Trends in Axillary Management of Breast Cancer in Auckland, New Zealand

Russell P, Gerred S. Department of General Surgery,

North Shore Hospital, WDHB, Auckland, New Zealand

Waitemata District Health Board

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Introduction

Axillary node dissection (AND) in breast cancer patients is known to cause significant morbidity. Several recent papers have challenged the previous notion that a positive sentinel node biopsy (SNB) is an absolute indication for surgical clearance of axillary nodes in all patients. The Z0011 trial by The American College of Surgeons Oncology Group (ACSOG) in 2011 randomized clinically T1/2, N0, M0 invasive breast cancer patients with 1-2 positive sentinel nodes to axillary node dissection or no further axillary treatment[1]. All patients had lumpectomy and tangential whole-breast irradiation. In 891 patients randomised, the authors found no significant difference in 5-year overall survival or 5-year disease-free survival.

Similar results have been reported elsewhere for patients with low risk cancer and a positive sentinel node[2,4]. Specifically, trials comparing AND vs. no AND when micrometastatic disease only is detected on SNB, continue to show non-inferiority in survival and disease free survival when AND is omitted[3]. The significance of these results is largely found in the reduced unnecessary morbidity associated with AND, such as lymphedema, restricted motion and parasthesia[4].

This change in dogma should be reflected in treatments and outcomes for individual patients. The current study aims to quantify any changing trends in management for patients with invasive breast cancer in Auckland, New Zealand. It compares treatment for Z0011-eligible patients before and after February 2011, which was the date of publication of the trial.

Methodology

The Auckland Breast Cancer Registry, covering pubic and private surgery across the Auckland region, was searched for all women with T1-2 invasive breast cancer who underwent sentinel node biopsy between January 2009 and June 2012. Patients who fulfilled eligibility to the Z0011 trial were identified and divided into patients with a histological diagnosis prior to February 2011 and those after. The two groups were compared to ensure adequate similarity between the groups. The proportion of eligible patients who proceeded to AND, as well as the proportion with micrometastatic disease only, was compared between the two groups. Lastly the number of total positive nodes was compared between groups. Analysis was performed using Fisher's exact test for P-values and binomial (Clopper-Pearson) 'exact' method for proportion confidence intervals.

Results

A total of 1,999 patients who underwent lumpectomy or mastectomy and SNB between January 2009 and June 2012 were identified from the registry database (Fig. 1). Using the Z0011 selection criteria, 151 (7.6%) patients were deemed eligible and were used for further analysis, 96 were diagnosed prior to February 2011 and 55 after. A comparison of patient and tumour characteristics between the groups showed no significant difference except a small difference in mean age (Table 1).

There was a decrease in the proportion of patients who underwent completion axillary node clearance from 89.6% (CI 81.7 – 94.9) prior to February 2011 to 65.5% (CI 51.4 – 77.8) post (P 0.0005) (Fig. 1). No significant trend was found when comparing rate of progression to AND per year (Fig. 2). There was a significant decrease in the proportion of patients with micrometastatic disease only who underwent AND from 68.2% (CI 45.1 – 86.1) prior to February 2011 to 28.6% (CI 11.3 – 52.2) post (P 0.0148).

Of the patients who had an AND (122 patients), 49 (40.2%) had further metastatic nodes detected. Of these, an average of 2.88 (range 1-17) nodes contained metastatic deposits. There was a non-significant increase in the proportion of patients with AND who had further metastatic nodes detected. Prior to February 2011, 30 of 86 patients (34.8%) had further positive nodes, and 19 of 36 patients (52.8%) after February 2011 (P 0.0724).

Table 1: Comparison of baseline patient and tumour characteristics

Characteristic	No. (%) 2009 - Feb 2011	No. (%) Feb 2011 - Jun 2012	P Value
Ethnicity			
NZ European / Other European	61 (63.5)	40 (72.7)	0.2840
Maori	14 (14.6)	3 (5.5)	0.1112
Pacific	8 (8.3)	3 (5.5)	0.7468
Asian / Indian	9 (9.4)	5 (9.1)	1.0000
Not stated	4 (4.2)	4 (7.3)	0.4631
Mean Age at Tissue Diagnosis (years)	56.84	59.38	0.0478*
Range	28.75 – 88.96	40.13 – 78.35	
1st Quartile	48.18	53.79	
Median	55.90	60.67	
3rd Quartile	63.44	65.28	
Clinical T stage			
T1	64 (66.7)	37 (67.3)	1.0000
T2	32 (33.3)	18 (32.7)	
Tumor size			
Median (range) mm	18 (1-40)	18 (6-46)	
Average	18.26	19.19	0.3178
Receptor status			
ER+/PR+	82 (85.4)	41 (74.5)	0.1276
ER+/PR-	4 (4.2)	7 (12.7)	0.0989
ER-/PR+	1 (1)	0 (0)	1.0000
ER-/PR-	9 (9.4)	6 (10.9)	0.7848
Missing data	0 (0)	1 (1.8)	0.3642
LVI			
Yes	37 (38.5)	21 (38.2)	1.0000
No	59 (61.5)	34 (61.8)	
Tumor Type			
Infiltrating ductal	88 (91.7)	48 (87.3)	0.4701
Infiltrating lobular	5 (5.2)	4 (7.3)	0.7243
Other	3 (3.1)	3 (5.5)	0.6687
Lymph node metastases (N grade)			
MIC	22 (22.9)	21 (38.2)	0.0607
1	56 (58.3)	29 (52.7)	0.1607
2	16 (16.7)	4 (7.3)	0.1354
3	2 (2.1)	1 (1.8)	1.0000
Adjuvant therapy			
Hormonal	46 (47.9)	26 (47.3)	1.0000
Chemo	9 (9.3)	6 (10.9)	0.7824
Both	32 (33.3)	20 (36.4)	0.7284

* = Statistically significant

Figure 1: Percentage of Patients Progressing to AND

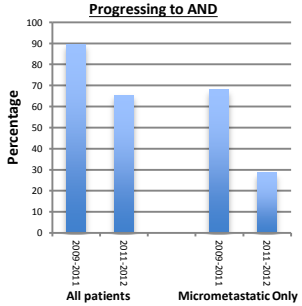
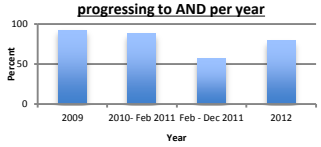


Figure 2: Percent of patients progressing to AND per year



Discussion

The results show a significant drop between the two time periods in rate of progression to AND among women in Auckland who would fulfil the Z0011 inclusion criteria. This drop was detected for both micro and macrometastatic disease. Of all women with T1-T2 invasive breast cancer in Auckland, only 7.6% would fulfil the criteria for the Z0011 study. However, given the large number of patients over 3.5 years (1,999 patients), the drop in rate of AND is a significant decrease, and would avoid the morbidity associated with AND for many women. The most likely cause for this trend, although unproven by this study, is the growing body of evidence against completion AND in all patients with a positive SNB. The fact there were no significant differences between the two groups at baseline, except a small difference in age, reinforces this. The date that separates the two groups in the study is the publication date of the Z0011 trial; February 2011. It is unclear from the study if it is a meaningful date to separate the groups as there is no trend continuing downwards from 2011 to 2012 (Fig. 2). However, the results of the study were well known post February 2011 and highly likely to be contributing to surgeon decision-making.

Similar results to Z0011 have been replicated elsewhere, including a large meta-analysis by Glechner et al.[4] However many argue against generalising the results of Z0011 to every patient that would fulfil the criteria. Gatzemeier & Mann list the main objections and criticisms against the trial[2]. These include early closure of the study, missing data and a high proportion lost to follow up. Interestingly there was a statistically significant difference in proportion of macrometastatic disease in the sentinel node between the two groups, with the SNB only group potentially having less tumour burden. There was also double the rate of axillary recurrence (although low, 0.9% vs. 0.5%) in the SNB group only. Concerns regarding generalizability arise from the actual population of the Z0011 trial which mainly included patients over 50, with small (T1), ER positive invasive ductal carcinomas. Notably this patient group is also over-represented in the present study, indicating natural variation in prevalence of breast cancer subgroups. Despite these reservations, the American Society of Clinical Oncology and National Comprehensive Cancer Network recommend considering no further surgery for patients who meet the eligibility criteria[5].

It can be presumed to be safer to omit AND when micrometastatic disease only is found in the sentinel node than macrometastatic disease. A meta-analysis in 2006 showed 53% of patients with a macrometastatic positive SNB had additional positive axillary nodes found on completion AND, compared with 20% for micrometastatic disease on SNB, and 12% for isolated tumour cells[6]. There is a growing body of evidence, in randomised trials and retrospective studies, supporting omission of AND for micrometatstaic disease only[3,7]. The current study reflects this trend with a significant decrease in the proportion of women with micrometastatic disease only on SNB who proceed to AND.

Studies have reported various rates of further metastatic disease in the axilla for SNB +ve women. In the Z0011 trial, 28% of patients in the AND arm were found to have further metastatic disease, which is presumed to be a similar rate in the SNB only arm[1]. The trial proposes that this number is unimportant for oncological outcome, which is counter-intuitive to many. In the present study the number was higher than that of Z0011, with 40% of patients who had an AND found to have further metastatic nodes. However a direct comparison is unreasonable of course as the present study was not randomised. There was a non-significant rise in the proportion of patients who had an AND with further metastatic nodes. It is possible this trend may reflect more accurate selection of which patient should require an AND. This has been aided by studies such as Z0011, as well as clinical nomograms such as MSKCC[8]. Unfortunately it is beyond the scope of this study to assess outcomes in comparison to number of metastatic nodes.

Conclusion

The rate of AND in Auckland patients who fulfill the Z0011 study criteria has dropped by 24% since the study was published. This signifies an improvement in morbidity associated with AND for these patients, however the findings remain applicable to only a small proportion of breast cancer patients.

References

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