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Predictors and Outcomes of Completion Axillary Node Dissection Among Older Breast Cancer Patients

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Abstract

Background—The role of completion axillary lymph node dissection (ALND) for older women who had sentinel lymph node-positive (SLN+) invasive breast cancer is unclear. We examined factors predictive of ALND and the association between ALND, adjuvant chemotherapy administration, and survival.

Methods—Using the Surveillance, Epidemiology, and End Results (SEER)-Medicare database, we reviewed records of women age >65 diagnosed with stage I/II breast cancer from 1998–2005. Adjusted Cox proportional hazards and multivariate logistic regression were used to identify patient and disease variables associated with ALND, and assess association between ALND and all-cause and breast cancer-specific survival.

Results—Among SLN+ patients, 88 % underwent ALND. Earlier diagnosis year, greater nodal involvement, younger age, registry location, and larger tumor size were all associated with a significantly higher likelihood of ALND. The ALND in SLN+ patients was not significantly associated with 5-year breast cancer-specific survival (hazard ratio [HR] 1.22, 95 % confidence interval [CI] 0.76–1.96). The SLN+ patients who underwent ALND were more likely to receive adjuvant chemotherapy (odds ratio [OR] 1.8, 95 % CI 1.45–2.24). However, younger age (OR 18.0, 95 % CI 14.4–23.9), estrogen receptor-negative (ER–) status (OR 4.2, 95 % CI 3.4–5.3), and fewer comorbidities (OR 2.6, 95 % CI 1.7–4.0) were all more strongly linked to receipt of chemotherapy.

Conclusions—ALND for older patients with SLN+ breast cancer is not associated with improved 5-year all-cause or breast cancer-specific survival. Younger age, fewer comorbidities, and estrogen receptor-negative (ER–) status were more strongly associated with receipt of chemotherapy than ALND. Consideration should be given to omitting ALND in older patients, particularly if findings of ALND will not influence adjuvant therapy decisions.

INTRODUCTION

Nearly half of all breast cancer cases diagnosed each year in the United States occur in women over the age of 65 years. By 2030, it is estimated that 20 % of Americans will be age 65 years or older.¹ The existing data to guide the management of breast cancer in older women is limited and is often based on large, randomized clinical trials that specifically excluded patients >65 years of age.²

Axillary node status is the single most powerful predictor of prognosis and remains a major factor in adjuvant therapy decision-making. Since the early 2000s, sentinel lymph node biopsy (SLNB) has largely replaced axillary lymph node dissection (ALND) as the preferred method of staging the axilla.^{3–5} The SLNB is minimally invasive, harboring only a 3–7 % risk of lymphedema in comparison to the 15–20 % risk associated with ALND.⁶ In the setting of positive SLNB, standard practice has been to perform ALND. The value of ALND has recently been challenged by the findings of the American College of Surgeons Z0011 (Z11) randomized clinical trial demonstrating no survival or locoregional recurrence benefit of ALND when performed in sentinel lymph node-positive (SLN+) patients undergoing breast-conserving therapy.⁷ However, nodal staging determined by ALND can influence both systemic adjuvant chemotherapy and locoregional radiotherapy decisions. It remains controversial whether ALND confers a cancer-specific survival advantage. The ALND is also associated with significant risks of chronic arm lymphedema, paresthesias, and impaired arm mobility.

Earlier studies have shown that elderly patients are less likely than younger patients to undergo either SLNB or ALND.^{8–16} However, the impact of axillary node surgery on survival and receipt of adjuvant therapy among older patients remains unclear. Utilizing Surveillance, Epidemiology, and End Results (SEER) registry data linked to Medicare, we report the factors associated with ALND among SLN+ patients, and the relationship of ALND to both survival and receipt of adjuvant chemotherapy.

METHODS

Data were obtained from the linked SEER-Medicare database. The SEER registries encompass approximately 25 % of the United States cancer population, and Medicare data provides health insurance coverage information for 97 % of Americans 65 years of age.¹⁷ A total of 251,240 patients in 16 SEER registries were diagnosed with breast cancer during the study period (1998–2005). We studied a subset of 24,023 patients that met the following inclusion criteria: >65 years old, clinical stage I/II cancer (T1–T2, N0), and had SLNB procedure. Figure 1 is the exclusion flow chart with details.

An algorithm to code SLNB and ALND described by Reeder-Hayes et al.¹¹ was utilized to combine SEER and Medicare lymph node category variables. In summary, patients were categorized as having undergone SLNB if their scope of regional node surgery in the SEER registries indicated sentinel node biopsy with or without subsequent ALND or if they had a Medicare Current Protocol Terminology (CPT) code for biopsy of an axillary node with lymphatic mapping. The ALND was ascertained on the basis of SEER data scope of lymph

node surgery specifying ALND or at least ten axillary nodes examined, or if Medicare codes for axillary lymphadenectomy, modified radical mastectomy, or radical mastectomy were used. In cases in which the SLNB was not coded in SEER data, but was coded as having an SLNB in Medicare, the patient was categorized as having SLNB.

The primary outcome of this study was the receipt of ALND after positive SLNB. Chi-square tests were used to determine whether unadjusted significant differences existed between those who were SLN+ patients having SLNB only versus SLNB + ALND. Factors examined included year of diagnosis, registry location, race, age, marital status, Charlson Comorbidity Index (CCI), tumor (T) stage, tumor grade, extent of nodal metastases, breast surgery type, adjuvant chemotherapy, and adjuvant radiation. A multivariate logistic regression model was used to explore the determinants of ALND among elderly patients who were SLN+ after adjusting for potential confounding by variables found to have significant association with ALND.

Secondary analyses were then conducted to evaluate the association between ALND and all-cause and breast cancer-specific survival among patient who were SLN+. Patients who died of causes other than breast cancer were excluded from the breast cancer-specific survival analysis. The survival times were calculated from the date of cancer diagnosis to the date of death or to the last follow-up date 31 December 2006. The Kaplan-Meier method was used to generate unadjusted survival curves by both the log-rank test and Wilcoxon tests. Cox proportional hazards regression analyses were conducted to estimate the association between ALND and survival after adjusting for exploratory variables found to have the significant effect on survival. Surgical treatments (extent of node surgery and breast surgery) were set as the time-dependent variables in the Cox models.

A multivariate logistic regression model was used to assess the adjusted association between the receipt of ALND and the receipt of adjuvant chemotherapy. Adjuvant chemotherapy receipt was the binary outcome. The model was adjusted by all available factors in the description tables (Tables 1 and 2).

All analyses in this study were conducted with a personal computer using SAS 9.2 software (SAS Institute Inc., Cary, NC).

RESULTS

Patient and Tumor Characteristics

Patient demographics are listed in Table 1. Most patients were white (90.5 %) and resided in large metro/metro areas. Most patients had few or no comorbidities (92 % CCI score 0 or 1). Patient tumor characteristics and clinical features are listed in Table 2. Most tumors were well or moderately differentiated (69.7 %), estrogen receptor-positive (ER+) (76.9 %), and small (78.1 % T1).

Trends In and Factors Associated with ALND

For the duration of the study period, 22 % of patients who underwent SLNB were SLN+, and 88 % of these SLN+ patients underwent ALND. However, the frequency of ALND

among SLN+ patients decreased from 98 % in 1998 to 83 % in 2005 (Table 1). Univariate analysis demonstrated that SLN+ patients undergoing SLNB only versus SLNB + ALND differed with respect to age at diagnosis, year of diagnosis, SEER registry, T stage, tumor grade, breast surgery type, and receipt of adjuvant chemotherapy. Race, CCI, and receipt of adjuvant radiation therapy did not significantly differ between groups.

Factors significantly associated with undergoing ALND included: node extent (macro versus micrometastasis), earlier year of diagnosis, younger age at diagnosis, registry location, and higher T stage (Table 3). Patients with macrometastases were more than three times as likely to undergo ALND compared to those with micrometastases. Patients aged 66–70 years were more than twice as likely to undergo ALND compared to those patients >80 years old. Rates of ALND varied markedly across SEER regions. In addition, patients who required more than one surgery (i.e., breast-conserving followed by mastectomy) were more likely to undergo ALND. Number of comorbidities (CCI) and ER status were not associated with the receipt of ALND.

ALND and Receipt of Adjuvant Chemotherapy

Twenty percent of all patients in the study period received adjuvant chemotherapy. Among SLN+ patients, 47 % received chemotherapy (Table 2). There was a significant trend toward decreased use of chemotherapy over time (Mantel-Haenszel Trend test; $p = 0.01$). In multivariate regression analyses, age at diagnosis was the most significant factor influencing receipt of chemotherapy. Younger patients (ages 66–70) were substantially more likely to receive chemotherapy than patients >80 years old after controlling for all confounding variables (odds ratio [OR] 18.0, 95 % confidence interval [CI] 14.4–23.9). Younger age was significantly linked to receipt of chemotherapy when comparing across each age stratum: 66–70 years old versus 71–75 years old (OR 1.95, 95 % CI 1.67–2.29), 66–70 years old versus 76–80 years old (OR 5.93, 95 % CI 4.96–7.1), 66–70 years old versus >80 years old (OR 18.58, 95 % CI 14.45–23.89), and 71–75 years old versus 76–80 years old (OR 3.04, 95 % CI 2.55–3.62). The ER– status was strongly associated with chemotherapy administration (OR 4.2, 95 % CI 3.4–5.3). Those who underwent ALND were more than 80 % more likely to receive chemotherapy than those who had SLNB alone (OR 1.80, 95 % CI 1.45–2.24), even after controlling for T stage, grade, ER status, and receipt of radiation. In addition, patients with a CCI score of zero were nearly three times more likely to receive chemotherapy than those with a CCI score of 3 (OR 2.6, 95 % CI 1.7–4.0).

Survival Analyses

After a median follow-up of 44 months, 14 % (727) of SLN+ patients had died. Of these, 42.2 % died of breast cancer. All-cause unadjusted survival did not differ between SLN+ patients who underwent SLNB only versus SLNB + ALND (5-year survival 84 % vs. 83 %; $p = 0.54$). Breast cancer-specific survival was also similar between SLN+ patients who underwent SLNB only versus SLNB + ALND over the first 3 years of follow-up, but diverged thereafter (Fig. 2) (5-year survival 94.6 % vs. 91.6 %, respectively; $p = 0.035$ log rank test; $p = 0.078$ Wilcoxon test).

After adjusting for factors associated with receipt of ALND, breast cancer-specific survival did not significantly differ between SLN+ patients who had SLNB only versus SLNB + ALND (hazard ratio 0.82, 95 % CI 0.52–1.31) (Table 4). Factors associated with a significantly higher risk of breast cancer-specific mortality included more advanced age, high tumor grade, higher CCI, macro/regional nodal disease, ER– status, and mastectomy versus breast-conserving surgery. The T stage was not associated with a higher breast cancer mortality. High tumor grade was the strongest predictor of breast cancer death.

DISCUSSION

Our study builds on a body of literature demonstrating that breast cancer care for older patients is highly variable. We demonstrated that national rates of ALND in the setting of positive SLNB for early stage breast cancer are high, but decrease significantly with increasing age, even when controlling for pathological and clinical variables. Several studies have demonstrated that elderly patients with breast cancer are less likely to receive standard curative therapies, including lower rates of breast radiation after breast conserving surgery, lower rates of adjuvant systemic chemotherapy, and lower rates of SLNB or ALND.^{18–22} This may be due to the concern that such therapies would be more toxic and may not provide benefit to older patients who may have competing comorbidities.

Interestingly, however, the number of comorbidities (CCI) in our study was not significantly associated with receipt of ALND among SLN+ patients, suggesting that age may play an independent role in surgical decision-making. In addition, rates of ALND were higher in those patients who had to return to the operating room for other reasons (e.g., inadequate lumpectomy margins), suggesting that the decision to proceed with ALND may have been at least partly influenced by convenience. Lastly, substantial variability in the rates of ALND observed points regionally to the lack of clarity as to what the standard of practice should be in elderly SLN+ patients.

The debate about the utility of ALND among the elderly and basis for some of the age-related disparity in its use stems from studies showing little survival or locoregional recurrence benefit associated with ALND in this population. In a randomized trial comparing ALND to no ALND in patients >65 years old who had T1N0 breast cancer, there was no difference in overall or breast-cancer specific survival at 15-year follow-up and a low (6 %) risk of axillary recurrence in the no ALND group.²³ A limitation of that study, however, was that it was underpowered to demonstrate noninferiority between the two arms. Additionally, patients were required to take 5 years of adjuvant tamoxifen therapy and <10 % of patients had hormone receptor-negative disease, both of which could have contributed to the low rates of recurrence and breast cancer mortality observed in this population that may not be generalizable to all elderly patients, especially those not on endocrine therapy. In a study using the SEER database, Aziz et al.¹⁰ also examined the use and impact of ALND among patients >70 years old. They found a trend toward survival benefit among those patients who underwent ALND, which became nonsignificant after conducting a propensity analysis adjusting for predictors of receipt of ALND. This study, however, was limited in that the analyses included clinically node-positive patients and was unable to adjust for important covariates known to impact survival and receipt of ALND, such as stage, ER

status, and tumor grade. Ours is the first study to utilize the more robust SEER-Medicare linked dataset to examine variability in receipt of ALND among older SLN+ patients and the association between ALND and survival and adjuvant chemotherapy, while controlling for potential confounders.

We found, similar to the findings of Martelli et al.²³ that neither all-cause nor breast cancer-specific mortality were associated with ALND. Another important question is whether ALND is associated with receipt of adjuvant systemic chemotherapy. Earlier studies have demonstrated that data gained from ALND does not alter treatment recommendations for elderly breast cancer patients, arguing against ALND for this purpose.^{24–26} The decision to advise chemotherapy depends not only on axillary lymph node status, which can be gleaned from SLNB, but also on the ER status, tumor grade, patient age, and genomic profile of the tumor (e.g., Oncotype DX). We found, in order of decreasing importance, that younger age, ER– status, CCI, node extent, and ALND were the strongest factors linked to the receipt of chemotherapy. The finding that those patients having an ALND were 80 % more likely to receive chemotherapy cannot be explained by selection bias (i.e., that the same older patients who were healthy enough to undergo ALND were also deemed healthy enough to tolerate chemotherapy) because age, CCI, and all other covariates were controlled for in this logistic regression analysis. A possible explanation for this is that among our cohort of SLN + elderly patients, medical oncologists may be less inclined to offer chemotherapy for limited SLN involvement, but more obliged to do so in the setting of several axillary nodes being positive on ALND.

The finding that ALND is still an important factor associated with receipt of systemic chemotherapy would be the argument for the continued practice of ALND after positive SLNB, assuming that systemic chemotherapy is beneficial to this population. However, in this population of elderly SLN+ patients, although 88 % underwent ALND after positive SLNB, only 47 % received chemotherapy. Just as we saw a trend toward declining rates of ALND over the study period, we also observed a trend toward decreasing use of chemotherapy. This may be linked to the falling rates of ALND. However, this is more likely attributable to the widespread adoption of systemic endocrine therapy during the study period, diminishing any relative benefit of cytotoxic chemotherapy for the ER + cancers predominant in this population. Furthermore, there remains a debate over whether chemotherapy is beneficial to older patients with breast cancer. A recent review of four randomized cancer and leukemia group B trials focusing on node-positive patients demonstrated that although the efficacy of various regimens did not differ by age, older patients had higher rates of nonbreast cancer-related mortality and treatment-related mortality.²⁷

This study has several limitations. First, coding of axillary surgery (scope of regional lymph node surgery) in the SEER database has been faulted with significant underreporting of both SLNB and SLNB plus ALND, likely stemming from abstractors' collection of data regarding surgical procedures largely from pathology reports.²⁸ In addition, the SEER database had a change in registry coding for lymph node surgery in 2003 (from SEER to FORDS), which could have resulted in altered trends or miscoding of SLNB, particularly in the 1–2 years immediately after this change. In an effort to mitigate these limitations, and

maximize the capture of SLNB, we considered SLNB as having been performed whether coded as such in the SEER database or in Medicare with CPT codes for axillary node biopsy and lymphatic mapping. Similarly, to be able to define those who underwent ALND, we considered ALND as having been performed if SEER documented > 10 axillary nodes removed or ALND in scope of regional node surgery or if in Medicare, CPT codes for axillary lymphadenectomy, modified radical mastectomy, or radical mastectomy were documented. This limitation is unfortunately inherent to any study of axillary lymph node surgery using either the SEER database or the National Cancer Database (NCDB), and was recently addressed through revision of coding instructions and dissemination of these instructions to abstractors and researchers beginning in 2012. Another limitation of the study is that the SEER-Medicare database does not capture data on endocrine therapy, Her2Neu status, or genomic profile of a tumor, and hence the relationship of these factors to survival and chemotherapy use could not be assessed. We also cannot parse out the details of whether patients did not receive treatment based on their own preference or a physician's recommendation, an important distinction. In addition, SEER does not capture data on locoregional recurrence, so we were not able to examine the relationship between ALND and recurrence.

In summary, rates of ALND after positive SLNB were high in elderly patients with early stage breast cancer in this study period preceding publication of the Z11 trial. However, breast cancer-specific mortality in this population was low (6.4 %) and not linked to ALND. Although ALND does appear to be positively associated with receipt of systemic chemotherapy, other factors appear to be more strongly linked, including patient age, comorbidities, and ER status. Given the lack of survival benefit shown in this and other studies, as well as lack of local recurrence benefit shown in others, ALND in older patients with early-stage SLN+ breast cancer may best be reserved for cases in which data from ALND would clearly impact adjuvant therapy decisions.

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FIG. 1.
Study eligibility and exclusion criteria

FIG. 2.
Adjusted breast cancer-specific survival among sentinel lymph node-positive patients >65 years of age from 1998–2005

TABLE 1

Patients Demographics

Patient characteristics	Cohort of patients undergoing SLNB number (%)	Sentinel node positive (SLN+)			Chi-square <i>p</i> value
		Number (%)	SLNB only row (%)	SLNB + ALND row (%)	
Total	24,023	5,198 (21.6)	629 (12.1)	4,586 (87.9)	
Diagnosis year					<0.0001
1998	634 (2.6)	151 (2.9)	<7.3 ^a	>92.7 ^a	
1999	899 (3.7)	220 (4.2)	5.5	94.6	
2000	2,409 (10.0)	604 (11.6)	7.5	92.6	
2001	3,096 (12.9)	763 (14.7)	10.1	89.9	
2002	3,635 (15.1)	857 (16.5)	12.4	87.6	
2003	4,045 (16.8)	898 (17.3)	12.9	87.1	
2004	4,575 (19.0)	821 (15.8)	14.0	86.0	
2005	4,730 (19.7)	884 (17.1)	17.2	82.8	
Age at diagnosis					<0.0001
66 ~ 70	7,381 (30.7)	1,658 (31.9)	9.7	90.3	
71 ~ 75	7,044 (29.3)	1,506 (29.0)	10.7	89.3	
76 ~ 80	5,758 (24.0)	1,176 (22.6)	12.0	88.0	
>80	3,840 (16.0)	858 (16.5)	19.0	81.0	
Race					0.2714
White	21,734 (90.5)	4,626 (89.0)	11.8	88.2	
Black	1,195 (5.0)	323 (6.3)	13.3	86.7	
Other	1,094 (4.5)	249 (4.8)	14.9	85.1	
Living area					0.4762
Big metro	14,689 (61.2)	3,240 (62.3)	11.5	88.5	
Metro	6,413 (26.7)	1370 (26.4)	13.1	86.9	
Urban	1,282 (5.3)	272 (5.2)	12.5	87.5	
Less urban	1,372 (5.7)	261 (5.0)	11.5	88.5	
Rural	267 (1.1)	55 (1.1)	<20.0 ^a	>80.0 ^a	

ALND axillary lymph node dissection, SLNB sentinel lymph node biopsy

^aCell is masked by the approximate percentage or not applicable to comply with privacy regulations

TABLE 2

Patients clinical diagnoses information

Clinical characteristics	Cohort of patients undergoing SLNB number (%)	Sentinel node positive (SLN+)			Chi-square <i>p</i> value
		Number (%)	SLNB only row (%)	SLNB + ALND row (%)	
Total	24,023	5,198 (21.6)	629 (12.1)	4,586 (87.9)	
Grade					0.0008
Well-differentiated	6,424 (26.7)	945 (18.2)	14.8	85.2	
Moderately differentiated	10,334 (43.0)	2,316 (44.6)	12.0	88.0	
Poorly differentiated	5,410 (22.5)	1,564 (30.1)	9.7	90.4	
Undifferentiated	229 (1.0)	55 (1.0)	<20.0 ^a	>80.0 ^a	
Not determined	1,626 (6.8)	318 (6.1)	15.1	84.9	
Charlson Comorbidity Index					0.9626
0	17,152 (71.9)	3,655 (70.8)	11.9	88.1	
1	4,742 (19.9)	1,059 (20.5)	12.3	87.7	
2	1,316 (5.5)	310 (6.0)	12.6	87.4	
3+	639 (2.7)	141 (2.7)	11.4	88.7	
Tumor stage					<0.0001
T1	18,754 (78.1)	3,051 (58.7)	13.8	86.2	
T2	5,157 (21.5)	2,041 (39.3)	9.3	90.7	
Unknown	112 (0.5)	106 (2.0)	14.2	85.9	
Extent of node involvement					<0.0001
Negative	18,825 (78.4)	0 (0)	(not include in test)		
Micrometastasis	1,399 (5.8)	1,399 (26.9)	22.2	77.8	
Macrometastasis	2,346 (9.8)	2,346 (45.1)	8.4	91.6	
Axillary/regional LN	1,438 (6.0)	1,438 (27.7)	8.1	91.9	
Others/unknown	15 (0.1)	15 (0.3)	N/A ^a	N/A ^a	
Estrogen receptor status					0.47
None done	473 (2.0)	87 (1.7)	13.8	86.2	
Positive	18,474 (76.9)	3,953 (76.1)	12.4	87.6	
Negative	2,943 (12.3)	660 (12.7)	11.2	88.8	
Borderline/undertermined	36 (0.2)	N/A ^a	N/A ^a	N/A ^a	
Unknown	2,097 (8.7)	490 (9.4)	9.8	90.2	
Breast surgery type					<0.0001
Breast conserving	17,392 (72.4)	3,064 (59.0)	14.3	85.7	
Mastectomy	1,191 (5.0)	492 (9.5)	10.6	89.4	
Conserving + mastectomy	5,440 (22.6)	1,642 (31.6)	8.3	91.7	
Chemotherapy					<0.0001
No	19,231 (80.2)	2,759 (53.1)	16.2	83.8	
Yes	4,745 (19.8)	2,435 (46.9)	7.3	92.7	

ALND axillary lymph node dissection, LN lymph node, N/A not applicable, SLNB sentinel lymph node biopsy

^aCell is masked by the approximate percentage or N/A to comply with privacy regulations

TABLE 3

Odds ratios of variables affecting the receipt of ALND after positive SLNB

Variables	Compared treatments	Adjusted hazard ratio (95 % CI)
Node extent	Axillary/regional LN vs. micro metastasis	2.73 (2.14, 3.47)
	Macro metastasis vs. micro metastasis	3.16 (2.56, 3.86)
	Macro metastasis vs. axillary/regional LN	1.16 (0.90, 1.50)
Diagnosis year	1998 vs. 2005	10.77 (3.33, 34.78)
	1999 vs. 2005	3.91 (2.08, 7.35)
	2000 vs. 2005	2.91 (2.02, 4.20)
	2001 vs. 2005	1.93 (1.42, 2.63)
	2002 vs. 2005	1.60 (1.20, 2.12)
	2003 vs. 2005	1.50 (1.14, 1.99)
	2004 vs. 2005	1.34 (1.01, 1.76)
	2005 vs. 2005	1.00 (0.77, 1.30)
Age at diagnosis	66 ~ 70 vs. >80	2.11 (1.64, 2.73)
	71 ~ 75 vs. >80	1.93 (1.50, 2.49)
	76 ~ 80 vs. >80	1.70 (1.31, 2.20)
Registry	Seattle vs. Utah	0.26 (0.12, 0.56)
	Hawaii vs. Utah	0.17 (0.06, 0.43)
Tumor stage	T1 vs. T2	0.73 (0.61, 0.89)
Breast surgery type	Conserving vs. mastectomy	0.78 (0.57, 1.08)
	Conserving + mastectomy vs. conserving	1.92 (1.54, 2.38)
	Conserving + mastectomy vs. mastectomy	1.50 (1.05, 2.13)

ALND axillary lymph node dissection, CI confidence interval, LN lymph node, SLNB sentinel lymph node biopsy, vs. versus

TABLE 4

Hazard ratios (HR) of variables affecting breast cancer mortality among SLN+ patients >65 years of age from 1998–2005

Variables	Compared groups	Breast cancer death hazard ratio (95 % CI)
Node surgery	SLNB only vs. SLNB + ALND	0.82 (0.52, 1.31)
Age at diagnosis	66 ~ 70 vs. >80 years old	0.48 (0.33, 0.70)
	71 ~ 75 vs. >80 years old	0.59 (0.41, 0.84)
	76 ~ 80 vs. >80 years old	0.85 (0.61, 1.18)
Tumor grade	Moderately differentiated vs. well-differentiated	2.19 (1.27, 3.77)
	Poorly differentiated vs. well-differentiated	3.85 (2.23, 6.64)
	Undifferentiated vs. well-differentiated	4.01 (1.54, 10.48)
	Not determined vs. well-differentiated	3.39 (1.78, 6.45)
Charlson comorbidity index	1 vs. 0	1.34 (1.02, 1.77)
	2 vs. 0	1.80 (1.20, 2.71)
	1 vs. 2	0.75 (0.48, 1.17)
Tumor stage	T1 vs. T2	0.84 (0.62, 1.13)
Node extent	Axillary/regional LN vs. micro metastasis	1.80 (1.25, 2.60)
	Macro metastasis vs. micro metastasis	1.90 (1.34, 2.71)
	Macro metastasis vs. axillary/regional LN	1.06 (0.82, 1.36)
Estrogen receptor status	Negative vs. positive	2.70 (2.04, 3.57)
	Negative vs. none done	2.27 (0.98, 5.26)
	Positive vs. none done	0.84 (0.37, 1.90)
Breast surgery type	Conserving vs. mastectomy	0.58 (0.42, 0.80)
	Conserving vs. conserving + mastectomy	0.71 (0.55, 0.92)
	Conserving + mastectomy vs. mastectomy	0.81 (0.59, 1.12)

ALND axillary lymph node dissection, CI confidence interval, LN lymph node, SLN+ sentinel node positive, SLNB sentinel lymph node biopsy, vs. versus