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Research Article

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Prediction capability of axillary nodal status by five node sampling in early invasive breast cancer

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ABSTRACT

Background: Management of axilla in early breast cancer is controversial with options being sentinel lymph node biopsy (SLNB), axillary sampling and axillary dissection. In our study we explored the possibilities of 5-node sampling as an alternative or adjunct to SLNB in early invasive breast cancer.

Methods: We did an observational study of the 45 patients, who underwent modified radical mastectomy and compared the initial 5-nodes pathology with standard axillary dissection in the excised breast tissue specimen.

Results: Out of 45 patients, first 5-nodes were found positive in 25 cases. In 8 cases only initial 5-nodes were involved. Sensitivity improved with increasing number of nodes examined in 5-node biopsy, approaching 100% with 5 nodes examined. In all pathological negative axilla, 5-node pathology was also negative.

Conclusions: Five node sampling of axilla has a comparable sensitivity and false negative rate as SLNB. It fairly represents axillary nodal status and could be a good adjunct to SLNB for further increasing accuracy of later. It can also be an alternative to SLNB in situation where lack of feasibility to perform it as in many developing countries. We also recommend further study directly comparing five-node sampling and SLNB in future.

Keywords: Breast cancer, Five node sampling, Sentinel node biopsy, Axillary sampling

INTRODUCTION

Breast cancer is the most commonly occurring female cancer in the world with an age-standardized incidence rate (ASR) of 39 per 100,000, which is more than double that of the second ranked cancer (cervical cancer ASR=15.2 per 100,000.¹ Though a large number of these patients presents in later stages of disease in Indian scenario, with increased awareness, disease presentation in early stage is on rise. Today with increasing use of adjuvant polychemotherapy, radiotherapy and hormonal therapy it has been possible to do breast conserving therapy, while achieving similar survival benefits and decreased recurrence rate as of radical surgery.

One such aspect of surgery is routine axillary lymph node dissection (ALND), which tells the extent of involvement of axillary nodes. Although a multitude of new prognostic factors has been proposed, the strongest one is still the axillary lymph-node status.² The down side of this procedure is the morbidity associated with axillary surgery. Its complications include lymphoedema, seroma, wound infection resulting in delayed wound healing, restriction of shoulder movement, intercostobrachial nerve syndrome, lymphoedema causing cellulitis, rarely lymphangiosarcoma and Stewart Treves syndrome. Although these complications mostly were described as

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mild, 39% of the women experienced an effect upon their daily lives.³ Thus in patients who do not have axillary lymph node metastasis there is a need for a procedure which can stage the axilla as accurately as conventional or modified ALND without complications of axillary dissection.

The alternatives available to axillary dissection for axillary staging are axillary sampling (AS) and sentinel lymph node biopsy (SLNB).^{4,5} Various techniques of axillary sampling include triple node biopsy, four or five node biopsy (4NAS), pectoral lymph node biopsy etc.⁶ The sentinel node biopsy is a new method for minimally invasive axillary surgery. By the means of peritumoral injections of blue dye and/or a radiolabeled colloid a few hours before surgery the lymph node that first receives the drainage from the breast can be identified visually and/or by a gamma probe. The false negative rate in one of the largest series from a single institution was 6-7%, whereas the corresponding figure in two other multicenter studies was 3-11%. 7,8 As it is a simple technique do not require expert training and hence can be a reasonable alternative to sentinel node biopsy especially in situations where SLNB is not feasible because of varied reasons.

There seems to be a role for AS when SLN is not identified while examining the axilla (4%) and when there is previous history of excision biopsy of tumor (draining lymphatics are divided and alternate channels open). Even when facilities are available for SLNB, it seems reasonable to complement the SLNB with AS to improve the accuracy of staging the axilla. In this study, we have staged the axilla in patients undergoing Modified radical mastectomy in early invasive breast cancer by five node biopsy, to assess its sensitivity.

METHODS

We did an observational study of the prediction capability of axillary node status by 5-node sampling in breast tissue specimen following modified radical mastectomy in patients of carcinoma breast, operated during September 2011 to December 2012. Women with clinical stage T0-3, N0, M0 breast cancer were eligible. They were included in the study after informed consent. Women with stage T4 / N1-2 / M1 breast cancer were not included, also the patients with recurrent breast cancers, male breast cancers and patients received neoadjuvant chemotherapy were not included in the study.

All patients underwent modified radical mastectomy (level I-II axillary dissection) and entire specimen of breast and axillary tissue was removed. These were the patients, who refused conservative surgery due to poor socioeconomic conditions and lack of desire to undergo further radiotherapy and attending long follow ups. The 5-node sampling began with dissection near the intercostal brachial nerve of the breast specimen until initial five lymph nodes had been removed (Figure 1).

Afterward this material was submitted in a separate box to the pathologist along with entire specimen. In this way the experimental method could be compared with the gold standard procedure in each patient. Biopsy results of 5 node sampling were compared with the final histopathology of entire specimen of breast and axilla including 5 separated nodes.



Figure 1: Specimen of modified radical mastectomy showing the axillary tail area, where initial 5nodes were searched.

RESULTS

Study enrolled 45 patients of early breast cancer operated in 1 year duration. Majority of women were in 30-50 years of age group. Average number of nodes examined in axilla was 10. Five-node biopsy was positive in 25 cases out of 45 cases. In 8 cases, initial 5-nodes were the only involved ones with no further positive nodes found in axilla, which were picked up by 5-node sampling. Further analysis showed sensitivity improved with number of nodes examined (Table 1).

Table 1: Sensitivity and false negative rate related to number of examined lymph nodes.

Nodes	Node + cases	False negative rate (%)	Sensitivity (%)
1-Lymph node	16	33	66
2-Lymph nodes	17	30	70
3-Lymph nodes	18	25	75
4-Lymph nodes	24	4	96
5-Lymph nodes	25	0	100

Five-node sampling was found positive in all positive axillary lymph node cases. False negative rate also decreased with number of examined nodes, 30% with 2 nodes to 4% with 4 nodes. In all 20/45 patients with negative axillary lymph node status, five-node sampling was also found negative. Tumor size correlated well with pathological nodal status (Table 2). Clinic-pathological features of the study patients revealed presentation of tumor with large size and of higher grade in young age

premenopausal patients (Figure 2), however no significant correlation to node positivity was observed.

Table 2: Correlation of node positivity to different variables in study.

Variables	Grouping	%	Node + cases
All Patients		100%	25/45
Age	<50 years	57%	10/26(38%)
	>50 years	43%	10/19(52%)
Menopause	Pre	55%	9/22(40%)
	Post	45%	11/23(47%)
T-size	<2 cm	4%	0/2
	2-5 cm	42%	5/19(24%)
	>5 cm	54%	15/24(62%)
Tumour type	Ductal	96%	
	Lobular	2%	18/43(42%)
	Others	2%	

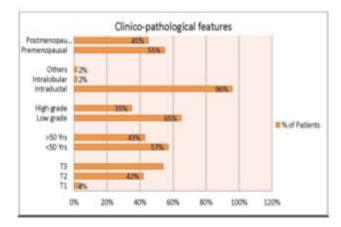


Figure 2: Clinicopathological features of the study patients.

DISCUSSION

Although there is hope that it will be possible to forgo axillary surgery in a low risk group, this subset comprises only a minority of newly diagnosed breast cancers in large Indian setup. Thus, in order to improve the management of the axilla for the vast majority of women with breast cancer other strategies are needed. One alternative is lymph-node sampling of the axilla, a method that is less extensive than axillary dissection. The Scottish trial on sampling versus axillary clearance showed a sensitivity of 100% of a four-node biopsy from the axilla. However, the estimation of sensitivity, which is a key parameter, was based on only 67 women. Moreover, the Scottish trial included patients with on average larger tumors than currently are seen in areas with well-functioning screening.

Our study of the 5-node sampling included 45 patients. The false negative rate in our study was fairly low despite small sample size, this estimate is encouraging since several studies of the sentinel node procedure have shown false negative rates of 6, 7-11, 4%. The positive

predictive value in our series was near 100%, probably due to larger tumor size presentation in our study, the corresponding estimate reported from the sentinel node procedure is 93-96%.

Axillary sampling versus sentinel lymph node biopsy

Macmillan et al., from 'Nottingham Breast Unit', studied 200 patients (T1-2/ N0) and directly compared SLNB using hot node technique (lymphoscintigraphy) with fournode axillary sampling (4NAS-Edinburgh technique). SLN was identified in 191 patients (96%). When compared with SLNB, 4NAS failed to identify metastasis in one patient (2%). On the contrary, SLNB failed to identify metastasis in eight (14%) patients in whom 4NAS detected axillary lymph node metastasis and hence under-staged the axilla. They concluded that SLNB performed using radiolabeled colloid has no advantage over 4NAS when nodes are assessed by standard histological technique. They affirmed that SLNB for breast cancer may have little to offer four-nodesamplers.¹² But this study has been criticized for its faulty design. Similarly, a comparative Japanese study (Sato et al.) of 206 patients of operable breast cancer undergoing SLNB and four-node sampling procedure (Edinburgh technique) showed that the accuracy and sensitivity of 4NAS (98 and 96%) was comparable to that of SLNB (99 and 98%) respectively. The study concluded that 4NAS can be considered an alternate safe and easy procedure for axillary staging. 13

An interesting aspect is that serial sectioning and/or immunohistochemical staining of the sentinel node (-s) often are employed, whereas only routine pathological examination was performed in our study.¹⁴ Serial sectioning and IHC are feasible when used in conjunction with the sentinel node procedure but have been considered too unpractical to be used in routine handling of specimens from level I-II dissections. The 5-node sampling represents something in between. One could speculate that the performance of the 5-node sampling could be improved by using these refined histopathological techniques. Although there seems to be a worse outcome for women with lymph node micrometastases compared with those without, 15 the longterm prognostic value of IHC-positive sentinel nodes is still unknown.

Although axillary surgery per se not seems to affect survival the risk of withholding adjuvant treatment for the women that were falsely defined as node negative must be considered. This problem has decreased during recent years since most breast cancer patients nowadays will be given adjuvant tamoxifen and even chemotherapy regardless of lymph-node status. Though we do not know the true incidence of arm symptoms after a 5-node biopsy, the Scottish group has reported less morbidity of 4-node sampling compared with axillary clearance of level I-III. Moreover, several studies indicate that increasing number of removed nodes causes increased

incidence of arm morbidity. ^{19,20} It is also most likely that the sentinel node procedure causes less arm morbidity than a 5-node biopsy.

The impact of complete ALND on long-term overall and disease-free survival is unclear from the literature. NSABPB- 04 did not show any survival advantage following complete axillary clearance in clinically negative axilla, 21 although the study has been criticized for not being adequately powered. 22 Although the sentinel node procedure probably is superior, in terms of less associated morbidity, the 5-node biopsy seems safe to use as an alternative to level I-II dissection in women not suitable for a sentinel node procedure, as mentioned earlier.

CONCLUSION

Five-node sampling of the axilla fairly predicts the axillary lymph node status and compares with results reported in the literature from the sentinel node biopsy procedure. It can be used as a good adjunct to SLNB to decrease false negative rates further and also as an alternative where feasibility to perform SLNB is not available as in peripheral setups of many developing countries. We also recommend a large randomized study directly comparing sentinel node biopsy and 5-node biopsy results in future.

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Ethical approval: The study was approved by the

 $institutional\ ethics\ committee$

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