ORIGINAL ARTICLE

LONG-TERM MORBIDITY OF AXILLARY LYMPH NODE DISSECTION: IMPLICATIONS FOR PATIENTS WITH CARCINOMA BREAST

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Background: To assess the long term complications of level II Axillary Lymph Node Dissection (AXLND) in patients with breast cancer and to see if they are high enough to warrant a Sentinel Lymph Node (SLN) biopsy in all patients presenting with carcinoma breast in our setup in Pakistan. **Methods:** This study was conducted at Surgical Unit IV, Department of Surgery, Combined Military Hospital, Rawalpindi. Upper, lower arm circumferences and body mass index were ascertained in post Modified Radical Mastectomy (MRM) with level II AXLND, in female patients who had undergone surgeries from 1992 to 2008. Patient's perception of degree of lymph oedema, arm function and other symptoms like pain, tingling and numbness was noted. The number of lymph nodes removed, number of positive nodes and post operative radiotherapy were also recorded from the hospital records. **Results:** Thus upper arm circumference in 85.7% patients and lower arm circumference in 89.2% patients was within 2 Cm of the unaffected side. No, moderate and severe arm swelling was described by 83.35% of patients, 11.6% of patients and one patient respectively and 41.5% of patients describing some arm swelling had positive lymph nodes. Thus even if they had gone (SLN) biopsy, these patients would have had a subsequent AXLND. Over 94% of patients had either good or excellent arm function with most in the excellent range. **Conclusion:** The patients at significant risk for positive nodal may be better served with an AXLND rather than the SLN technique.

Keywords: Breast carcinoma, Sentinel lymph node biopsy, Axillary Lymph Node Dissection

INTRODUCTION

Axillary Lymph Node Dissection (AXLND) as part of the surgical therapy for breast cancer has come under increased scrutiny over the last several years, mainly due to the introduction of the Sentinel Lymph Node (SLN) biopsy technique to assess the status of the axillary nodes. This technique has the advantage of avoiding AXLND in those patients with pathologically negative nodes and of identifying those nodes at highest risk of disease. This allows the pathologist to focus their efforts more thoroughly on those nodes most likely to be positive. The principal downside of the SLN biopsy technique is the possibility of false negative result, i.e., the sentinel node is negative, but there is disease elsewhere within the axilla that is not identified. Consequently, disease is left behind and the patient's disease status is down staged with resultant under treatment.

As with all new surgical procedures, there is an associated learning curve for the SLN biopsy technique. As a result, the false negative rate seems to be inversely proportional to the experience of the surgeon. The false negative rate based on a review of the current literature ranges from 0–16.7%, with an estimate of approximately 5% for the experienced surgeons.[1]

Other factors that make SLN biopsy technique a less favourable option in Pakistan are the fact that women with breast cancer in our country present late with advanced disease and very few stage I tumours are seen[2–4] resulting in high rates of tumour positive lymph nodes[5], and large tumour size at presentation.[6]

Added to all this, the need for a second operation in patients whose sentinel node is positive and a second anaesthesia with its attendant risks makes SLN of limited use in our setup.

The long term morbidity of AXLND in experienced hands is minimal, as there are multiple factors in addition to the extent of axillary dissection contributing to the morbidity. AXLND should remain a reasonable treatment option (especially in Pakistan) until long term recurrence and survival data are available with the SLN technique, particularly for patients with invasive cancers more than 2 Cm in size.

MATERIAL AND METHODS

Women treated for breast cancer were seen in routine follow-up in CMH, Rawalpindi. They were eligible for our retrospective study of the long-term complications from AXLND if they were a minimum of one year out of Modified Radical Mastectomy (MRM) with axillary level II clearances. The patients studied had undergone surgeries over a 16 year period (1992–2008) the axillary level was determined according to the relationship of axillary tissue to the Pectoralis minor muscle.[7] In level II AXLND all axillary tissue lateral, inferior to the muscle was removed. Objective measurements including upper and lower arm circumferences and body mass index

were ascertained. Patients were divided into three BMI categories that correspond to the definitions of normal weight (18.5–24.9 Kg/m^2), overweight (25–29.9 Kg/m^2) and obesity (30 Kg/m^2 or greater), as proposed by the WHO.[8] A subjective evaluation from the patients was conducted. This included the patient's perception of degree of lymph oedema or arm swelling (none, minimal, moderate, severe and incapacitating), arm function (including range of motion, strength and overall function) and other symptoms like pain, tingling and numbness. Additional information including the number of lymph nodes removed number of positive nodes, stage of the disease (American Joint Committee on Cancer, AJCC, staging system was used) and postoperative radiotherapy was also taken down from hospital records.

Means for continuous variables as well as frequencies and percentages for categorical variables were calculated. Stepwise regressions were performed to evaluate patient variables that might be predictive of either lymph oedema measured clinically or arm swelling perceived by the patient.

RESULTS

Fifty-three percent of the patients at the time of the AXLND were less than 50 years of age and only two patients were 70 years or older (Table-1). Majority of the patients were less than 5 years post surgery (Table-2). Adequate number of lymph nodes (14 or more) was removed in 71.4% of patients and 34% of patients were with positive nodes (Table-3). Only 4 patients had a more than 2 Cm difference in both upper and lower arm circumference. Thus 96 (85.7%) of 112 patients had an upper arm circumference within 2 Cm of the unaffected side and 100 (89.2%) of 112 patients had a lower arm circumference within 2 Cm of the unaffected side (Table-4, 5).

The BMI was normal in 23 (20.5%) patients; 10 (9%) had a BMI in the underweight range; 37 (33%) had a BMI in the overweight range; and 42 (37.5%) were in the obese range. The objective measurements on 19 of the 27 patients with minimal subjective swelling demonstrated less than a 2 Cm difference between the affected and the unaffected side. Thus 90 (83.35%) of 112 patients had virtually no arm swelling (Table-6). Of the 41 patients who felt that they have some degree of arm swelling 17 (41.5%) had positive nodes. Thus even if they had gone SLN biopsy, 17 of 41 patients would have had a subsequent AXLND. Thirty-four of the 41 patients received postoperative radiotherapy. Twenty-eight (68.2%) of the 41 patients with subjective arm swelling had a BMI more than 24.9. The most common long term symptom was numbness involving mainly the upper inner aspect of the affected arm. This was mentioned by 30 (26.8%) of 112 patients and had no effect on lifestyle.

Over 94% of the patients had either good or excellent arm function with most in the excellent range (Table-7). All variables including age, BMI, years of follow up, number of nodes positive for metastasis disease and whether or not the patient received chemotherapy, radiation or anti-oestrogen therapy were analysed, especially in patients who described themselves as having moderate or severe arm swelling (Table-8). No patient variables were statistically significant in predicting which patient would develop clinically measurable lymph oedema or subjective swelling of the affected arm, although there was a trend demonstrating an association of arm swelling with obesity (9 out the 14 patients who had a subjective moderate or severe arm swelling had a BMI of >24.9).

Table-1: Age of patients

Age (years)	Patients
20–29	7
30–39	23
40–49	29
50–59	28
60–69	23
70–79	2

Table-2: Duration out of surgery (Years)

Duration	Patients	%
Less than 5 years	87	78.0
5–10 years	19	17.0
More than 10 years	6	5.35

Table-3: Breakdown of lymph nodes removed

Lymph nodes/patients	Number
AXLNDS	112
Average nodes removed	17.5
Range of nodes removed	4–34
14 or more nodes removed	80 (71.4%)
Positive nodes	38 (34%)
>4 Positive nodes	18 (16%)

Table-4: Upper arm circumference

Difference from unaffected side	Patients	%
Within 1 Cm	66	58.93
Within 2 Cm	30	26.79
> 2 Cm	16	14.28

Table-5: Lower arm circumference

Different from unaffected side	Patients	%
Within 1 Cm	77	68.75
Within 2 Cm	23	20.54
More than 2 Cm	12	10.71

Table-6: Patient's perception of arm swelling

Values	Size (Cm)	Patients	%
No	1	71	63.39
Minimal	2	27	24.11
Moderate	4	13	11.61
Severe	1	1	0.89
Incapacitating	0.5	0	0

Table-7: Overall arm function

	Range of motion	Strength	Overall function
Excellent	95	98	60
Good	9	8	45
Fair	6	5	4
Bad	2	1	1
Poor	0	0	2

Table-8: Details of patients with moderate and severe arm swelling (n=14)

Parameter	Patients
Age <60 years	13
Age >60 years	1
BMI >24.9	9
Positive nodes	9
Radiation therapy	12
Chemotherapy	14
Tamoxifen therapy	7

DISCUSSION

Our data on long term complications of a complete (level II) AXLND indicate that this operation can be performed with minimal long-term morbidity. Some degree of numbness was the most common symptom and was observed in 26.8% of our patients. It occurred mainly in the upper inner aspect of the inter-costal-brachial nerve(s). Obesity as an important variable in lymph oedema after AXLND was described by Petrek *et al* from Memorial Sloan-Kettering Cancer Center.[9] Of 15 potential predictive factors that they analysed, only 2, arm infection/injury and weight gain (obesity), were statistically associated with lymph oedema. In another study from the same institution, Werner *et al*[10] reported that the level of node dissection was not statistically related to the development of arm oedema; the only factor that was significantly associated was an elevated BMI. We believe that the SLN technique has an important role to play in patients with breast cancer, particularly those with high grade ductal carcinoma-in-situ (DCIS) and small T1 invasive cancers. In both cases, risk of positive node disease is very low, thus the SLN technique obviates the need for AXLND in these low risk patients. However, with lesions >1.0 Cm, the risk for positive node disease becomes substantial, at least 30% and increases with increasing size of tumour.[11] At the same time, the false negative rate of the SLN technique increases. Other complications specific to the SLN technique include the rare allergic reaction to the dye[12,13] and the need for a second operation (not forgetting its initial cost) in the substantial percentage of patients whose sentinel node is positive, since the diagnosis of positive nodal disease is not often made on frozen section at the time of initial operation; and a second anaesthesia with its attendant risks makes SLN of limited use in our setup.

Most of the patients presenting to doctors in Pakistan have stage III (34.8%) or stage II (32.2%) disease at the time of diagnosis.[14] In a recent study[15] only 3.3% patients had stage II disease. In another study[16], 2 (3.9%) patients had TNM stage II, 42 (82.4%) had TNM stage III and 8 (15.9%) had TNM stage IV disease.

Previous studies carried out at our hospital show that majority of breast carcinomas were bigger than 2 Cm (92%).[3] They also show that 74% of the patients had axillary lymph node metastasis at the time of first diagnosis and in 30% of these patients there were more than 3 axillary lymph nodes which had tumour metastasis.[3] With an intra operative (frozen section) false negative rate for identifying metastatic disease in the SLN of 45–60% for T1 lesions, the volume of re-operative axillary surgery that needs to be performed to say the least is considerable.

There is no question that the surgical complications of a SLN biopsy are less than that of an AXLND; however, to compare the SLN technique with AXLND, the potential consequences of the SLN technique must also be taken into account including the morbidity associated with the extension of the radiation field to include the axilla in a patient whose has undergone segmental mastectomy and negative SLN biopsy in an effort to cover the possibility of a false negative result.[17] Radiation delivered to an axilla in a patient found to have positive SLN on permanent section in an effort to avoid a second operation has also become increasingly common and understated in the west. Not reporting on a patient with appositive SLN would leave residual disease behind in a substantial number of patients. In two studies carried out at our hospital on 100 and 280 patients 74 and 79% of patients had positive lymph nodes respectively, out of which 71 and 30% of patients had more than 3 positive lymph nodes positive respectively.[3,4]

Veronesi *et al* pointed out that if level I lymph nodes were positive, the statistical chance that level II-III lymph nodes would be positive was 41%. This percentage increases with increasing tumour size.[18] Moreover, the control of loco regional disease in node positive patients improves survival. The University of Chicago group noted that in patients with T1 lesions with fewer than 4 positive nodes, the long-term disease free survival was comparable to that for patients who were node negative.[19] The result was the same even for patients that did not receive systemic chemotherapy, indicating that the AXLND was not only diagnostic, but also therapeutic. The recently published radiation trials[20,21] in high risk (positive nodes or T3); pre-menopausal breast cancer patients also concluded that improved regional disease control prolongs survival. Thus, the axilla must be adequately treated to obtain the best oncological results.

We believe that the complication rate of AXLND has been overestimated and the negative aspects of the AXLND technique underestimated in the understandable enthusiasm surrounding the development of a new technique. Even though we assessed patients with level II axillary clearance, the resultant morbidity was minimal; thus, a long-term complication rate of 60% for the standard level I-II AXLND as reported by Singletary[22] is an entirely unacceptable surgical result and simply fuels the fear of our patients. The question remains that should we jump

on to conclusions made in developed countries without collecting our own data and carrying out our own research?

CONCLUSION

The SLN technique is a major advance in the treatment of early stage breast cancer. However, we believe that the long term complication rate of AXLND is sufficiently low not to dessert AXLND completely. Therefore, the patients at significant risk for positive nodal disease and patients who are unlikely to turn up for long term follow-ups may be better served with an axillary dissection rather than the SLN technique.

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