of cancer are eligible for Medicare/Medicaid, it takes approximately 90 days for that to become effective in Illinois. Therefore patients without insurance are not scheduled into clinic.

All information entered was reviewed by a data manager and an Attending Gynecologic Oncologist (ST, EL). As a result there was no missing data and we were able to obtain 100% verification of all outcomes. For this analysis, we only included patients with epithelial ovarian cancer who were identified as either white or African American. The ovarian cancer database was approved by the Institutional Review Board at the University of Chicago.

Statistical analyses

All analyses were performed using STATA v 9.2 (College Station, TX). Descriptive statistics described patient demographic and clinico-pathologic variables. We compared the relationships between demographic and clinico-pathologic variables to see if they differed by race using χ^2 -test of independence and Pearson's R. Continuous variables were analyzed with *t* tests. Median survival was calculated in months for each group. Kaplan-Meier survival curves were plotted for both overall survival and disease free survival by race; these were compared with log-rank tests. A Cox proportional hazard model was used to calculate hazard ratios for both overall survival and disease recurrence while adjusting for potential confounders. A *p*-value of less than 0.05 was considered significant for all tests.

RESULTS

The analysis is based upon 209 patients treated for epithelial ovarian cancer at the University of Chicago who were identified as either African American or white. These patient included 163 (78%) white and 46 (22%) African American women. There was no difference between African American and white women in terms of family history, insurance status or age at the time of diagnosis. The distribution of clinico-pathologic variables, such as patient age, family history, insurance status, tumor type, American Society of Anesthesiologists (ASA) class and residual tumor mass after completion of surgery is shown in Table 1. The most common histology was papillary-serous cancer, which comprised over 70% of cancers. 149 (71%) of the patients had a high grade tumor and 177 (85%) had either FIGO stage III or IV disease (Table 1). There was no statistical difference between the two groups. An equal number of women in each group received first line adjuvant chemotherapy (Carboplatin and Paclitaxel). Response to chemotherapy was similar in both groups (Table 2).

Median survival time for all patients was 35 months. In bivariate survival analysis, age, grade, stage, ascites volume, and residual disease were correlated with survival. Optimally debulked patients (*n*=122) had a significant survival advantage (median survival time 50 months) over patients with suboptimal debulking surgery (*n*=87) (median survival time 22 months). There was no difference in disease free survival and overall survival. The median time to recurrence was 13.2 months (95% CI: 10.9, 17.0) for white patients and 14.4 (10.3, 21.0) months for African Americans; time to death was 34.1 (27.4, 42.6) months for whites and 37.2 (22.5, 52.9) for African Americans. Kaplan-Meier curves showed similar rates of both recurrence and survival (Figure 1 and Figure 2). In multivariate analysis adjusted for FIGO stage, optimal debulking, platinum sensitivity, preoperative CA-125, age at diagnosis and ASA class, race was not a prognostic factor. African Americans had 1.00 times the hazard of dying (95% CI: 0.57, 1.77) compared with whites and 0.95 times the hazard of disease recurrence (0.0.56, 1.60) (Table 3 and Table 4). Platinum resistance and public insurance were both associated with an increased hazard of both dying and disease recurrence independent of race. ASA class (I–II vs III–IV) was significantly associated with an increased hazard of dying but was not independently associated with recurrence.

DISCUSSION

We compared ovarian cancer treatment and survival among African American and white women and found that treatment type and outcome of patients with advanced ovarian cancer

cared for at one specific tertiary academic center is independent of race. White and African American women were equally likely to receive optimal debulking surgery, similar chemotherapies, and there was no difference in either overall or disease free survival between the groups.

Our results differ from many previously reported studies looking at the interplay of race and outcome in ovarian cancer. They have found that African Americans present with more advanced disease (7;8;13). We had a similar distribution of cancer stage and mean pre-operative CA-125 levels in the two groups. Also, the proportion of African Americans in other studies ranges from only 3.5–12.4% (17;18) and is typically lower than that of the national population (12.3%). Such low proportions of the primary exposure call into question the stability of the statistical model especially when used in multivariable analyses (19). In our study, African Americans made up 22% of the total number of patients presenting to our institution with ovarian cancer. Prior studies describe race as an independent prognostic factor for survival in ovarian cancer (7;10;12;13;20). Chan and colleagues, using the SEER database after controlling for age, stage, grade, and histology, found that African Americans had 1.18 times the hazard of death compared with white women. While this difference is statistically different, the magnitude of the effect is small and no interpretation of the result is offered aside from a reference to racial disparities as “genetic” (8).

Several limitations that affect the utility of SEER data in the investigation of disparities in ovarian cancer are worth noting. First, pertinent risk factors such as residual disease or platinum sensitivity, two well established risk factors for survival, are not captured. Secondly, no information on physician specialty in the provision of ovarian cancer care is included in SEER. Women who receive care from a gynecologic oncologist are known to have improved survival (21;22). In fact, in the study by Earle and colleagues (21), the effect of race on survival vanished when the type of surgeon was taken into account. Universal access to a Gynecologic Oncologist may have accounted for a least part of our finding of equivalent outcomes regardless of race in this study. Lastly and perhaps most importantly, the geographic distribution of the African Americans population in SEER is markedly different from that of whites. In an analysis of 9 SEER sites from 1988 – 1997, 84% of all African American cases came from only 3 sites (range per site for all the sites <1–42%) whereas white cases were far more equitably distributed (range per site 2–17%) (7).

The complex relationship between hospital setting, teaching status and surgery volume should not be ignored when looking at disparities in ovarian cancer treatment and survival. Minority race, older age, and admission to a rural, non-teaching or low surgery volume hospital all predict that a patient will receive incomplete surgical care for ovarian cancer (12;23). There is currently no cancer surveillance system or administrative data system (including SEER) in the United States that collects socioeconomic data. Consequently, the majority of the cancer literature addressing disparities concentrate on only those variables that are easily available, namely age and race and, more recently, Hispanic origin. More complex social inequalities, such as socioeconomic gradients in health and the contribution of economic deprivation to racial disparities are rendered invisible. These issues should be included in order to accurately assess disparities within our health care system and are largely controlled for in single institution settings.

Several limitations to this study must be noted. First, prior to 2004 our dataset was collected retrospectively. Second, the proportion of African Americans with private insurance was similar to that of whites in our study population. This is in contrast with insurance trends in the United States where greater than 70% of whites are insured compared with around 50% of African Americans (24). Although this may be seen as a limitation in terms of generalizability, the fact that our patient population was equal in all measured demographic characteristics aside

from race strengthens the conclusion that equal care yields equal outcomes. Finally, this study is based on a single institution which may be seen as limiting the finding's generalizability. Yet, a single institution studies can capture essential survival cofactors such as residual disease that are not available in national data sets. Indeed, a large review of racial disparities in breast, colon and cervix cancer treatment noted that, although a majority of studies reported disparities in cancer treatment, those that focused on a single institution or an equal access system described far fewer disparities (20).

Our findings should be generalizable to other large medical centers. The standardization of care within a single practice reduces the heterogeneity of treatment that clouds population based studies. In fact, the other published studies that have demonstrated no racial disparity in survival are also from single institutions (18;25). In a review of ovarian cancer patients treated at the University of Pennsylvania from 1989 to 1993, Morgan and colleagues demonstrated no difference in stage at presentation and overall survival between white and African American patients (25). In our study patients all received the same standard of clinical and surgical care. In addition, we were able to analyze essential clinical factors such as residual disease and platinum sensitivity, as well as insurance status, which serves as a marker of socio-economic status, and ASA class, a proxy for medical comorbidity. After controlling for these variables, race was not an independent prognostic determinant of survival in women with ovarian cancer.

The purpose of this study was to investigate whether racial disparities in ovarian cancer outcome exist when white and African American women are treated for epithelial ovarian cancer under similar conditions at a single institution with equal access to medical care. We found that these women had similar outcomes. These observations call into question the assumption that genetic differences or different tumor biology underlie ovarian cancer outcomes and point instead to social and institutional variables as leading contenders. Indeed, any residual effect of race would be small and non-modifiable. Our study highlights the importance of access to quality care in the treatment of ovarian cancer and in the elimination of outcome disparities.

Acknowledgments

We would like to thank Melissa Gilliam MD MPH and Erica Smith MPH for their help with the manuscript and Amy Becker PhD who supports the University of Chicago Ovarian Cancer Data Base.

Financial Support: This work was at least in part supported by the Ovarian Cancer Research Fund (Liz Tilberis Scholars Program), the National Cancer Institute - R01 CA111882 (to E.L.). Ernst Lengyel holds a Clinical Scientist Award in Translational Research from the Burroughs Wellcome.

Reference List

1. ACS. Cancer Facts & Figures 2007. Atlanta, GA: American Cancer Society; 2007.
2. HHS. Healthy People 2010. Department of Health and Human Services 2008. [cited 2008 Jan 15]. Available from: URL: <http://www.healthypeople.gov/About/goals.htm>
3. Reis, LAG.; Melbert, D.; Krapcho, M.; Stinchcomb, DG.; Howlader, N.; Horner, MJ., et al. SEER Cancer Statistics Review, 1975–2005. Bethesda, MD: National Cancer Institute; 2008.
4. Surveillance Research Program CSB. Surveillance, Epidemiology, and End Results (SEER) Program. National Cancer Institute, DCCPS 7 A.D; Apr 2 [cited 2008 Jan 15]. Available from: URL: www.seer.cancer.gov
5. Harper, S.; Lynch, J. NCI Cancer Surveillance Monograph Series. Bethesda, MD: National Cancer Institute; 2005. Methods for Measuring Cancer Disparities: Using Data Relevant to Healthy People 2010 Cancer-Related Objectives. Ref Type: Serial (Book, Monograph)
6. McGuire V, Herrinton L, Whittemore AS. Race, epithelial ovarian cancer survival, and membership in a large health maintenance organization. *Epidemiology* 2002;13(2):231–234. [PubMed: 11880767]

7. Barnholtz-Sloan JS, Tainsky MA, Abrams J, Severson RK, Qureshi F, Jacques SM, et al. Ethnic differences in survival among women with ovarian carcinoma. *Cancer* 2002;94(6):1886–1893. [PubMed: 11920552]
8. Chan JK, Zhang M, Hu JM, Shin JY, Osann K, Kapp DS. Racial disparities in surgical treatment and survival of epithelial ovarian cancer in United States. *J Surg Oncol* 2008;97(2):103–107. [PubMed: 17979133]
9. Parham GP, Hicks ML. Racial disparities affecting the reproductive health of African-American women. *Med Clin North Am* 2005;89(5):935–943. 941. [PubMed: 16129105]
10. Barnholtz-Sloan JS, Schwartz AG, Qureshi F, Jacques S, Malone J, Munkarah AR. Ovarian cancer: changes in patterns at diagnosis and relative survival over the last three decades. *Am J Obstet Gynecol* 2003;189(4):1120–1127. [PubMed: 14586365]
11. Du X, Sun C, Milam M, Bodurka D, Fang S. Ethnic differences in socioeconomic status, diagnosis, treatment, and survival among older women with epithelial ovarian cancer. *Int J Gynecol Cancer*. 2007
12. Harlan LC, Clegg LX, Trimble EL. Trends in surgery and chemotherapy for women diagnosed with ovarian cancer in the United States. *J Clin Oncol* 2003;21(18):3488–3494. [PubMed: 12972525]
13. Parham G, Phillips JL, Hicks ML, Andrews N, Jones WB, Shingleton HM, et al. The National Cancer Data Base report on malignant epithelial ovarian carcinoma in African-American women. *Cancer* 1997;80(4):816–826. [PubMed: 9264366]
14. Cress RD, O'Malley CD, Leiserowitz GS, Campleman SL. Patterns of chemotherapy use for women with ovarian cancer: A population-based study. *Journal of Clinical Oncology* 2003;21(8):1530–1535. [PubMed: 12697877]
15. Sawada K, Radjabi AR, Shinomiya N, Kistner E, Kenny HA, Salgia R, et al. C-Met overexpression is a prognostic factor in ovarian cancer and an effective target for inhibition of peritoneal dissemination and invasion. *Cancer Res* 2007;67(4):1670–1680. [PubMed: 17308108]
16. Sawada K, Radjabi AR, Bhaskar V, Kistner E, Tretiakova MS, Jagadeeswaran S, et al. Loss of E-cadherin promotes ovarian cancer metastasis via alpha 5-integrin, which is a therapeutic target. *Cancer Res* 2008 Apr 1;68(7):2329–2339. [PubMed: 18381440]
17. O'Malley CD, Cress RD, Campleman SL, Leiserowitz GS. Survival of Californian women with epithelial ovarian cancer, 1994–1996: a population-based study. *Gynecol Oncol* 2003;91(3):608–615. [PubMed: 14675685]
18. Smith JP, Day TG Jr. M.D. Anderson Hospital and Tumor Institute. Review of ovarian cancer at the University of Texas Systems Cancer Center. *American Journal of Obstetrics & Gynecology* 1979;135(7):984–993. [PubMed: 507137]
19. Fisher RA. On the Interpretation of Chi-Square from Contingency Tables and the Calculation of P. *Journal of the Royal Statistical Society* 1922;85(1):87–94.
20. Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. *Natl Cancer Inst* 2002;94(5):334–357.
21. Earle CC, Schrag D, Neville BA, Yabroff KR, Topor M, Fahey A, et al. Effect of surgeon specialty on processes of care and outcomes for ovarian cancer patients. *J Natl Cancer Inst* 2006;98(3):172–180. [PubMed: 16449677]
22. Schrag D, Earle C, Xu F, 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(3):163–171. [PubMed: 16449676]
23. 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(10):2031–2042. [PubMed: 17420977]
24. Agency for Health Care Research and Quality. U.S. Department of Health and Human Services. Rockville, MD: 2008 Feb 1. Report No.: 08-0041.
25. Morgan MA, Behbakht K, Benjamin I, Berlin M, King SA, Rubin SC. Racial differences in survival from gynecologic cancer. *Obstetrics & Gynecology* 1996;88(6):914–918. [PubMed: 8942827]

Figure 1. Overall Survival by Race
See attachment

Figure 2. Disease Free Survival by Race
See attachment

Table 1

Characteristics of study population

Variable	White N (%) N=163	Black N (%) N=46	p-value
Family History			0.72
Breast/Ovarian cancer	32 (19.6)	10 (21.7)	
Uterine cancer	10 (6.1)	1 (2.2)	
No cancer history	89 (54.6)	27 (58.7)	
Insurance status			0.52
Private	60 (39.7)	21 (47.7)	
Medicare/private	60 (39.7)	13 (29.6)	
Medicare	17 (11.2)	4 (9.1)	
Medicaid	14 (9.3)	6 (13.6)	
ASA Class			0.47
I	7 (4.6)	0 (0.0)	
II	72 (47.7)	20 (45.5)	
III	70 (46.4)	23 (52.3)	
IV	2 (1.3)	1 (2.3)	
Mean Age (SD)*	60.9 (11.2)	61.2 (11.3)	0.42
Type of Surgery			0.51
Primary Debulking (no prior chemotherapy)	141 (86.5)	38 (82.6)	
Interval Debulking (neo-adjuvant chemotherapy)	22 (13.5)	8 (17.4)	
Pathology (histoloige subtype)			0.75
Serous-papillary	117 (71.8)	34 (73.9)	
Endometrial	20 (12.3)	7 (15.2)	
Clear cell	17 (10.4)	4 (8.7)	
Mucinous	9 (5.5)	1 (2.2)	
Grade of Tumor			0.56
Low	10 (6.2)	1 (2.2)	
Moderate	37 (22.8)	11 (23.9)	
High grade	115 (71.0)	34 (73.9)	
FIGO stage			0.17
I	15 (9.2)	6 (13.0)	
II	6 (3.7)	5 (10.9)	
III	98 (60.1)	22 (47.8)	
IV	44 (27.0)	13 (28.3)	
Residual Disease[†]			0.71
Absent	96 (59.6)	26 (56.5)	
Present	65 (40.4)	20 (43.5)	
Pre-operative levels of CA-125*			0.59
Mean (sd)	2320 (7912.4)	1579 (2156.8)	
Median	399.5	1044.0	
Range	1–4826	14–9630	
Inter-quartile Range	98–1126	151–1695	
Post-operative levels of CA-125*			0.31
Mean (sd)	994.9 (3933.3)	396.8 (758.3)	
Median	154.0	90.0	
Range	0–42546	4–4193	
Inter-quartile Range	34–450	25.5–407.5	

* Continuous variables, mean (standard deviation) presented

[†] Residual disease defined as mass ≥1cm at the completion of surgery

Table 2

Chemotherapy and response by race

Variable	White N (%)	Black N (%)	p-value
Type of Chemotherapy			0.54
Neo-adjuvant	24 (14.8)	8 (17.4)	
Adjuvant	127 (78.4)	32 (69.6)	
Platinum sensitivity			0.32
Resistant	71 (43.6)	15 (32.6)	
Sensitive	79 (48.5)	24 (52.2)	

Table 3

Hazard Ratio for Survival

Variable	Hazard Ratio	95% Confidence Interval
Race		
White	1	
Black	1.00	0.57–.77
Insurance		
Any Private	1	
Public	1.61	0.88–2.96
Age*	1.00	0.98–1.02
Pre-operative levels of CA125*	1.00	1.00–1.00
Residual Disease		
Absent	1	
Present	1.56	0.93–2.60
FIGO Stage		
I/II	1	
III/IV	1.24	0.44–3.45
Platinum Sensitivity		
Yes	1	
No	10.85	5.62–20.96
ASA Class		
I or II	1	
III or IV	1.91	1.15–3.18

* Modeled as continuous variables

Table 4

Hazard Ratio for Recurrence

Variable	Hazard Ratio	95% Confidence Interval
Race		
White	1.0	
Black	0.95	0.56 – 1.60
Insurance		
Any Private	1.0	0.50 – 1.54
Public	1.88	
Age*	1.01	0.99– 1.03
Pre-operative levels of CA125*	1.00	1.00 – 1.00
Residual Disease		
Absent	1.0	0.96 – 1.75
Present	1.10	
FIGO Stage		
I/II	1.0	
III/IV	1.82	0.74 – 4.48
Platinum Sensitive Disease		
Yes	1.0	
No	24.85	11.66 – 52.96
ASA Class		
I or II	1.0	
III or IV	1.38	0.88 – 2.17

* Modeled as continuous variables