Axillary Reverse Mapping for Preservation of Arm Lymphatics during Axillary Lymph Node Dissection in Cases of Breast Cancer

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Abstract: Background: Axillary lymph node dissection represents the standard surgical treatment for breast cancer patients with clinically or histologically involved axillary lymph nodes. However, it is associated with significant morbidity, including postoperative arm lymphedema and neuropathy of the involved extremity, and seroma formation in the axilla. Recently, the axillary reverse mapping technique has been developed to map and preserve arm lymphatic drainage during axillary lymph node dissection. Patients and Methods: In a prospective study, in our surgical department, we attempted to preserve arm lymphatics during axillary lymph node dissection in 50 breast cancer patients, between December 2010 and March 2012. All patients undergoing axillary reserve mapping (ARM) by injection of 2-5 mL blue dye dermally or subcutaneously into the upper inner arm of the ipsilateral arm on average 30 minutes before axillary exposure. RESULTS: The average time between blue dye injection and axillary exposure was 30 minutes (range, 10-50 minutes). ARM procedure successful in 34 patients(68%) and failed in 16 patients(32%). The number of ARM lymph nodes histological were negative in 30 patients (60%) and positive in 4 patients (8%). No lymphedema recorded in this study but Tattooing in 3 patients (6%).CONCLUSIONS**:** ARM appears to be a feasible technique for identification of upper arm lymphatics during axillary surgery. On the other hand, it is not always possible to preserve ARM nodes and/or lymphatics during axillary lymph node dissection. However, the presence of lymph node metastasis involving ARM lymph nodes in this study suggested that preservation of these lymphatics is not oncologically safe during axillary lymph node dissection in patients with breast cancer and clinically palpable axillary lymph nodes and however success ARM rate was relatively high.

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Key words: Sentinel lymph node biopsy, Axillary lymph node dissection, Arm Lymphedema.

1. Introduction:

Axillary lymph node dissection (ALND) is a standard surgical treatment in patients with involved axillary lymph nodes. Unfortunately, arm lymphedema develops in 2.7–5.0% of patients treated by partial ALND (levels I and II), in 3.1–9.6% of those undergoing total ALND, and in 26–38% of patients treated with ALND and radiotherapy[(1).]

The risk of lymphedema is often used as an argument against ALND. Currently, sentinel lymph node (SLN) biopsy has become a highly utilized and widely accepted method for surgical staging of axillary lymph nodes in breast cancer. It can avoid an unnecessary ALND in patients with node-negative breast cancer, thereby preventing arm lymphedema. Nevertheless, recent short-term studies demonstrated that lymphedema develops in 2–7% of patients even with SLN biopsy alone[(2).]

Transection of the arm lymphatics during ALND most likely results in lymphedema, but the ALND technique has changed little over the decades, and involves purely anatomical dissection. It is generally thought that the lymphatics reside juxtaposed to the vein, and the risk of lymphedema can be minimized if the surgeon takes care to avoid skeletonizing the vein. However, lymphatics with this positioning are rarely seen and SLN biopsy does not correct the problem of lymphedema, although it is less morbid than ALND[(3).]

With the purpose of minimizing arm lymphedema after axillary staging surgeries in breast cancer patients, the axillary reverse mapping (ARM) technique has been developed to identify and preserve arm drainage system during axillary surgery[(4).]

This technique of axillary reverse mapping (ARM) uses the injection of blue dye in the upper extremity to allow visualization and preservation of blue lymphatic channels and lymph nodes from the upper extremity during the course of axillary lymph node dissection. Initial reports of this technique suggested that blue lymph nodes did not contain tumor and thus could be safely preserved[(5)].

A recent report by Nos *et al.,* suggested that metastatic deposits may be observed in as many as 14% of ARM lymph nodes. Thus, there is debate regarding the oncologic safety of this technique[(6)].

The arm and breast lymphatic drainage can be separated, allowing safe removal of only the lymphatics of the breast (SLN or ALND) and protection of the lymphatic channels draining the upper extremity[(7)]. This

study will tell us the feasibility, success rate and safety of the ARM technique.

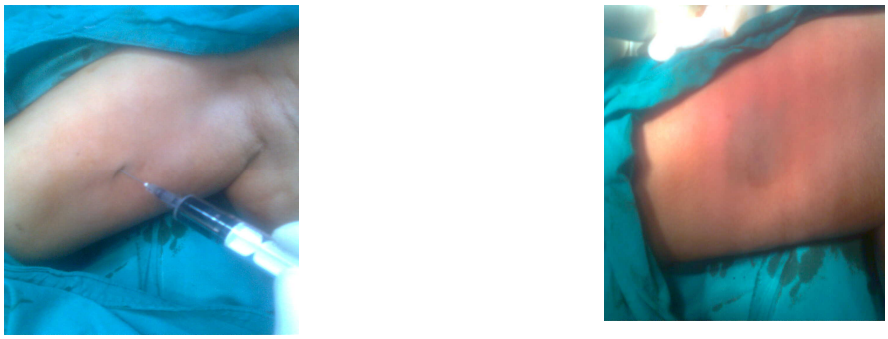
2.Patients and Methods

In a prospective study, in our surgical department, we attempted to preserve arm lymphatics during axillary lymph node dissection in 50 breast cancer patients, between December 2010 and March 2012. A preoperative multiparameter evaluation were done for all patients including, clinical evaluation (general and local examination), imaging evaluation (Mammography, Ultrasound for breast and axilla, Chest x-ray), and tissue diagnosis (by FNA, excisional biopsy or frozen section).

All patients undergoing axillary reserve mapping (ARM) by injection of 2-5 mL blue dye dermally or subcutaneously into the upper inner arm of the ipsilateral arm on average 30 minutes before axillary exposure (range, 10-50 minutes).

After injection, the site was massaged and the arm elevated for 5 minutes to enhance arm lymphatic drainage (Figure,1). Axillary lymph node dissection was performed in a standard anatomic manner to remove all lymph node-bearing tissue extending from the thoracodorsal neurovascular bundle laterally to the chest wall medially, from the axillary vein superiorly to the insertion of the thoracodorsal vessels into the latissimus dorsi muscle distally, and from the anterior aspect of the axillary vein down to the subscapularis muscle posteriorly (Figure,2). The arm and breast lymphatic drainage can be separated, allowing safe removal of only the lymphatics of the breast during axillary lymph node dissection (ALND) and protection of the lymphatic channels draining the upper extremity (blue lymphatics and blue nodes) (Figure,3). Any blue lymphatic channels and/or blue lymph nodes identified in the course of the axillary lymph node dissection were noted. Blue lymph nodes were dissected from the remainder of the surgical specimen and sent for separate pathologic evaluation.

Breast operations included mastectomy in 25 patients (50%), wide local excision in 20 patients (40%) and quadrantectomy in 5 patients (10%).All patients received chemotherapy and radiotherapy.



(A) ***(B)***

Figure(1): A - Injection of 3 mL blue dye subcutaneously into the upper inner arm.
B - 5 minutes after injection of blue dye.

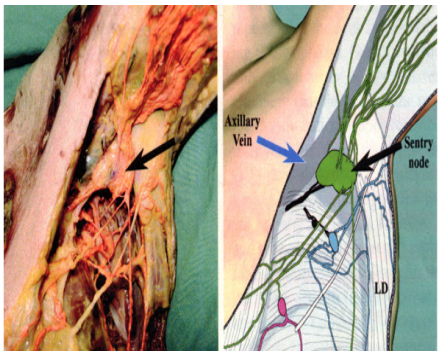


Figure (2): Lymphatics anatomy in the axilla. Left: The left axilla region of the dissected male specimen; Right: a schematic diagram of the same area. (Reprinted from Suami *et al.)* [8].

(A) (B)

Figure (3): Successful identification of blue Lymphatics (A) and blue lymph node (B) in ARM procedure

Inclusion Criteria:

Females(30-70 years) median age (46.5)years old with Stage II, 40 patients and stage III, 10 patients (after successful down staging by neoadjuvant chemotherapy), invasive breast cancer with clinically palpable axillary lymph nodes who are scheduled to undergo an ALND.

Exclusion Criteria:

Patients with a clinically negative axilla undergoing sentinel lymph node biopsy were excluded from enrollment, prior ipsilateral axillary surgery, prior ipsilateral axillary radiation, prior ipsilateral breast radiation, allergy to isosulfan blue dye, history of ipsilateral upper extremity lymphedema, prior history of surgical excision of the upper outer quadrant of the ipsilateral breast, prior history of neoadjuvant chemotherapy for current breast cancer and bulky axillary disease at presentation.

3. Results

Fifty female pateints with age range (46.5) years, diagnosed as breast cancer were included in this study in the period between December 2010 and March 2012.

The following tables show the results of our study according to clinical stage, method of diagnosis of primary tumor, breast surgery, histology, Neoadjuvant treatment**,** positivity and negativity of ARM lymph node, success and failure of mapping and complications(Tables 1-3).

Table (1) Details of The Study:

Characteristics	No. of patients	Percentage
Clinical stage		
II	40	80%
III	10	20%
Methods of diagnosis of patients with primary tumor		
FNA	40	80%
Excisional biopsy	8	16%
Frozen section	2	4%
Histology		
Ductal	46	92%
Lobular	3	6%
Papillary	1	2%
ARM lymph node		
Positive (in identified cases)	4	8%
Negative(in identified cases)	30	60%
Neoadjuvant treatment		
Chemotherapy	10	20%
None	40	80%
Breast surgery		
Mastectomy	25	50%
Wide local excision	20	40%
Quadrantectomy	5	10%

Table(2): Results of lymphatic mapping(ARM) in 50 patients with breast cancer

Results of mapping	Number of cases	Percentage
Successful identification of blue Lymphatics and/or lymph nodes In ARM procedure	34	68%
Failure of identification of blue Lymphatics and/or lymph nodes in ARM procedure	16	32%

Table(3): Complications which recorded in our study.

Complications	Number of cases	Percentage
Seroma	5	10%
Wound infection	2	4%
Scar formation	1	2%
Tattooing	2	4%
lymphedema	0	0%
Nerve injury	0	0%

4. Discussion

Approximately 30% of patients diagnosed with breast cancer will present with regional lymph node metastasis. For these patients, complete levels I and II axillary lymph node dissection remains the standard of cure. However, this operation is associated with significant morbidity, the most functionally debilitating of which is lymphedema. Lymphedema is reported to occur in 20% to 50% of patients undergoing axillary lymph node dissection and is believed to result from disruption of the lymphatic drainage of the arm as it enters into the axilla[9].

Axillary reverse mapping (ARM) is a novel technique to preserve upper extremity lymphatics that may reduce the incidence of lymphedema after axillary lymph node dissection. Early reports have suggested that ARM lymph nodes do not contain metastatic disease from breast cancer; however, these studies were conducted in early stage patients with low likelihood of lymph node metastasis[10].

Variations in arm lymphatic drainage put the arm lymphatics at risk for disruption during axillary lymph node surgery. Mapping the drainage of the arm with blue dye (axillary reverse mapping, ARM) decreases the likelihood of disruption of lymphatics and subsequent lymphedema[11]. The average time between blue dye injection and axillary exposure was 35 minutes (range, 15-60 minutes). Blue lymphatics were identified in 21 patients (70%) and blue lymph nodes in 15 patients (50%)[10].

In 11 of 18 ALNDs (61%) blue lymphatics or blue nodes were identified in the axilla. In the initial seven cases with positive lymph nodes in the axilla, the blue node draining from the arm was biopsied and all were negative[11]. During ALND, the blue lymphatics draining the arm were visible in 8 out of 9 patients (88.9%). All ARM blue nodes removed during ALND were negative for malignancy. At 9-months follow-up, no patient had lymphedema[12].

In our study the average time between blue dye injection and axillary exposure was 30 minutes (range, 10-50 minutes). Blue lymphatics and/or lymph nodes were identified in 34 patients (68%) and failed in16 patients(32%) and 10 patients(20%) went on to receive neoadjuvant chemotherapy.

Initial studies showed that no cancer cells were found in the ARM nodes even when the patients had many positive axillary nodes Subsequently, they preserved the axillary reverse mapping nodes in patients in the later series [13]. It is important to confirm that the ARM nodes are not involved with metastatic foci, even in patients at high risk of axillary nodal involvement. Nevertheless, 3 of 21 patients (14%) in a study by Nos *et al.* showed metastatic involvement of the ARM sampling, although the ARM nodes had no metastatic involvement in the remaining 18 patients[14].

In current study the number of ARM lymph nodes histological negative 30 patients (60%) and positive in 4 patients (8%). There were no intraoperative complications noted to be related to the use of isosulfan blue dye or the ARM technique. Postoperatively, all patients returned to the surgery clinic within a 3-week for reassessment. Two patients (4%) were noted to have persistence of mild blue dye staining at the site of blue dye injection.

To minimize prolonged seroma and prevent arm lymphedema, on the other hand, *Kodama* routinely performed lower axillary dissection without using either axillary reverse mapping or sentinel lymph node biopsy. The lower axillary dissection is defined

as dissecting axillary lymph nodes only below the second intercostal brachial nerve[15].

To improve the identification rate of the axillary reverse mapping nodes and to prevent a persistent blue stain at the site of injection, Nos *et al;* injected an isotope into the web space of the ipsilateral hand. During axillary lymph node dissection, the radioactive axillary reverse mapping node was localized above the second intercostal brachial nerve, and then blue dye was injected directly into the node to visualize the efferent ducts constituting the lymphatic axillary reverse mapping chain[6].

Thus, radioisotope labeling seems to be more sensitive for detecting axillary reverse mapping nodes than use of blue dye alone. Identification rates of axillary reverse mapping nodes were improved by using radioisotope with or without blue dye [16].

However, radioisotope alone does not permit the visual mapping of axillary reverse mapping lymphatics [6].

It is important to point out that the proposed technique of ARM, even if oncologically safe, has not been rigorously tested to determine whether its adoption would reduce rates of lymphedema. Cadaveric studies suggest that lymphatic drainage from the upper extremity drains into a dominant sentry lymph node in the axilla [7].

If this is the case, and if this dominant lymph node often overlaps with breast lymphatic drainage, as is suggested by some of the sentinel lymph node concordance data, then it appears unlikely that the ARM technique will reduce the likelihood of upper extremity lymphedema. In an adaptation of the ARM procedure, Boccardo *et al.,* have described a microsurgical technique in which disrupted ARM lymphatics are anastamosed to venous tributaries draining into the axillary vein [17].

It is not always possible to preserve ARM nodes and/or lymphatics during axillary lymph node dissection or sentinel lymph node biopsy. Therefore, Casabona *et al.* performed microsurgical lymphatic-venous anastomosis using lymphatic collectors coming from the arm and one of the collateral branches of the axillary vein [12].

Lymphatic collectors were introduced inside the vein and the inferior edge of the lymphatics introduced into the vein lumen acted as valves to avoid backflow of blood into the lymphatics, thus preventing the occurrence of thrombosis. In fact, lymphatic microsurgery techniques have been shown to be effective in the treatment of peripheral lymphedema [18].

5. Conclusions

The axillary reverse mapping procedure is not completely accurate in differentiating between the arm and breast lymphatic pathways. The ARM node is involved with metastatic foci in some patients with extensive axillary lymph node metastasis. It is oncologically unacceptable to preserve a metastatic axillary reverse mapping node in axillary lymph node dissection. Further studies are needed before this technology can be accepted as a standard procedure in the surgical management of breast cancer. On the other hand, it is not always possible to preserve ARM nodes and/or lymphatics during axillary lymph node dissection. Therefore, microsurgical lymphatic-venous anastomosis may be effective for prevention of arm lymphedema in patients who underwent axillary lymph node dissection with removal of axillary reverse mapping nodes. long-term follow-up studies are required before we can conclude that this microsurgical technique is effective to prevent arm lymphedema. Therefore, further studies are needed to determine whether the ARM technique can prevent arm lymphedema during ALND.

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