

Utilization of Lymph Node Dissection, Race/Ethnicity, and Breast Cancer Outcomes

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Involvement of axillary lymph nodes is the most important prognostic factor in women with invasive breast carcinoma.¹ Sentinel lymph node biopsy (SLNB), a rapidly adopted and less morbid alternative to axillary lymph node dissection (ALND) for nodal staging, has been used since the late 1990s. Based on SLNB, patients are grouped into those with regional nodal metastasis who are likely to benefit from ALND and those without nodal metastases who are unlikely to benefit from ALND.² Compared with SLNB alone, SLNB with complete ALND was not associated with greatly improved survival for breast cancer (BC) patients with micrometastasis^{3,4} and macrometastasis.⁴

Recent studies reported that patient race/ethnicity affects receipt and/or quality of sentinel lymph node dissection (SLND).^{5,6} Variation in compliance with a sentinel lymph node dissection quality measure was supported by a few additional studies. For example, being African American was associated with lower odds of receiving initial SLNB.⁷ African American or Hispanic women were less likely to undergo initial SLNB with complete ALND,¹ and disparities in receipt of SLNB persisted for African American and Hispanic women with BC in a study that looked at temporal differences in use of SLNB from 1998 to 2005.⁸ Although large differences by race/ethnicity in BC survival are well established,^{9,10} it is unknown whether disparities in nodal surgery utilization explain the racial/ethnic disparities in survival among women with micrometastasis and macrometastasis in sentinel lymph nodes.

Because the majority of BC diagnoses occur after age 65 years and because increased life expectancy and advances in treatment mean that more women will be BC survivors,¹¹⁻¹⁵ we report the impact of nodal surgery utilization on survival among white, black, Hispanic, and Asian women in a large population-based cohort of women with BC diagnosed from 1998 through 2005 who were enrolled in fee-for-service Medicare plans A and B.

MATERIALS AND METHODS

Population

We used the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute to identify BC patients who underwent SLNB alone or SLNB with a complete ALND between 1998 and 2005. As previously de-

Objectives: Although large differences by race/ethnicity in breast cancer survival are well established, it is unknown whether disparities in nodal surgery utilization explain the racial/ethnic disparities in survival among women with micrometastasis and macrometastasis in sentinel lymph nodes (SLNs).

Study Design: Retrospective cohort study.

Methods: Women with breast cancer who underwent sentinel lymph node biopsy (SLNB) and who were found to have nodal metastases were identified from the Surveillance, Epidemiology, and End Results database (1998-2005). Outcomes data were examined for patients who underwent SLNB alone versus SLNB with axillary lymph node dissection (ALND).

Results: Proportions of patients receiving SLNB alone or receiving SLNB with a complete ALND were not statistically different among women of different racial/ethnic backgrounds ($P = .8$). Patients of African American descent or Hispanic origin had reduced overall survival, whereas patients of Hispanic origin had reduced disease-specific survival after adjusting for selected covariates. Adjusting for nodal surgery did not reduce racial/ethnic disparities in overall survival or disease-specific survival.

Conclusions: The disparities in survival among African American and Hispanic women with breast cancer are not explained by nodal surgery utilization among women with micrometastasis and macrometastasis in SLNs.

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It is unknown whether nodal surgery utilization explains the racial/ethnic disparities in survival among breast cancer patients with micrometastasis and macrometastasis in sentinel lymph nodes (SLNs). We found that among Medicare beneficiaries, disparities in survival are not explained by nodal surgery utilization among women with micrometastasis and macrometastasis in SLNs.

- Race/ethnicity had no effect on the nodal surgery utilization among Medicare beneficiaries with node-positive breast cancer.
- Adjusting for nodal surgery utilization did not reduce racial/ethnic disparities in breast cancer outcomes for Medicare beneficiaries of Hispanic (disease-specific survival and overall survival) and African American (overall survival) heritage.

follows: micrometastatic disease (>0.2-2 mm) and macrometastatic disease (>2.0 mm).¹⁶ Survival was calculated as the number of months between the date of diagnosis and the date of death, the date last known to be alive, or December 31, 2005, whichever occurred first. The day of diagnosis was defined as the 15th of the month, because SEER only reports the month and year of diagnosis. The survival end points for the present study were overall survival (OS) and disease-

specific survival (DSS). Patients who were lost to follow-up or who survived beyond December 31, 2005, were coded as censored observations. Kaplan-Meier survival curves for survival by treatment were parallel per visual inspection as well as by log-rank test supporting the proportionality assumption. There were no significant interactions among the variables.

scribed,^{3,4} patients were categorized according to their primary surgical procedure (breast-conservation surgery or mastectomy) and according to their axillary lymph node assessment as follows: no nodal evaluation, ALND only, SLNB only (without complete ALND), and SLNB with complete ALND. If a patient underwent SLNB and a modified radical mastectomy, the patient was categorized as having undergone complete ALND. Patients were excluded if they underwent ALND only (without SLNB), did not undergo a lymph node evaluation or if evaluation status was not specified in SEER data, or did not undergo primary surgery. Patients were also excluded if they had stage IV disease. We used the American Joint Committee on Cancer pathologic N category subclassifications to categorize patients according to the degree of nodal metastatic disease as follows: macrometastatic disease (>2.0 mm) and micrometastatic disease (>0.2-2.0 mm). Patients reported only as N1 were classified as having macrometastatic nodal disease as described earlier by Yi and colleagues.⁴ The final sample included 24,961 patients.

Statistical Analysis

We used SEER categories of non-Hispanic white, non-Hispanic black, Hispanic, and non-Hispanic Asian/Pacific Islander. Patients who underwent surgical resection of the primary breast tumor were categorized as having had mastectomy or breast conservation therapy. Beginning in 1998, SEER started recording information about the type of lymph node assessment. The SEER variable “scope of regional lymph node surgery” was used to capture the patients’ lymph node assessment. Patients were categorized according to their lymph node assessment: no nodal evaluation, ALND only, SLNB without complete ALND (the SLNB-only group), and SLNB with complete ALND (the ALND-group, node-positive women).¹³ Patients who underwent SLNB and a modified radical mastectomy were considered as having undergone complete ALND. To categorize patients according to their degree of nodal metastatic disease, the American Joint Committee on cancer pathologic N category subclassifications were used as

We used χ^2 testing to compare the differences in categorical variables and proportions between patients who underwent SLNB alone and patients who underwent SLNB with complete ALND. In preliminary analyses, we compared the outcomes of patients undergoing SLNB alone with those of patients undergoing SLNB with complete ALND. We also performed univariate analyses to determine the influence of patient, tumor, and treatment factors with known or potential prognostic value on OS and DSS as determined by the Kaplan-Meier method. Variables subjected to univariate analysis included age (continuous); socioeconomic status; comorbidity index¹⁷⁻²¹; tumor grade (low/intermediate vs high); tumor size (T1-T3); estrogen receptor and progesterone receptor status (positive, negative, unknown); use of chemotherapy; use of radiotherapy after surgery (yes vs no); year of diagnosis (split, before 2000 and after 2000); and use of ALND. Significant factors from the univariate analysis were included in a multivariate Cox proportional hazard model to identify significant predictors of OS and DSS. In the unadjusted model (model 1) race is the only predictor. The covariates age and tumor size were analyzed as continuous variables in the multivariate models. Covariates added in our regression models included patient and tumor characteristics (age, year of diagnosis, treatment [chemotherapy, surgery, radiation], tumor stage, tumor size, tumor grade and number of positive lymph nodes, diameter of positive lymph nodes, comorbidities, socioeconomic status) (model 2); and receipt of nodal surgery (model 3). Hazard ratios (HRs) and 95% confidence intervals (CIs) were obtained for all regressions. Analyses were performed using SAS release 9.2 (SAS Institute Inc, Cary, North Carolina). All tests were 2-tailed with statistical significance set at $P < .05$.

RESULTS

Of the 24,961 women in the SEER database who underwent SLNB as part of their surgical treatment for BC from 1998 to 2005, 5364 (21%) had nodal metastases and comprised the cohort we analyzed. Of the patients in the cohort, 1028 (19%) underwent SLNB alone and 4336 (81%) underwent SLNB with a complete ALND. Most patients ($n = 4098$) had macrometastasis, and 1831 patients had micrometastasis.

Proportions of patients receiving SLNB alone or receiving SLNB with a complete ALND were not statistically different among women of different racial/ethnic backgrounds ($P = .8$) in a cohort of BC patients restricted to those with nodal metastases. A higher proportion of patients underwent SLNB alone if they were diagnosed after 2000 (81.7% vs 18.3%). Patients who underwent SLNB alone rather than SLNB with complete ALND were more likely to have smaller (median tumor size, 15 mm vs 20 mm) or low-grade tumors (69.2% low/intermediate vs 23.6% high grade) (**Table 1**). Most patients (84.2%) who underwent SLNB alone had breast-conservation surgery. The median number of lymph nodes removed during surgery was 2 in the patients who underwent SLNB alone and 12 in those who underwent SLNB with complete ALND ($P < .0001$). The mean number of lymph nodes removed was 3.9 (range, 1-32 nodes) in the SLNB-alone group and 13 (range, 1-52 nodes) in the SLNB plus ALND group.

Of the patients undergoing SLNB alone, 52.4% had micrometastases, compared with only 22.1% of the patients undergoing SLNB with complete ALND. **Table 2** shows a multivariate analysis for factors associated with undergoing SLNB alone. Patients were more likely to undergo SLNB alone compared with SLNB with complete ALND if they had smaller or low-grade tumors, had micrometastases, had positive estrogen receptor status, and were undergoing segmental mastectomy. Of the study population, 551 patients (10.5%) had died of any cause, and 297 patients (5.5%) had died of BC. Overall survival was not greatly different for patients undergoing SLNB alone compared with those undergoing SLNB with complete ALND in the entire cohort and in patients with micrometastases or macrometastases. **Table 3** shows the clinical and pathologic factors affecting OS and DSS.

Patients of African American descent or of Hispanic origin had reduced OS after adjusting for selected covariates. Older women or those with macrometastases, high-grade tumors, larger tumors, negative estrogen receptor status, or more positive lymph nodes found during surgery had reduced OS. Adjusting for nodal surgery did not reduce

racial/ethnic disparities in OS. Patients of Hispanic origin who were older or who had high-grade tumors, larger tumors, or negative estrogen receptor or progesterone receptor status; who underwent complete ALND after SLNB; or who had more positive lymph nodes found during surgery had reduced DSS. Disease-specific survival was decreased in patients with macrometastasis (not statistically significant). Adjusting for nodal surgery did not reduce racial/ethnic disparities in DSS.

DISCUSSION

Yi and colleagues⁴ recently examined differences in survival for patients with nodal disease undergoing SLNB alone versus SLNB with complete ALND. Similar to their results, we found no significant differences in utilization of SLNB alone or SLNB with a complete ALND between Caucasian and African American older BC patients in a cohort restricted to those with micrometastasis and macrometastasis in sentinel lymph nodes. In our study, this observation also held true for Hispanics and Asians/Pacific Islanders. Our study is unique in that it is one of the first reports of health outcomes in older BC patients with nodal disease for Hispanics, Asians, and Pacific Islanders. Previously mentioned studies did observe racial/ethnic disparities in utilization or quality of nodal surgery.^{1,5-8} This difference probably reflects the fact that their purpose was not to address BC survival with receipt of nodal surgery; therefore, they did not restrict their study population to only those with nodal disease. Similar to the findings reported by Bili-moria and colleagues³ and Yi and colleagues,⁴ our study suggests that patients are more likely to receive SLNB alone if they undergo breast-conservation therapy, are older, and have smaller primary tumors.

We observed that adjusting for receipt of nodal surgery did not reduce racial/ethnic disparities. Being of African American descent was associated with reduced OS, while being of Hispanic origin was associated with reduced DSS and OS compared with being Caucasian. This finding is consistent with the findings of Ooi and colleagues,⁹ who used SEER data to study women diagnosed with invasive breast carcinoma between 2000 and 2006. Ooi and colleagues showed elevated risk of BC-specific mortality among Hispanic whites and blacks that persisted after adjustments for important outcome predictors.

Yi and colleagues⁴ found a statistically significant hazard of mortality (HR = 1.3; 95% CI, 1.1-1.6) for women aged 18-99 years undergoing a complete ALND compared with those undergoing SLNB only. They attributed this difference to more advanced disease in patients undergoing SLNB

■ **Table 1.** Demographic and Clinical Characteristics of Study Population^a

Characteristic	SLND Alone (n = 1028)	SLNB and ALND (n = 4336)	P
Age, y			.08
Mean	74.6	74.3	
Median	74 (66-89)	74 (66-89)	
Positive lymph node diameter, n (%)			
Micrometastasis	539 (52.4)	960 (22.1)	
Macrometastasis	489 (47.6)	3376 (77.9)	
Race, n (%)			.8
Non-Hispanic white	860 (83.7)	3649 (84.2)	
Non-Hispanic black	55 (5.4)	202 (4.7)	
Asian/Pacific Islander	65 (6.3)	290 (6.7)	
Hispanic	43 (4.2)	173 (3.9)	
Other	5 (0.5)	22 (0.5)	
Year of diagnosis, n (%)			.03
Before 2000	188 (18.3)	920 (21.2)	
After 2000	840 (81.7)	3416 (78.8)	
Surgery, n (%)			<.0001
Breast conservation	866 (84.2)	2352 (54.2)	
Mastectomy	162 (15.8)	1984 (45.8)	
Tumor stage (AJCC), n (%)			<.0001
II	989 (96.2)	3972 (91.6)	
III	39 (3.8)	364 (8.4)	
Tumor size, mm			<.0001
Mean	21.2	29.1	
Median	15 (1-998)	20 (1-998)	
Tumor stage, cm, n (%)			<.0001
0-2	738 (71.8)	2339 (53.9)	
>2 to 5	259 (25.2)	1719 (39.6)	
>5	31 (3.0)	271 (6.3)	
Unknown	<5	7 (0.2)	
Tumor grade, n (%)			<.0001
Low/intermediate	711 (69.2)	2620 (60.4)	
High	243 (23.6)	1421 (32.8)	
Unknown	61 (5.9)	246 (5.7)	
Missing	13 (1.3)	49 (1.1)	
Estrogen receptor status, n (%)			<.0001
Positive	794 (77.2)	3192 (73.6)	
Negative	93 (9.1)	624 (14.4)	
Unknown	141 (13.7)	520 (12.0)	
Progesterone receptor status, n (%)			.01
Positive	611 (59.4)	2508 (57.8)	
Negative	238 (23.2)	1177 (27.1)	
Unknown	179 (17.4)	651 (15.1)	
No. of positive lymph nodes removed			<.0001
Mean	1.3	3.0	
Median	1 (1-13)	2.0 (1-36)	
No. of lymph nodes removed			<.0001
Mean	3.9	13.0	
Median	2 (1-32)	12 (1-52)	
Radiotherapy, n (%)			<.0001
None/before surgery	366 (36.7)	2083 (49.3)	
After surgery	628 (63.1)	2122 (50.2)	
Unknown	<5 (0.2)	23 (0.5)	

AJCC indicates American Joint Committee on Cancer; ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy; SLND, sentinel lymph node dissection.

^aWhen cases numbered fewer than 5, they were reported as <5 as required by the National Cancer Institute.

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with complete ALND. In our study of Medicare beneficiaries 65 years and older, we obtained similar results, with the hazard of BC-specific mortality of a slightly higher magnitude (HR = 1.6; 95% CI, 1.1-2.5).

This study has several limitations, as previously described.^{4,22} Medicare beneficiaries in the fee-for-service program represent a self-selected population. Our data set does not include beneficiaries enrolled in health maintenance organizations. Hispanic women are more likely to be in Medicare health maintenance organizations (because of the residence area),²³ which might lead to selection bias. Both Hispanic and African American women are less likely than white women to have supplemental coverage, and they are more likely to have Medicaid.²³ Comparisons of the accuracy of Medicare's race codes with self-report (using the Medicare Current Beneficiary Survey data) suggested that the primary error is in mistakenly identifying some Asians, Native Americans, and Hispanics as white.²⁴ The impact of the misclassification has not been examined to date. Because patient comorbidity is identified from diagnoses coded on claim forms, BC survivors' greater interaction with care providers may explain their higher measured comorbidity. Income, supplemental insurance, and availability of providers all significantly affect access to care and are not included in our models except as grossly approximated by census tract socioeconomic status quartile and urban-rural status.

In summary, this study examined the effect of nodal surgery, an initial part of longitudinal healthcare for older BC patients, on racial disparities in survival. Overall survival is comparable for those who undergo SLNB alone and those who undergo SLNB with complete ALND among women with BC. African American women have lower OS and women of Hispanic origin have a lower DSS and OS com-

■ **Table 2.** Multivariate Analysis of Factors Associated With Undergoing SLNB Alone

Characteristic	Odds Ratio (95% CI)	P
Surgery		
Total mastectomy	Reference	<.0001
Segmental mastectomy	2.9 (2.4-3.4)	
Positive lymph node diameter^a		
Micrometastasis	Reference	<.0001
Macrometastasis	3.1 (2.7-3.6)	
Tumor stage, cm		
T2/T3	Reference	.007
T1	1.2 (1.1-1.5)	
Tumor grade		
High	Reference	.02
Low/intermediate	1.3 (1.1-1.5)	
Estrogen receptor status		
Negative	Reference	.003
Positive	1.4 (1.1-1.8)	

CI indicates confidence interval; SLNB, sentinel lymph node biopsy.
^aMacrometastasis is greater than 2.0 mm; micrometastasis is greater than 0.2 to 2.0 mm.

■ **Table 3.** Associations Between Survival, Race/Ethnicity, and Receipt of Lymph Node Dissection in Women With Breast Cancer Who Underwent Surgery, 1998-2005^a

Type of Survival	Model 1 ^b		Model 2 ^c		Model 3 ^d	
	HR	95% CI	HR	95% CI	HR	95% CI
Disease-specific survival						
Whites	1.00	Reference	1.00	Reference	1.00	Reference
African Americans	1.1	0.7-1.7	0.9	0.5-1.3	0.9	0.5-1.3
Hispanics	1.7	1.1-2.5	1.7	1.1-2.6	1.7	1.1-2.6
Asians/Pacific Islanders	0.8	0.4-1.5	1.0	0.5-1.8	1.0	0.5-1.8
Overall survival						
Whites	1.00	Reference	1.00	Reference	1.00	Reference
African Americans	1.5	1.1-2.0	1.2	0.9-1.7	1.2	0.9-1.7
Hispanics	1.4	1.1-1.9	1.4	1.1-1.9	1.4	1.02-2.0
Asians/Pacific Islanders	0.8	0.5-1.3	0.9	0.6-1.5	0.9	0.6-1.5

CI indicates confidence interval; HR, hazard ratio.
^aBoldface denotes statistical significance.
^bModel 1 presents unadjusted point estimates and 95% CI.
^cModel 2 was adjusted for patient and tumor characteristics (age, Surveillance, Epidemiology, and End Results registry, year of diagnosis, treatment [chemotherapy, surgery, radiation], tumor stage, tumor size, tumor grade and number of positive lymph nodes, diameter of positive lymph nodes, comorbidities, and socioeconomic status).
^dModel 3 was adjusted for nodal surgery and factors in model 2.

pared with their white counterparts. These disparities in survival are not explained by differences in utilization of ALND among women with micrometastasis and macrometastasis in sentinel lymph nodes.

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