

Patterns in Utilization of Axillary Operations in Patients with Node-Positive Breast Cancer Following Neoadjuvant Chemotherapy: A National Cancer Database (NCDB) Analysis



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Introduction

• ACOSOG Z1071 and SENTINA trials demonstrated significant false negative rates of sentinel node biopsy for node positive breast cancer treated with neoadjuvant chemotherapy (NAC)

Objective

• To evaluate trends in axillary operations before and after publication of these trials

Methods

- Patients from National Cancer Database (NCDB) with clinical T0 through T4, N1 and N2, M0 breast cancer receiving NAC from 1/1/2012 to 12/31/2015 and sentinel lymph node biopsy (SNB) or axillary lymph node dissection (ALND) were analyzed
- Patients were divided into three groups based on the type of axillary operation: SNB, ALND, or Both (SNB + ALND)
- Groups were compared with respect to pt characteristics, facility type, and time trends

Results

- 32,036 evaluable patients were identified. 5,565 patients had a SNB, 19,930 had an ALND, and 6,541 had both
- Compared with the ALND group, the SNB group were younger, had more invasive ductal cancers, and lower clinical T and N stage (p<0.001)
- Pts in the SNB group had a higher rate of ER positive and triple negative breast cancers, but a lower rate of HER2 positive cancer (p<0.001) [Table 1]

Results

Table 1: Demographics and Clinical Detail

	All patients (N = 32,036) 100.0%	SNB (N = 5,565) 17.4%	ALND (N = 19,930) 62.2%	Both (SNB & ALND) (N = 6,541) 20.4%	P Value
Age (years, mean±SD)	54 (13)	53 (12)	54 (13)	53 (12)	<0.001*§
Histology					
Ductal	26,280 (82.0)	4,827 (86.7)	16,134 (81.0)	5,319 (81.3)	<0.001*§
Lobular	1,966 (6.1)	235 (4.2)	1,210 (6.1)	521 (8.0)	
Clinical T Stage					<0.001*§
0	13 (0.0)	2 (0.0)	9 (0.0)	2 (0.0)	
1	4,654 (14.8)	917 (16.7)	2,652 (13.6)	1,085 (16.8)	
2	14,736 (46.9)	3,067 (55.8)	8,438 (43.4)	3,231 (50.1)	
3	7,306 (23.3)	1,154 (21.0)	4,630 (23.8)	1,522 (23.6)	
4	4,695 (15.0)	360 (6.5)	3,723 (19.1)	612 (9.5)	
Clinical N Stage					<0.001*§
1	27,300 (85.2)	5,128 (92.1)	16,398 (82.3)	5,774 (88.3)	
2	4,736 (14.8)	437 (7.9)	3,532 (17.7)	767 (11.7)	
Estrogen Receptor Positive	13,528 (42.5)	2,838 (51.3)	8,291 (41.9)	2,399 (36.8)	<0.001*§
Progesterone Receptor Positive	16,729 (52.6)	3,314 (60.0)	10,328 (52.2)	3,087 (47.4)	<0.001*§
HER2 Receptor Positive	23,689 (74.9)	3977 (72.4)	14,708 (74.8)	5,004 (77.2)	<0.001*§
Triple Negative Breast Cancer	8,242 (26.7)	1,710 (31.7)	5,045 (26.3)	1,487 (23.5)	<0.001*§
Type of operation					<0.001*§
Partial mastectomy	9,510 (29.8)	2,651 (47.8)	4,804 (24.2)	2,055 (31.5)	
Mastectomy	22,377 (70.2)	2,897 (52.2)	15,010 (75.8)	4,470 (68.5)	
Chemotherapy					<0.001*§
Neoadjuvant alone	16,512 (57.8)	3,511 (63.1)	11,422 (57.3)	3,579 (54.7)	
Neoadjuvant + Adjuvant	13,524 (42.2)	2,054 (36.9)	8,508 (42.7)	2,962 (45.3)	

*Post-hoc testing using Bonferroni correction identified significance between SNB and ALND group.
 †Post-hoc testing using Bonferroni correction identified significance between SNB and Both group.

• Pathologic complete response (PCR) rate was 66.5% in the SNB group and 33.1% in the ALND group [Table 2]

Table 2: Pathologic yN Stage and Lymph Node Results

	All patients (N = 30,173)	SNB (N = 5,157)	ALND (N = 18,787)	Both (SNB & ALND) (N = 6,229)	P Value
Pathologic yN Stage					
0	11,566 (38.3)	3,429 (66.5)	6,226 (33.1)	1,911 (30.7)	<0.001*§
1	11,215 (37.2)	1,563 (30.3)	6,895 (36.7)	2,757 (44.3)	
2	5,325 (17.6)	142 (2.8)	4,016 (21.4)	1,168 (18.8)	
3	2,056 (6.8)	23 (0.4)	1,550 (8.3)	393 (6.3)	
Nodes examined	11 (IQR 5-18)	3 (IQR 2-5)	13 (IQR 8-19)	11 (IQR 6-17)	
Nodes positive	2 (IQR 1-5)	1 (IQR 0-2)	2 (IQR 1-7)	2 (IQR 1-5)	

*Post-hoc testing using Bonferroni correction identified significance between SNB and ALND group.
 †Post-hoc testing using Bonferroni correction identified significance between SNB and Both group.
 §Post-hoc testing using Bonferroni correction identified significance between ALND and Both group.
 Abbreviations: SNB, Sentinel lymph node biopsy; ALND, Axillary lymph node dissection;

• Since 2013, the rate of ALND has decreased from 88.7% to 77.1% in both community and academic institutions (p<0.001) [Table 3, 4]

Table 3: Rates of Axillary Lymph Node Dissection by Year pre-Z1071/SENTINA and post-Z1071/SENTINA Trials by Type of Program

	All patients (N = 23,047)	Community Cancer Program (CCP) (N = 2,084)	Comprehensive CCP (CCCP) (N = 9,974)	Academic/ Research Program (N = 7,986)	Integrated Network Cancer Program (N = 3,003)	P Value
2012 (pre-trial)	5978 (88.7)	444 (86.5)	2524 (87.2)	2162 (91.2)	848 (87.8)	<0.001*
2013 (post-trial)	5598 (85.7)	573 (87.2)	2392 (84.8)	1932 (87.5)	701 (82.9)	
2014	5678 (80.9)	548 (83.9)	2495 (80.3)	1895 (81.3)	740 (80.0)	
2015	5793 (77.1)	519 (76.8)	2563 (76.9)	1997 (78.7)	714 (74.1)	

*Post-hoc testing using Bonferroni correction identified significance between CCP vs. CCCP group, CCP vs. Academic/Research group, CCP vs. Integrated group, and CCP vs. Integrated group. Adjusted p-value for CCP vs. Academic/Research group (p=0.0530) and Academic/Research vs. Integrated (p=0.2796) were not significant.

Abbreviations: CCP, Community Cancer Program; CCCP, Comprehensive Community Cancer Program;

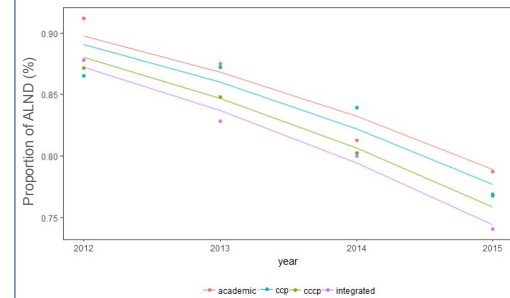
Table 4: Rates of Axillary Lymph Node Dissection by Year pre-Z1071/SENTINA and post-Z1071/SENTINA Trials

	Pre-Trial (N = 5,978)	Post-Trial (N = 17,069)	P Value
CCP	444 (86.5)	1,540 (82.6)	0.037
CCCP	2,524 (87.2)	2,450 (80.4)	<0.001
Academic/Research	2,162 (91.2)	5,824 (82.3)	<0.001
Integrated	848 (87.8)	2,155 (78.8)	<0.001

Abbreviations: CCP, Community Cancer Program; CCCP, Comprehensive Community Cancer Program;

Results

• Figure 1. Model Estimates in Trends of ALND from 2012 to 2015 by Facility Type



• Model estimates of trends of ALND by facility type show a decrease in the rate of ALND over time among all facility types

• A logistic regression model of the facility types adjusted for year showed fewer ALND performed at:

- CCCP compared to Academic/Research (OR 0.839, 95% CI 0.763-0.923, p<0.001)
- Integrated compared to Academic/Research (OR 0.778, CI 0.683-0.887, p<0.001), &
- Integrated compared to CCP (OR 0.836, CI 0.702-0.996, p=0.043) facilities

Conclusion

• Since publication of the results of the ACOSOG Z1071 and SENTINA trials, national rates of ALND in node positive breast cancer treated with NAC have decreased despite significant false negative SNB rates and no study demonstrating safety of ALND omission