Outcomes after Sentinel Lymph Node Biopsy and Radiation Therapy in Elderly Women with Estrogen Receptor-Positive, Early-Stage Breast Cancer

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OBJECTIVES

To describe rates and association with disease recurrence of SLNB and RT in elderly breast cancer.

INTRODUCTION

- The incidence of cancers in elderly patients is predicted to rise, which are expected to account for nearly 70% of all cases diagnosed by 2030 in the United States[1].

- Oncologists often make treatment decisions with uncertainty in elderly patients with breast cancer since few guidelines exist for the clinical treatment of this age group due to their lack of representation in randomized controlled trials (RCTs).

- The Society of Surgical Oncology (SSO) adopted the American Board of Internal Medicine (ABIM) Foundation's *Choosing Wisely* guidelines, recommending against routine use of sentinel lymph node biopsy (SLNB) for axillary staging in patients who are over 70 years with hormone receptor (HR)-positive, clinically node negative, early-stage breast cancer in case of overtreatment[2].

- Adherence to these guidelines remains low, as nearly 60%-80% receive SLNB, and there is conflicting evidence on trends and perceived benefits of SLNB use in this population of patients[3-6].

- Despite the *Choosing Wisely* guidelines, limited conclusive evidence exists for definitive omission, and the large institutional data is lacking.

- This study aims to retrospectively compare trends in mortality in patients who received SLNB against those that did not, as well as in patients who received RT against those that did not.

- We focus on evaluating whether further de-implementation of SLNB and RT is feasible in women aged over 70 years who present with early stage, clinically node negative, ER+, HER2- breast cancer using the highly annotated data derived from the cancer registry and electronic health record (EHR) of a multisystem academic and community health care network.

METHODS

Data Source

- Clinical data was obtained from the UPMC Network Cancer Registry including patients seen across the health care system with age at diagnosis, clinical and pathologic TNM staging, axillary staging procedures, breast surgical procedures, and adjuvant therapies (RT, hormone therapy, and chemotherapy).

Study Population and Outcomes
UPMC Network

> N = 7,328
> Women invasive breast cancer between diagnosed with ER+, HER2- 2010 and 2018

↓ ≥ 70 years old
Clinically node-negative (cN0)

> N = 3,361 between 2010 and 2018 (for SLNB and RT rate)
> N = 2,109 between 2010 and 2014 (for outcome analysis)

- *Locoregional recurrence-free survival (LRFS):* the time from diagnosis to the time to an event, including a local or regional recurrence or censoring if lost to follow up.

- *Disease Free Survival (DFS):* the time from diagnosis to the time to any disease recurrence; DFS does not include second primary cancers. Non-breast cancer specific mortality events that occurred before a recurrence were considered censored events.

- *Modified Charlson comorbidity index score (mCCI score):* weighted sum of comorbidities.

Statistical Analysis

Descriptive statistics for summarizing baseline characteristics of patients; Propensity score matching for minimizing the potential bias of treatment allocation and confounding; Cox proportional hazard model for survival analysis estimating the association of treatment with LRFS and DFS.

RESULTS

Rates of SLNB and RT
Rates of SLNB steadily increased (1.0% per year), a trend that persisted in 2017 and 2018 even after SSO's 2016 adoption of the *Choosing Wisely* SLNB de-implementation guideline. During the same time period, rates of RT declined (3.4% per year).
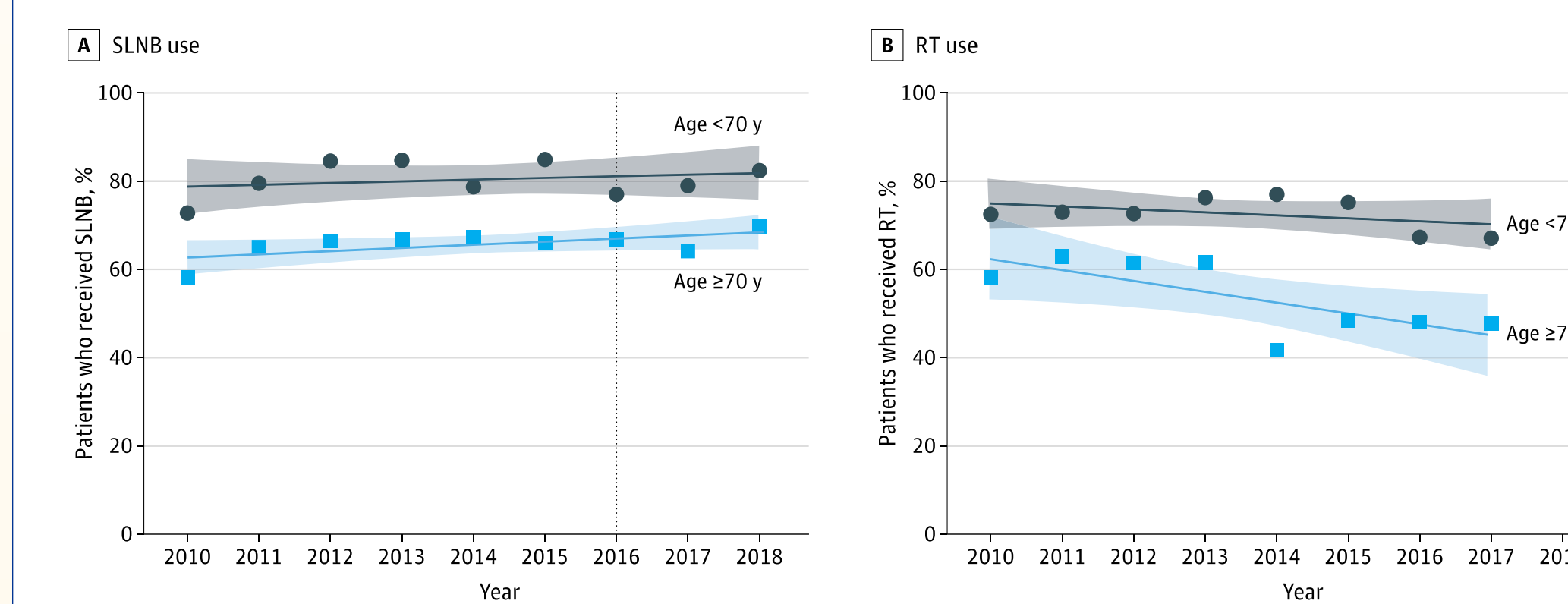
Patient Characteristics

Patients who did not undergo SLNB and RT, compared to patients who did, were older, had shorter median follow up times, had larger tumors, had higher mean mCCI scores, had varied treatment courses, and had differences in treatment sites.
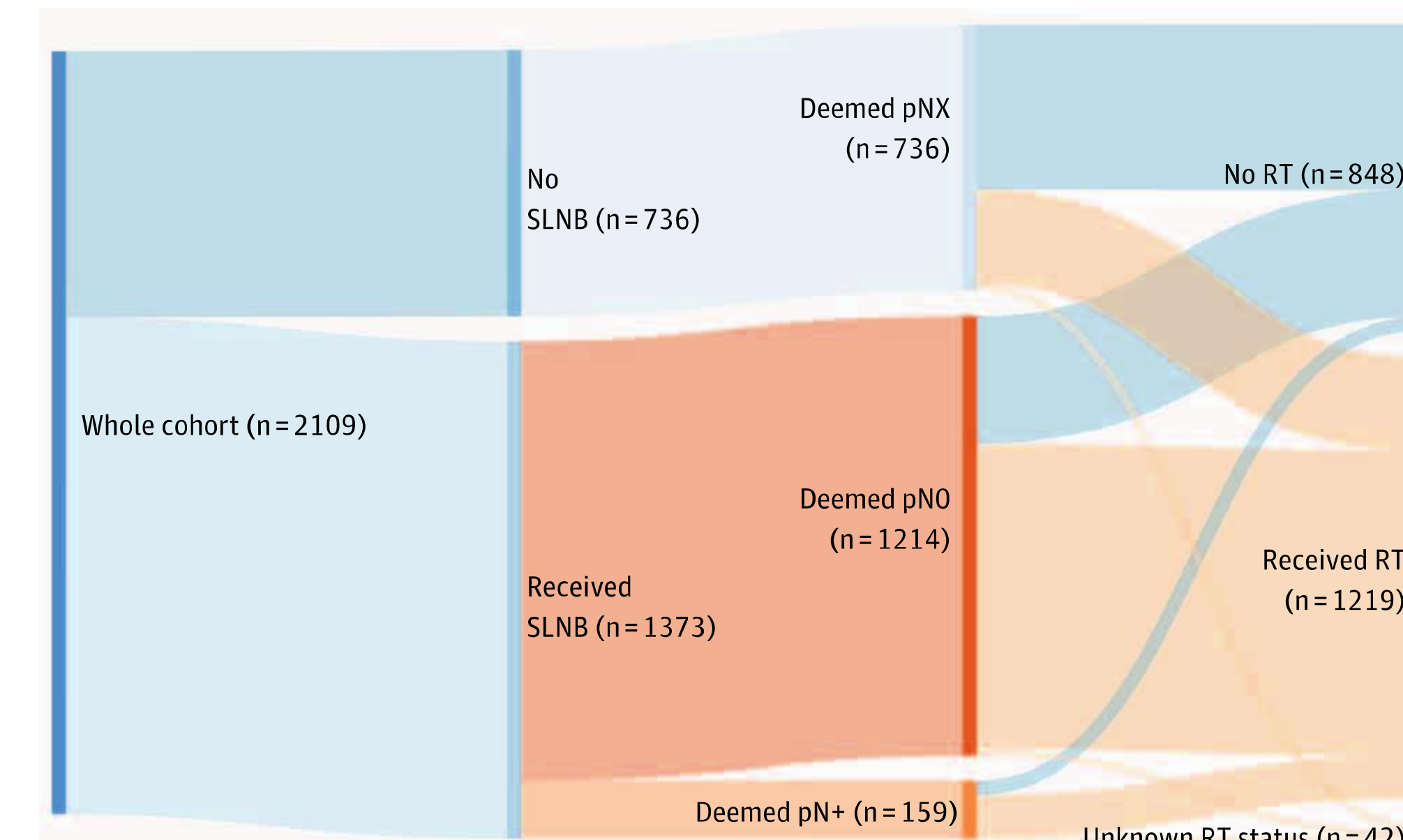
Association Between Receipt of SLNB/RT and Disease Recurrence

In Cohort A, which was used to evaluate the association of SLNB receipt and outcomes, SLNB was not associated with DFS (HR = 1.92, CI = [0.86, 4.32], P = 0.11) or LRFS (HR = 1.26, CI = [0.37, 4.30], P = 0.71) in the Cox-PH model adjusting for age, grade, stage, comorbidity score, patient income, area deprivation index, and insurance status.

In Cohort B, RT again did not have a significantly lower hazard for either DFS (HR = 0.99, CI = [0.46, 2.10], P = 0.97) or LRFS (HR = 0.33, CI = [0.09-1.24], P = 0.10) in the Cox-PH model adjusting for the variables mentioned above.

Variable	LRFS HR (95% CI)	LRFS P-Value	DFS HR (95% CI)	DFS P-Value
Results for Cohort A matched to evaluate SLNB.				
SLNB	1.26 (0.37, 4.30)	0.71	1.92 (0.86, 4.32)	0.11
Age	0.99 (0.88, 1.11)	0.87	1.05 (0.98, 1.12)	0.14
mCCI Score	1.63 (0.98, 2.69)	0.06	1.34 (0.97, 1.85)	0.08
Grade 2 vs. 1 Disease	2.08 (0.45, 9.68)	0.35	2.90 (0.85, 9.87)	0.09
Grade 3 vs. 1 Disease	3.35 (0.41, 27)	0.26	6.27 (1.68, 23)	0.006
T2 vs. T1 Tumor	1.58 (0, 100)	0.89	11.84 (1.57, 89)	0.017
T3 vs. T1 Tumor	30.31 (0, 100)	0.29	30.39 (3.47, 100)	0.002
Results for Cohort B matched to evaluate RT.				
Radiation Therapy	0.33 (0.09, 1.24)	0.10	0.99 (0.46, 2.10)	0.97
Pathologic Node Status*	--	--	0.86 (0.26, 2.86)	0.81
Age	1.19 (1.05, 1.35)	0.007	1.20 (1.11, 1.30)	< 0.001
mCCI Score	1.26 (0.54, 2.92)	0.59	1.35 (0.89, 2.08)	0.16
Grade 2 vs. 1 Disease	0.42 (0.10, 1.78)	0.24	1.36 (0.48, 3.86)	0.56
Grade 3 vs. 1 Disease	0.25 (0.03, 2.50)	0.24	1.55 (0.46, 5.18)	0.48
T2 vs. T1 Tumor	1.65 (0, 100)	0.93	12.15 (1.32, 100)	0.03
T3 vs. T1 Tumor	8.47 (0, 100)	0.69	5.77 (1.15, 100)	0.04

CONCLUSIONS

(1) SLNB can safely be omitted, in accordance with the *Choosing Wisely* guidelines, in elderly patients with cN0, ER+ breast cancer.

(2) RT can safely be omitted, in accordance with results of CALBG 9343 trial and NCCN guidelines, in elderly patients with cN0, ER+ breast cancer based on LRFS and DFS.

(3) Rates of RT and SLNB still remain quite high, suggesting additional studies are needed to investigate why this is the case.

(4) In accordance with the CALGB 9343, we show low rates of locoregional recurrence with (2.2%) and without RT (2.5%) and low rates of pathologic node positivity after SLNB (11.5%), adding further evidence for the omission of both interventions.

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