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ORIGINAL ARTICLE – BREAST ONCOLOGY

American College of Surgeons Oncology Group (ACOSOG) Z0011: Impact on Surgeon Practice Patterns

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ABSTRACT

Introduction. The ACOSOG Z0011 trial has been described as practice-changing. The goal of this study was to determine the impact of the trial on surgeon practice patterns at our institution.

Methods. This is a review of practice patterns comparing the year before release of Z0011 to the year after an institutional multidisciplinary meeting discussing the results. Patients meeting Z0011 inclusion criteria were identified. Clinicopathologic data were compared between the cohorts.

Results. There were 658 patients with clinical T1-2 tumors planned for breast conservation: 335 in the pre-Z0011 cohort and 323 post-Z0011. Sixty-two (19 %) patients were sentinel lymph node (SLN) positive in the pre-Z0011 group versus 42 (13 %) post-Z0011 ($p = 0.06$). Before Z0011, 85 % (53/62) of SLN-positive patients underwent axillary node dissection (ALND) versus 24 % (10/42) after Z0011 ($p < 0.001$). After Z0011, surgeons were more likely to perform ALND on patients with larger tumors (2.2 vs. 1.5 cm, $p = 0.09$), lobular histology ($p = 0.01$), fewer SLNs (1 vs. 3, $p = 0.09$), larger SLN metastasis size (4 vs. 2.5 mm, $p = 0.19$), extranodal extension present (20 vs. 6 %, $p = 0.16$), or a higher probability of positive non-SLNs ($p = 0.03$). Surgeons were less likely to perform intraoperative nodal assessment post-Z0011 (26 vs. 69 %, $p < 0.001$) resulting in decreased median operative times for SLN-negative patients (79 vs. 92 min, $p < 0.001$).

Conclusions. Surgeons at our institution have implemented Z0011 results for the majority of patients; however, clinicopathologic factors still impact the decision to perform ALND. Z0011 results have significantly impacted practice by decreasing rates of ALND, use of intraoperative nodal evaluation, and operative times.

The management of breast cancer has evolved significantly, with increasing recognition that less aggressive surgical techniques provide equivalent local-regional control with reduced morbidity. This principle has guided the transition from the Halsted radical mastectomy to breast conservation therapy, an oncologically sound and cosmetically favorable option.[1] Mirroring this trend has been the adoption of sentinel lymph node dissection (SLND) as the standard technique for nodal assessment in clinically node-negative patients. SLND is associated with lower morbidity compared with axillary lymph node dissection (ALND) and improved sensitivity in detecting nodal metastases.[2,3]

The use of SLND has identified a population of patients with small-volume nodal disease in whom there is debate regarding the optimal management. Whereas previous consensus statements from the American Society of Clinical Oncology published in 2006 and the National Comprehensive Cancer Center Network in 2008 recommended ALND in patients with a positive SLN, studies evaluating practice patterns from 1998–2005 demonstrate trends toward omitting ALND in selected patients.[4–8] The

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American College of Surgeons Oncology Group (ACOSOG) Z0011 trial was designed to determine whether ALND impacted survival in selected SLN positive patients.[9] The trial enrolled patients with clinical T1-2N0M0 breast cancer undergoing breast-conserving surgery and adjuvant whole breast radiotherapy who were found to have one or two positive SLN(s) on standard hematoxylin and eosin (H&E) staining. At median follow-up of 6.3 years, there were no differences in locoregional recurrence or overall survival (OS) between the two groups.[9,10]

The Z0011 trial has been touted as "practice-changing" and has been the focus of discussion and debate in the breast oncology community, which is reflected in the updated NCCN guidelines incorporating the Z0011 findings.[11–14] After the trial results were released, our group convened a multidisciplinary conference to discuss the results and published our institutional interpretation and recommendations for implementation into clinical practice. The goal of this study was to determine the impact of the Z0011 data and our multidisciplinary discussion on the practice patterns of breast surgical oncologists at our institution.

METHODS

A review of practice patterns of 17 surgical oncologists at a comprehensive cancer center was performed. Patients presenting with clinical T1-2N0M0 invasive breast cancer who underwent breast conservation therapy (BCT) and SLND (thus reflecting some of the Z011 inclusion criteria[9]) were identified and separated into two cohorts: those that underwent surgery in the year before initial report of the Z0011 results at the American Surgical Association annual meeting (April 2009–March 2010), and those who underwent surgery in the year after our institutional multidisciplinary discussion (September 2010–August 2011). Patients who had neoadjuvant chemotherapy ($n = 146$), node-positive patients converted to mastectomy ($n = 7$), and patients with tumors >5 cm ($n = 11$) were excluded. All patients in both cohorts were initially staged based on physical examination, mammography, breast and nodal ultrasound, and pathological assessment of biopsies. Suspicious-appearing lymph nodes identified on ultrasound routinely underwent fine needle aspiration (FNA) biopsy.[15] Positive SLN were defined as metastasis seen on standard H&E staining as per the Z0011 criteria. Patients with metastasis seen only on immunohistochemistry were considered negative. Data were collected from review of electronic medical records, including clinical, pathological, and radiologic reports, as well as operative logs.

Comparisons were made between groups using Fisher exact test for categorical variables and the Mann-Whitney test or logistic regression for continuous variables as appropriate. *P* values shown are two-sided values. This study was approved by the Institutional Review Board.

RESULTS

A total of 658 patients were identified who presented with clinically node negative T1-2 tumors undergoing BCT: 335 before Z0011 and 323 after Z0011. Clinicopathologic features were similar between groups (Table 1); however, there were more postmenopausal subjects in the post-Z0011 group (80 vs. 72 %, $p = 0.02$) and higher rates of lymphovascular invasion (LVI) in the pre-Z0011 group (16 vs. 10 %, $p = 0.02$). Sixty-two (18.5 %) patients were found to have a positive SLN in the pre-Z0011 group compared with 42 (13 %) patients in the post-Z0011 group ($p = 0.06$). The low rate of positive SLN(s) is likely attributable to routine use of nodal ultrasound and FNA biopsy.

Management of Sentinel Lymph Node-Positive Patients

The SLN-positive patients in the two cohorts were comparable with the exception of differences in histology; the pre-Z0011 cohort had a higher proportion of ductal histology (Table 2). Eighty-five percent (53/62) of SLN-positive patients underwent ALND pre-Z011 versus 24 % (10/42) post-Z0011 ($p < 0.001$). This trend became more pronounced over time. In the first 6 months after discussion of the Z0011 results, 28 % (7/25) of SLN-positive patients underwent ALND compared with 18 % (3/17) in the subsequent 6 months ($p = 0.44$).

Pre-Z0011 Cohort

Patients who did not undergo ALND in the pre-Z0011 cohort were similar to patients who had an ALND with respect to patient and tumor features (Table 3). The decision to omit ALND may have been driven by SLN characteristics. Patients who did not have an ALND were more likely to have a single positive SLN (100 vs. 74 %, $p = 0.04$), had smaller metastatic foci (1.4 vs. 3 mm, $p = 0.07$), and more often had micrometastasis (78 vs. 40 %, $p = 0.07$). Using a previously published validated nomogram that predicts risk of having non-SLN metastases,[16] the median predicted risk of having additional disease in the pre-Z0011 cohort was 18 % (range 0–94) in patients who underwent ALND versus 5 % (range 2–37) in those who did not have ALND ($p = 0.12$). In the patients who had ALND, 21 % (11/53) were found to have additional nodal disease.

TABLE 1 Clinicopathologic characteristics

	Pre-Z0011 ($N = 335$)	Post-Z0011 ($N = 323$)	p
Median age (yr)	58 (25–89)	60 (28–90)	0.06
Menopausal status			
Pre	94 (28 %)	66 (20 %)	0.02
Post	241 (72 %)	257 (80 %)	
Median clinical tumor size (cm)	1.6 (range 0.2–5)	1.5 (range 0.2–5)	0.31
Clinical T stage			
T1	229 (68 %)	239 (74 %)	0.12
T2	106 (32 %)	84 (26 %)	
Histology			
Ductal	259 (77 %)	236 (73 %)	0.1
Lobular	29 (9 %)	40 (12 %)	
Mixed	30 (9 %)	21 (6.5 %)	
Other	17 (5 %)	26 (8 %)	
Nuclear grade			
Low	62 (18.5 %)	77 (24 %)	0.16
Intermediate	184 (55 %)	177 (55 %)	
High	86 (26 %)	68 (21 %)	
Missing	2 (0.6 %)	1 (0.3 %)	
Median path size (cm)	1.2 (range 0–5)	1.2 (range 0–4.5)	0.39
Pathologic T stage			
T1	262 (78 %)	271 (84 %)	0.07
T2	72 (22 %)	51 (16 %)	
Missing	1 (0.3 %)	1 (0.3 %)	
Hormone receptor status			
ER/PR positive	310 (92.5 %)	295 (91 %)	0.77
ER/PR negative	25 (7.5 %)	28 (9 %)	
HER2 receptor status			
HER2 positive	21 (6 %)	20 (6 %)	1.00
HER2 negative	314 (94 %)	303 (94 %)	
Lymphovascular invasion			
Present	53 (16 %)	32 (10 %)	0.02
Absent/missing	282 (84 %)	291 (90 %)	
Positive SLN	62 (18.5 %)	42 (13 %)	0.06

ER estrogen receptor, *PR* progesterone receptor, *SLN* sentinel lymph node

TABLE 2 Clinicopathologic characteristics: sentinel lymph node-positive patients

	Pre-Z0011 ($N = 62$)	Post-Z0011 ($N = 42$)	p
Median age (yr)	54.5 (25–84)	53.5 (42–75)	0.6
Menopausal status			
Pre	25 (40 %)	14 (33 %)	0.54
Post	37 (60 %)	28 (67 %)	
Median clinical tumor size (cm)	2 (0.8–5)	2 (0.8–4.8)	0.7
Clinical T stage			
T1	33 (53 %)	24 (57 %)	0.69
T2	29 (47 %)	18 (43 %)	
Histology			
Ductal	50 (81 %)	30 (71 %)	0.05
Lobular	7 (11 %)	4 (10 %)	
Mixed	5 (8 %)	3 (7 %)	
Other	0	5 (12 %)	
Nuclear grade			
Low	6 (10 %)	9 (21 %)	0.15
Intermediate	39 (63 %)	21 (50 %)	
High	16 (26 %)	12 (29 %)	
Missing	0	0	
Median path size (cm)	1.75 (0.2–5)	1.6 (0.9–4)	0.98
Pathologic T stage			
T1	41 (66 %)	26 (62 %)	0.83
T2	21 (34 %)	15 (36 %)	
Missing		1 (2 %)	
Hormone receptor status			
ER/PR positive	59 (95 %)	38 (90 %)	0.44
ER/PR negative	3 (5 %)	4 (10 %)	
HER2 receptor status			
HER2 positive	6 (10 %)	2 (5 %)	0.47
HER2 negative	56 (90 %)	40 (95 %)	
Lymphovascular invasion			
Present	25 (40 %)	10 (24 %)	0.09
Absent/missing	37 (60 %)	32 (76 %)	
Median positive SLN	1 (1–5)	1 (1–2)	0.19
No. of positive SLN			
1	48 (77 %)	34 (81 %)	0.09
2	8 (13 %)	8 (19 %)	
≥3*	6 (10 %)	0	
Median total number SLN	2.5	2	0.26
Median largest metastatic foci in SLN	2.5 mm (micro-24)	3 mm (micro-10)	0.46
Extranodal extension in SLN	11 (18 %)	4 (10 %)	0.33
Micrometastasis?			
Yes	30 (48 %)	19 (45 %)	0.84
No	32 (52 %)	23 (55 %)	
Median predicted probability of positive non-SLN by nomogram	27.5 (0–94)	18 (3–70)	0.44

* Due to intraoperative randomization in the Z0011 trial, a small percentage of patients had ≥3 positive SLNs on final pathologic evaluation and were included in the analysis. Therefore, these patients are included in the current study

Post-Z0011 Cohort

In the post-Z0011 cohort, there were no differences between patients who underwent ALND compared with those that did not with respect to age, menopausal status, nuclear grade, receptor status, or presence of LVI (Table 3). However, there was a significant difference with respect to histology; 75 % (3/4) of patients with lobular histology underwent ALND and 67 % (2/3) of those with mixed histology underwent ALND versus 17 % (5/30) of patients with ductal histology ($p = 0.01$). There also was a nonsignificant difference in the median tumor size; patients who underwent ALND had larger tumors (2.5 vs. 1.7 cm,

TABLE 3 Comparison of clinicopathologic features of SLN positive patient who did and did not undergo ALND before and after Z0011

	Pre-Z0011			Post-Z0011		
	ALND ($N = 53$) (85 %)	No ALND ($N = 9$) (15 %)	p	ALND ($N = 10$) (24 %)	No ALND ($N = 32$) (76 %)	p
Median age (yr)	55 (25–82)	54 (45–84)	0.54	54.5 (44–75)	53.5 (42–75)	0.95
Menopausal status						
Pre	22 (42 %)	3 (33 %)	0.73	3 (30 %)	11 (34 %)	1.0
Post	31 (58 %	6 (67 %)		7 (70 %)	21 (66 %)	
Median clinical tumor size (cm)	2.1 (1–5)	1.7 (0.8–2.9)	0.16	2.5 (0.9–4.8)	1.7 (0.8–4)	0.09
Clinical T stage						
T1	27 (51 %)	6 (67 %)	0.48	4 (40 %)	20 (63 %)	0.14
T2	26 (49 %)	3 (33 %)		6 (60 %)	12 (37 %)	
Median pathologic size	1.7 (0.2–5)	1.8 (0.9–3)	0.56	2.2 (1.4–3.8)	1.5 (0.9–4)	0.09
Pathologic T stage						
T1	34 (64 %)	7 (78 %)	0.71	4 (40 %)	22 (69 %)	0.25
T2	19 (36 %)	2 (22 %)		5 (50 %)	10 (31 %)	
Missing	0	0		1 (10 %)	0	
Histology						
Ductal	44 (83 %)	6 (67 %)	0.28	5 (50 %)	25 (78 %)	0.01
Lobular	5 (9 %)	2 (22 %)		3 (30 %)	1 (3 %)	
Mixed	4 (7.5 %)	1 (11 %)		2 (20 %)	1 (3 %)	
Other	0	0		0	5 (16 %)	
Nuclear grade						
Low	5 (9 %)	1 (11 %)	1.0	2 (20 %)	7 (22 %)	1.0
Intermediate	33 (62 %)	6 (67 %)		5 (50 %)	16 (50 %)	
High	14 (26 %)	2 (22 %)		3 (30 %)	9 (28 %)	
Missing data	1 (2 %)	0		0	0	
Hormone receptor status						
ER/PR positive	50 (94 %)	9 (100 %)	1.0	8 (80 %)	30 (94 %)	0.24
ER/PR negative	3 (6 %)			2 (20 %)	2 (6 %)	
HER2 receptor status						
HER2 positive	5 (9 %)	1 (11 %)	1.0	0	2 (6 %)	1.0
HER2 negative	48 (91 %)	9 (89 %)		10 (100 %)	30 (94 %)	
Lymphovascular invasion						
Present	24 (45 %)	1 (11 %)	0.11	1 (10 %)	9 (28%)	0.54
Absent/missing	29 (55 % %)	8 (89 %)		9 (90 % % %)	23 (72 %)	
Median no. SLN (range)	3 (1–13)	2 (1–5)	0.66	1 (1–4)	3 (1–9)	0.09
No. positive SLN						
1	39 (74 %)	9 (100 %)	0.04	10 (100 % %)	24 (75 %)	0.17
2	8 (15 %)	0		0	8 (25 %)	
≥3	6 (12.5 %)	0			0	
Median largest SLN metastasis (mm)	3 (0.25–24)	1.4 (0.5–3)	0.07	4 (0.6–10)	2.5 (0.22–9.5)	0.19
Micrometastasis						
Yes	21 (40 %)	7 (78 % %)	0.07	4 (40 %)	15 (47 %)	1.0
No	32 (60 %)	2 (22 %)		6 (60 %)	17 (53 %)	
Extranodal extension						
Yes	10 (19 %)	1 (11 %)	0.60	2 (20 %)	2 (6 %)	0.16
No/missing data	43 (81 %)	8(89 %)		8 (80 %)	30 (94 %)	

TABLE 3 continued

	Pre-Z0011			Post-Z0011		
	ALND ($N = 53$) (85 %)	No ALND ($N = 9$) (15 %)	p	ALND ($N = 10$) (24 %)	No ALND ($N = 32$) (76 %)	p
Median predicted risk of positive non-SLN by nomogram (range)	18[a] (0–94)	5 (2–37)	0.12	25[a] (8–70)	14[b] (3–34)	0.03

[a] One patient could not be included because size of SLN metastasis not listed

[b] One patient could not be included because size of tumor not listed

$p = 0.09$). Using our nomogram, the median predicted probability of having additional nodal disease was 25 % in patients who underwent ALND compared with 14 % in the group that did not have ALND ($p = 0.03$). In the ACOSOG Z0011 trial, the rate of positive non-SLNs in the ALND arm was 27 %.[10] In our post-Z0011 group, 94 % (29/31) of the patients who did not undergo ALND had predicted scores <27 %. One patient (1/9, 11 %) who underwent ALND was found to have additional positive lymph nodes.

Adjuvant Therapy Decisions

One consideration regarding the Z0011 data is the impact on adjuvant therapy decisions. The number of patients who received adjuvant chemotherapy was similar in the cohorts (82 % pre-Z0011 vs. 76 % post-Z0011, $p = 0.47$). Another point of consideration has been radiation field design.[17,18] The radiation plans of the SLN-positive patients treated at our institution ($n = 52$ in pre-Z0011 cohort and $n = 28$ in post-Z0011 cohort) were

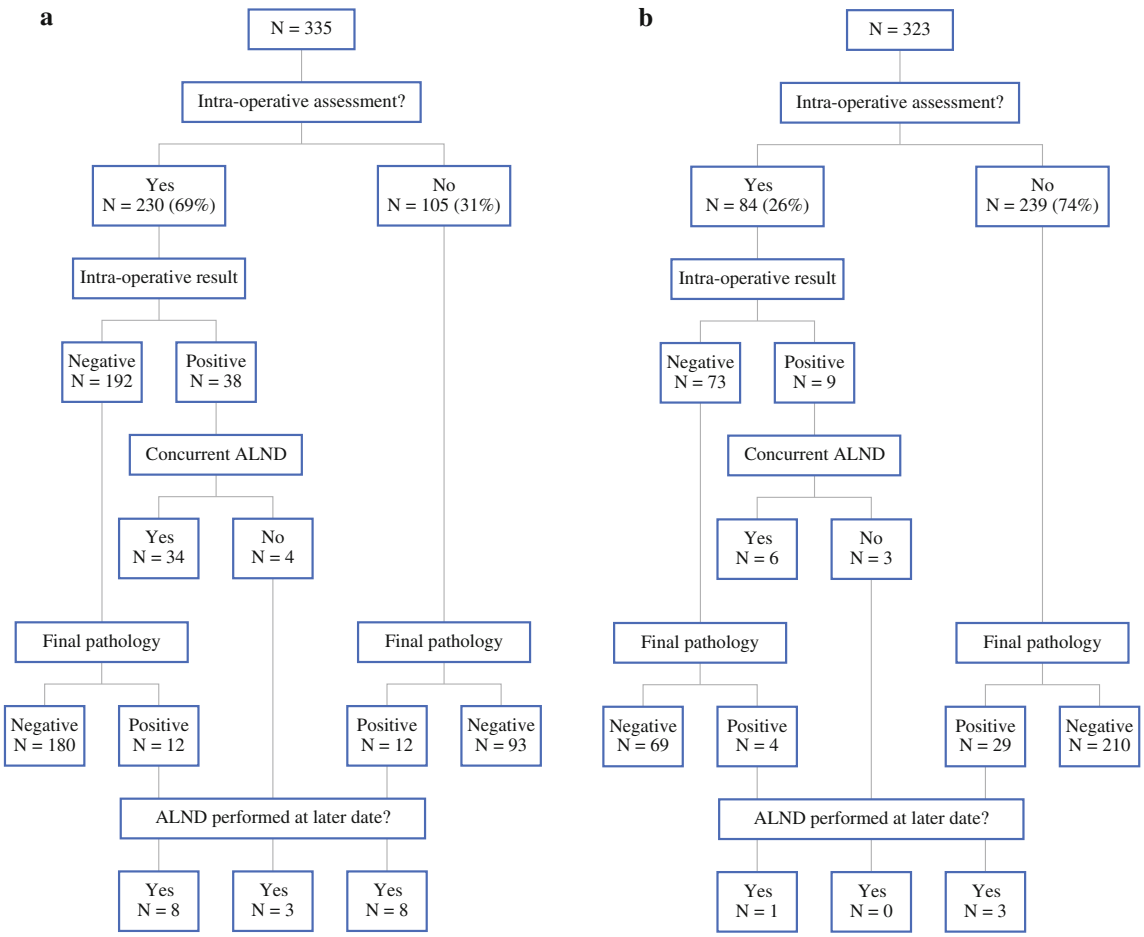

FIG. 1 **a** Intraoperative decisions in pre-Z0011 cohort. **b** Intraoperative decisions in post-Z0011 cohort

TABLE 4 Use of intraoperative assessment

Intraop assessment?*	Pre-Z0011			Post-Z0011		
	Yes ($N = 230$) (69 %)	No ($N = 105$) (31 %)	p	Yes ($N = 84$) (26 %)	No ($N = 239$) (74 %)	p
Median age (range)	57 (25–88)	60 (33–89)	0.02	59 (28–78)	61 (34–90)	0.02
Menopausal status						
Pre	74 (32 %)	20 (19 %)	0.01	19 (23 %)	47 (20 %)	0.64
Post	156 (68 %)	85 (81 %)		65 (77 %)	192 (80 %)	
Median clinical tumor size (cm)	1.75 (0.4–5)	1.4 (0.2–5)	<0.01	1.6 (0.2–4.8)	1.5 (0.2–5)	0.03
Clinical T stage						
T1	149 (65 %)	80 (76 %)	0.04	55 (65 %)	184 (77 %)	0.04
T2	81 (35 %)	25 (24 %)		29 (35 %)	55 (23 %)	
Histology						
Ductal	183 (80 %)	76 (72 %)	0.36	72 (86 %)	164 (69 %)	0.03
Lobular	16 (7 %)	13 (12 %)		6 (7 %)	33 (14 %)	
Mixed	20 (9 %)	10 (10 %)		3 (4 %)	18 (8 %)	
Other	11 (5 %)	6 (6 %)		3 (4 %)	24 (10 %)	
Nuclear grade						
Low	33 (14 %)	29 (28 %)	<0.001	13 (15 %)	64 (27 %)	0.03
Intermediate	121 (53 %)	63 (60 %)		46 (55 %)	131 (55 %)	
High	74 (32 %)	12 (11 %)		25 (30 %)	43 (18 %)	
Hormone receptor status						
ER/PR positive	209 (91 %)	101 (96 %)	0.06	74 (88 %)	221 (92 %)	0.24
ER/PR negative	21 (9 %)	4 (4 %)		12 (12 %)	18 (8 %)	
Her2 receptor status						
HER2 positive	16 (7 %)	5 (5 %)	0.63	9 (11 %)	11 (5 %)	0.06
HER2 negative	214 (93 %)	100 (95 %)		75 (89 %)	228 (95 %)	
Lymphovascular invasion						
Present	43 (19 %)	10 (10 %)	0.07	11 (13 %)	21 (9 %)	0.44
Absent/missing	187 (81 %)	95 (90)		73 (87 %)	218 (91 %)	

* There was a significant difference ($p < 0.001$) between the rate of intraoperative assessment in the pre-Z0011 and post-Z0011 cohorts

reviewed to assess the impact on radiation field design. Radiation oncologists at our institution generally use high tangent breast radiation fields that purposely target level I and II of the axilla for the treatment of SLN-positive patients who do not undergo ALND.[12,18] The proportion of patients treated with high tangents increased from 10 % (6/52) in the pre-Z0011 cohort to 43 % (18/28) post-Z0011 ($p < 0.001$). This reflects changes in surgical practice as only 2 % (1/54) of patients who underwent ALND had high tangents versus 88 % (23/26) of those who did not undergo ALND ($p < 0.001$). The proportion of patients treated with regional nodal irradiation was similar in the pre- (21 %, 13/52) and post-Z0011 cohorts (17 %, 7/28; $p = 1$) and similar between patients who underwent ALND (26 %, 14/54) and those who underwent SLND alone (23 %, 6/26; $p = 0.51$).

Other Practice Changes

Historically, our practice has been to perform intraoperative assessment of SLNs and proceed with concurrent ALND if positive. Given the Z0011 data showing that completion ALND is not required in all patients with a positive SLN, the routine use of intraoperative assessment is unnecessary. We therefore sought to determine differences in the use of intraoperative assessment of the SLN between the two cohorts (Fig. 1). Intraoperative nodal assessment was used significantly more in the pre-Z0011 cohort (69 %) compared with the post-Z0011 (26 %) cohort ($p < 0.001$). The rate of intraoperative assessment decreased from 55 % (56/102) in the first 6 months of the post-Z0011 time period to 22 % (28/127) in the subsequent 6 months reflecting increasing surgeon comfort with

implementing the Z0011 data. The decrease in use of intraoperative nodal assessment translated to a decrease in median operative time from 91.5 minutes pre-Z0011 ($n = 234$) to 79 minutes after the results ($n = 247$; $p < 0.001$) (we excluded patients with a positive SLN identified on intraoperative assessment who went on to completion ALND during the index procedure, had concurrent tissue rearrangement by a plastic surgeon, had bilateral procedures, or who had other unrelated procedures performed at the same operation from this analysis of operative times). Surgeons were more likely to perform intraoperative SLN assessment for patients with higher clinical T stage ($p = 0.03$), ductal histology ($p = 0.03$), and high-grade ($p = 0.03$) tumors (Table 4).

DISCUSSION

The ACOSOG Z0011 trial has defined a select cohort of patients in whom a completion ALND may be safely omitted. At MD Anderson, after a multidisciplinary discussion we began counseling the majority of women with clinical T1-2N0M0 tumors with a positive SLN undergoing BCT with whole breast irradiation that they may forgo ALND without a negative impact on oncologic outcomes. The current study suggests that the Z0011 data has resulted in practice changes at our institution. In women with positive SLN(s) meeting the Z0011 eligibility criteria, the rate of ALND decreased from 85 % in the year before the results were reported to 24 % in the post-Z0011 cohort. It is likely that this will continue to decrease, because the rate of ALND decreased from 28 % in the first 6 months after Z0011 to 18 % in the last 6 months.

Before the Z0011 trial, there was considerable debate regarding the benefit of extensive nodal surgery in patients with small volume nodal metastasis, especially in an era of improved systemic and radiation therapy. This is seen in multiple studies evaluating practice patterns. In an examination of 26,986 patients with positive lymph nodes in the Surveillance, Epidemiology, and End Results database from 1998–2004, 16.4 % underwent SLND alone without ALND with no difference in OS.[6] Similarly, an analysis of 97,314 patients in the National Cancer Data Base from 1998–2005 demonstrated that 20.8 % underwent SLND alone with no detriment to OS. Patients selected for omission of ALND tended to be older, had smaller tumors, or were treated at non-National Cancer Institute-designated cancer centers.[7] A study from our institution showed 26 % of SLN positive patients who did not undergo ALND with no axillary recurrences at 29.5-month follow-up. These patients had predominantly T1/T2 tumors (95.4 %) that were of ductal histology (74 %) and were ER-positive (82 %) with a median of one positive SLN and a median size of nodal disease measuring 1 mm.[8] These studies represent heterogeneous patient populations who received different surgical and adjuvant regimens; however, they suggest that, even before report of the Z0011 trial, surgeons were omitting completion ALND in select patients. An important contribution of the Z0011 trial is that it helps to define the population in whom this practice is appropriate.

One debate regarding the Z0011 trial is the applicability of the results to subsets of patients who were underrepresented or undefined in the trial such as young patients, patients with lobular histology, hormone receptor negative tumors, or HER2-positive tumors. This is reflected in the current study where some patients who qualified for omission of ALND by strict Z0011 eligibility criteria still underwent ALND. For instance, in the post-Z0011 cohort 75 % of patients with lobular histology underwent ALND compared with 17 % with ductal histology. Although histology was not predictive of recurrence in the Z0011 trial, patients with lobular histology made up only 6.5 % of the ALND group and 8.5 % of the SLND alone group.[9] Whereas the retrospective nature limits our analysis regarding decision making, surgeons seem less comfortable in omitting ALND in these patients, potentially reflecting the lack of data for this subset as well as data showing that even isolated tumor cells may be clinically relevant with lobular histology.[19] Although there has been discussion regarding the applicability of the Z0011 results to women with hormone receptor negative tumors, patients with ER negative tumors are routinely given neoadjuvant chemotherapy at our institution, resulting in a small subset included in this study (3 patients in the pre-Z0011 cohort and 4 patients in the post-Z011 cohort).

Surgeons at our institution often use our validated nomogram to predict the likelihood of nonsentinel lymph node metastases and to aid in clinical decision-making.[16] This also might be influencing decision-making as patients who underwent ALND had a higher predicted probability of additional nodal disease. There have been critics of using retrospectively created nomograms for patients meeting the Z0011 criteria.[11] However, patients enrolled in the Z0011 trial had favorable disease characteristics and accordingly had a lower (27.4 %) risk of additional axillary disease than the 53 % reported in a previous meta-analysis.[20] Although it is unknown whether surgeons used this nomogram in their decision-making, the different predicted probabilities between patients who underwent ALND versus those that did not reflects the possibility that either the nomogram or characteristics captured in the nomogram might have influenced the decision. We would therefore suggest that a nomogram could be helpful in guiding decisions for patients who meet Z0011 eligibility criteria but may not completely meet the characteristics of those

who enrolled on the trial or groups that were underrepresented in the trial.

Findings from the Z0011 trial are important for many reasons, inlcuding that a significant number of breast cancer patients will be spared the morbidity of ALND, such as lymphedema. Although the follow-up period for the current study is too short to determine lymphedema rates, a previous report of patients enrolled on the Z0011 study showed that lymphedema rates were lower in the SLND alone group (2 vs. 15 %).[21] In one case-control study comparing medical costs in the 2 years after breast cancer diagnosis, total costs were $22,153 higher in patients who developed lymphedema. Whereas there was a $8,560 difference in cancer-related costs ($p = 0.008$), there was a $14,600 difference between the groups in non-cancer-related costs, such as treatment for infections and physical therapy ($p = 0.001$).[22] Thus, sparing breast cancer patients from ALND should decrease morbidity related to ALND, which translates into cost savings. Further savings should result from the decreased use of intraoperative nodal assessment and the corresponding decreased operative time for patients with negative SLNs. These observations are vital in an era that emphasizes cost containment and clinician productivity.

In conclusion, the ACOSOG Z0011 trial has been practice-changing at our institution. For patients who meet the Z0011 eligibility criteria, we are omitting ALND in the majority of patients, although management decisions are left to individual surgeons, some of whom are performing ALND on selected patients who have unfavorable biological or tumor characteristics.

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