



Regional variation in surgical assessment of lymph nodes for staging among women with early-stage epithelial ovarian cancer



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HIGHLIGHTS

- Significant regional variation in lymphadenectomy for early ovarian cancer exists in the U.S.
- Variation in care by region and socioeconomic status shows a disparity in access and outcomes.
- Future work should focus on target interventions aimed at reducing the observed variation.

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ABSTRACT

Objective. To investigate geographical and socioeconomic variations in performance of lymph node dissection for the evaluation of patients with early-stage epithelial ovarian cancer.

Methods. A population-based, retrospective cohort study was conducted using data from the National Cancer Institute's SEER Program for 15 geographic registries and county-level measures. Women with early-stage epithelial ovarian cancer registered between 2000 and 2008 with known lymph node assessment status were studied. A multiple logistic regression analysis was used to evaluate the differences in the likelihood of lymph node assessment according to geographic SEER region.

Results. After adjusting for tumor characteristics, demographics, and area-based socioeconomic measures, a significant relationship between SEER region and lymph node dissection remained. Compared to the region with the highest proportion of lymph node dissection, there is a significantly lower probability of surgical assessment of lymph nodes in 8 of the remaining 14 geographical regions.

Conclusions. The variation in ovarian cancer surgical care by region reported in this study has implications for access and outcomes for patients with early-stage disease. Study findings merit further investigation and should be characterized to permit targeted interventions aimed at reducing the observed disparities.

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Introduction

The National Institutes of Health (NIH) Consensus Development Conference in 1994 was dedicated to ovarian cancer and its screening, treatment, and follow-up. Recommended guidelines and the standard of care for the primary treatment of a pelvic mass proven to be malignant consist of complete surgical staging, accurate diagnosis and optimal cytoreduction followed by adjuvant chemotherapy [1–4]. Roughly three quarters of women with ovarian cancer present with metastases, and National Comprehensive Cancer Network (NCCN) guidelines state that comprehensive surgical staging should be performed to rule out

occult metastases for women with apparent early disease [5]. Surgical staging procedures include removal of the uterus, ovaries and omentum as well as sampling of the peritoneum, peritoneal washings, and dissection of pelvic and para-aortic lymph nodes [1,6,7].

Approximately 25–30% of patients with cancer grossly confined to the ovaries at exploration who complete surgical staging are upstaged [8–11]. Powless found that among patients with presumed early-stage ovarian cancer: 32% had positive pelvic nodes, 48% had positive para-aortic nodes, and 20% had both positive [5]. The Centers for Disease Control and Prevention's National Program of Cancer Registries (CDC-NPCR) population-based, ovarian cancer patterns of care study assessed the adequacy of surgical staging and its impact on survival. Only lymph node assessment had a statistically significant association with improved survival. The 5-year survival for women with node sampling was 84.2% versus 69.6% for those without, and patients who did not have lymph node assessment had nearly twice the risk of death as those who did [12].

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The relative contribution of geography in the management of ovarian cancer is important in describing the pattern of care that exists in the United States. The Dartmouth Atlas Report continues to state geography as an important factor in the health care and outcome of various diseases. In regard to ovarian cancer, Polsky et al. investigated the geographical variation in receipt of chemotherapy among Medicare patients with ovarian cancer [13]. The study found large variations in chemotherapy treatment between geographic areas. Another study by Fairfield et al. using the Surveillance, Epidemiology and End Results (SEER) database looked at the regional variation in cancer-directed surgery and mortality among Medicare patients with epithelial ovarian cancer from 1998 to 2005 [14]. They found regional variation in cancer-directed surgery, which also helped to explain the variation in mortality. However, these studies did not describe the specific variations between regions.

Additionally, area-based socioeconomic measures have been found to be significantly associated with performance of lymph node dissection for staging in early-stage ovarian cancer patients. Goff et al. showed that patients with a better socioeconomic status were more likely to undergo surgical staging [15]. However, Cress et al. reported conflicting results that socioeconomic factors had no demonstrable impact effect on the receipt of surgical staging procedures including lymph node dissection [12]. The reasons for these discrepant findings are not apparent; however, identification of an association of socioeconomic factors with the performance of indicated staging procedures could help guide interventions to increase the frequency of comprehensive surgical staging and, thereby, improve outcomes.

Studies have shown the effectiveness of surgical assessment of lymph nodes as part of staging, resulting in better prognosis, better treatment and overall survival for women with early-stage ovarian cancer. Variations in comprehensive surgical staging, including lymph node dissection, exist. This study investigates geographical and socioeconomic variations in performance of lymph node dissection for the evaluation of patients with early-stage epithelial ovarian cancer.

Methods

A population-based, retrospective cohort study was conducted using data from the National Cancer Institute's SEER Program. The SEER Program collects cancer incidence and survival data from population-based cancer registries covering approximately 28% of the U.S. population. In the SEER 17 Registry, seventeen geographic areas across the United States contribute to the data: states (Greater California, Connecticut, Hawaii, Iowa, New Mexico, Utah, Kentucky, Louisiana, and New Jersey), metropolitan areas (Atlanta, the Greater Bay Area [San Francisco–Oakland and San Jose–Monterey], Los Angeles, Seattle, and Detroit), rural Georgia, and the Alaskan Native Tumor Registry. However, Alaska and Rural Georgia regions were excluded from analysis due to small sample sizes. The SEER database is linked to information about a patient's county of residence from the 2000 census data. County-level measures are calculated using the Census 2000 SF files [16].

Patients registered between 2000 and 2008 were included in the study. Early-stage was defined using the SEER Summary Stage classification as 'localized' – an invasive malignant neoplasm confined entirely to the organ of origin, women with involved nodes were not included. Analysis was restricted to women with microscopically confirmed malignant epithelial ovarian cancer. Histological cell types by International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) were categorized as: serous (8441, 8442, 8460–8462, 9014), endometrioid (8380–8383), mucinous (8470–8473, 8480–8482) and other (8050–8052, 8140, 8141, 8143, 8147, 8260–8263, 8310, 8313, 8440, 8450, 8451, 8560, 8562, 8570–8575, 8950, 8951, 8980–8982, 9000, 9015). Non-invasive tumors and tumors of low malignant potential were not included. Women with no cancer-directed surgery performed under SEER variable, "reason no cancer-directed surgery," were not included

in analysis. Lastly, women with unknown lymph node assessment were also excluded.

Receipt of surgical assessment of lymph nodes for staging was the outcome of interest in our analyses of variation according to geographic region. SEER data recorded the number of regional lymph nodes examined as: 'no nodes examined' (00), 'one node examined' (01) to 'ninety or more regional lymph nodes examined' (90), and 'unknown' (95–99). Surgical assessment of lymph nodes was analyzed as a dichotomous variable, 'no nodes examined' (00) versus 'one or more lymph nodes examined' (01–90). The number of resected nodes that defines an adequate dissection has not been determined for ovarian cancer. We chose to use one node as evidence that the effort to stage was made. If a higher number of resected nodes were selected, the findings could be somewhat different.

Additional covariates included clinical, sociodemographic and area-based socioeconomic factors. Clinical factors included tumor histologic cell type and tumor grade. Histologic cell type was categorized into 4 categories: serous, endometrioid, mucinous and other cell types. Tumor grade was classified as well differentiated (Grade I), moderately differentiated (Grade II), poorly differentiated (Grade III), and undifferentiated (Grade IV). Tumor grade was collapsed into 3 categories: Grades I and II, Grades III and IV, and unknown grade.

Sociodemographic factors included age and race. Age at diagnosis was transformed from a continuous into a categorical variable based on previous studies [17,18]. The race variable was defined by SEER as White, Black, Asian or Pacific Islander, American Indian/Alaska Native, other unspecified and unknown and was kept as such categories in the study analyses.

SEER does not collect individual level socioeconomic indicators, however aggregate-level measures from the U.S. Census are linked to each subject's county of residence. The 2000 county attributes included in the study were: median household income, educational attainment, unemployed percent of persons, percent of persons below poverty level, and rural–urban characteristic. These measures were calculated using the Census 2000 SF files and are provided as percentages of the population of the county where the subject resides. Based on census categorization, median household income was divided into 3 groups: lowest (<\$40,000), middle (\$40,000–57,999), and top tertiles (\geq \$58,000). Education was categorized into 3 levels: an undereducated county level as \geq 25% of the population with less than a high school degree (based on Krieger and colleagues' definition of "undereducated neighborhood"), and two degrees of educated levels, between 15–24% and below 15% [19]. The unemployed variable was categorized into 3 levels according to the national unemployment rate in 1999, into counties below 4.2% and two degrees above the national unemployment rate, between 4.2–6.7% and \geq 6.8%. The poverty variable was also categorized into 3 levels based on Krieger and colleagues' 1997) definition of a poverty area, \geq 20% of the population, and two degrees of non-poverty areas, between 10–19% and below 10% [19].

The Rural–Urban Continuum Code information linked from the 2000 census was used to form the rural–urban variable. It distinguishes metropolitan counties by the size of the population within their metropolitan area. Nonmetropolitan counties are distinguished by degree of urbanization and adjacency to metropolitan areas [20]. A total of 9 subdivided categories are available for analysis of trends; we collapsed the variable into 3 categories: metropolitan, urban and rural. This was done to better describe the area characteristics of the sample cohort.

Characteristics of the 5243 women with early-stage ovarian cancer were obtained using descriptive statistical techniques. Univariate analysis using a Pearson's chi-square test was used to determine if the main predictor variable and each covariate were independent of the outcome variable, lymph node assessment. A Pearson's Chi-square p-value was reported for each predictor variable, with <0.05 demonstrating a significant association. Univariate logistic regression analyses were performed to investigate the association between each independent variable and lymph node assessment. Significant associations

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