Lymphatic Microsurgical Preventing Healing Approach (LYMPHA) for Prevention of Breast Cancer-Related Lymphedema—a Preliminary Report

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ORIGINAL ARTICLE

Lymphatic Microsurgical Preventing Healing Approach (LYMPHA) for Prevention of Breast Cancer-Related Lymphedema—a Preliminary Report

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Abstract
Lymphatic microsurgical preventing healing approach (LYMPHA) for prevention of breast cancer-related lymphedema (BCRL)—a preliminary report BCRL—is a chronic debilitating condition which impairs quality of life of breast cancer survivors. The aim is to study the feasibility of preventing lymphedema by performing "Lymphatic Microsurgical Preventive Healing Approach (LYMPHA)." Patients undergoing breast cancer surgery with complete nodal dissection were taken up for the study. After the standard axillary nodal dissection, lymphatics were identified by the help of blue dye and were anastomosed with a tributary to the axillary vein. Post-operatively, patients were followed up clinically for development of lymphedema and lymphoscintigraphy was performed after treatment completion. A total of 35 patients were enrolled for the study. The average BMI was 29.5. LYMPHA was feasible in all cases. The number of lymphatics identified was 1 to 5 per axilla. Two patients developed transient lymphedema which resolved with conservative therapy and patients were able to discontinue the compression garment. Follow-up lymphoscintigraphy is performed in two patients, which showed normal lymphatic flow. LYMPHA is a feasible technique, not difficult to perform, takes a short time, is accomplished in same general anesthesia as for axillary dissection, and gives no extra scar. The early results are promising and long-term follow-up may make the procedure as a routine.

Keywords Lymphovenous anastomosis · Microsurgery · Axillary lymph node dissection · Breast cancer · Secondary lymphedema

Introduction

Breast cancer-related lymphedema (BCRL) is emerging as a common and very debilitating sequel of treatment for breast cancer, more so with the increase in breast cancer survivorship [1]. It causes functional, cosmetic, and psychological problems leading to a negative impact on overall quality of life [2, 3]. In a recent review published in Lancet Oncology, it is estimated that more than one woman in five who survive breast cancer has a chance of developing breast cancer-related lymphedema [4].

With high incidence of breast cancer in India and more patients presenting with node-positive disease, complete axillary dissection becomes a common practice. This directly poses women to higher risk of developing BCRL. If it can be prevented during the primary surgery, a lifelong morbidity in the form of lymphedema can be avoided.

The current study is designed to prevent BCRL by doing microsurgical lymphovenous anastomosis at the time of axillary dissection. This technique was first described by Boccardo et al. in 2009 [5], and later he conducted a randomized controlled trial in 49 patients and has a follow-up period of 18 months. The incidence of lymphedema in the study group was 4.34% [6].

This is a report on the feasibility of the technique and its early outcome in Indian patients at a single center. The literature search did not show any previous study from the Indian sub-continent so the authors believe that it is first of its kind.

This study reports about feasibility of preventive microsurgical lymphovenous anastomosis in the axilla at the time of axillary dissection for breast cancer. The early results of this procedure are encouraging.

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Methods

Patients with breast cancer undergoing planned axillary dissection with or without mastectomy were selected for the study and offered LYMPHA. Patients with locally advanced breast cancer who have received neo-adjuvant chemotherapy and then planned for modified radical mastectomy (MRM) were also included in the study. Exclusion criteria were sentinel lymph node biopsy, previous surgery to the axilla, pregnancy, allergy to iso-sulfan blue dye, and patients undergoing MRM along with any other surgery at the same time.

Pre-operatively, an informed consent was obtained from all the patients and the study was approved by the institutional review board of the hospital. All patients had their limb circumference measured at 4-cm intervals and compared with opposite side. Lymphoscintigraphy was not performed before surgery.

Under general anesthesia, modified radical mastectomy or breast conservation surgery with complete axillary dissection was performed by the onco-surgeon in the routine manner except preservation of a long segment of a tributary to the axillary vein in the axilla. After the specimen is taken out, axillary lavage with normal saline is done.

The iso-sulfan blue dye is then injected on the medial aspect of the upper arm, approximately 5 cm lateral to the axillary hair line. Around 2 ml of the dye is given at three spots; at each spot, the dye is given at three levels; intradermally, subcutaneously, and sub-fascially (Fig. 1). The vein preserved is then prepared for the anastomosis and backflow of blood is observed from the cut end of the vein. The chosen vein should not have any backflow of the blood which ensures a long-term patency of the lymphovenous anastomosis. The mere anatomical presence of a proximal valve does not ensure its competence. If there is no backflow of blood from cut end and saline can be easily injected into the vein, the proximal valve competence is confirmed. If backflow of the blood is seen, external valvuloplasty of the valve is performed. Sometimes, in spite of external valvuloplasty, the direct tributary to the axillary vein still shows backflow. In such cases, one of the venae-commitantes of the thoracodorsal branch supplying the serratus anterior muscle is used. These veins have consistently shown to have a good patent proximal valve.

The lymphatics are visualized, around 5–10 min after the injection and blue dye is occasionally seen oozing out in the axilla (Fig. 2). The visualized lymphatics are dissected keeping a thin layer of adipose tissue around them and clipped distally. In cases where lymphatics are visualized scattered around the area and a single pedicle is difficult to be developed for anastomosis, the larger ones and ones which can be clustered together are used for anastomosis. In few cases, one bundle of lymphatics is anastomosed to the main vein and other smaller bundle is anastomosed to a branch of the same vein, both by the technique described below.

The anastomosis technique followed is as described by Campisi et al. [7] where multiple lymphatics are telescoped into a large vein by the help of a "U" stitch. Then, the vein is sutured with the adipose tissue around the lymphatics by the help of 6–8 stitches and then the "U" stitch is removed (Fig. 3). Passage of blue dye in the vein confirms the patency of the anastomosis (Supplementary material –Video 1).

Fig. 1 The site of blue dye injection

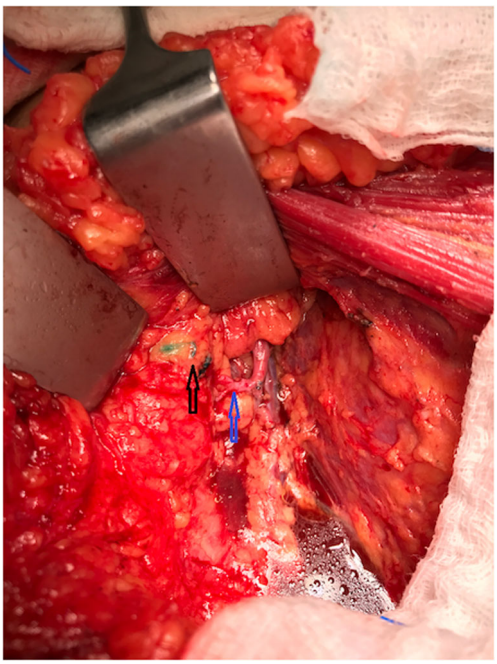

Fig. 2 Vein with no backflow (blue arrow) and dye-stained lymphatics to be anastomosed (black arrow)

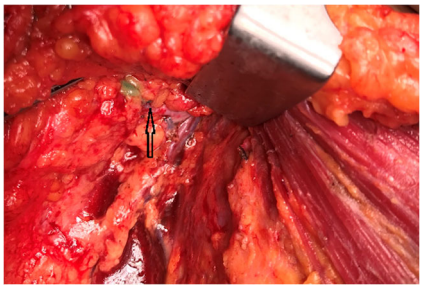

Fig. 3 Completion of anastomosis

A suction drain is inserted into the axilla and wound is closed in layers. Routine post-operative protocol for wound care, drain care, and physiotherapy is followed.

The variables studied include age, stage of disease, BMI, neo-adjuvant chemotherapy (CT), number of nodes excised, number of lymphatics identified, time duration for the procedure, adjuvant CT, and radiotherapy (RT).

Patients are followed up for the appearance of arm swelling and duration. Lymphoscintigraphy is performed post-operatively after completion of adjuvant treatment (CT and/or RT).

Results

A total of 35 patients were taken up for LYMPHA surgery during axillary dissection from December 2016 to November 2017. The mean age of the patients was 54.31 years (range 33 to 74 years). Body mass index (BMI) ranged from 17.7 to 41.27 (average 29.5). Seventeen patients had right sided disease, 16 had left side breast cancer and 2 had bilateral disease where LYMPHA were performed on one side only. Fourteen out of 35 patients received neo-adjuvant chemotherapy. The stage wise distribution of the patients is given in Tables 1 and 2.

All patients underwent complete axillary nodal dissection (level I, II, and III). LYMPHA was feasible in all the patients. Two milliliters of iso-sulfan blue dye (0.1%) was injected approximately 5 cm lateral to the axillary hair line. The dye was injected in sub-facial, sub-cutaneous, and intradermal planes at three points separated by each other by 2 cm vertically. The average duration of time from injecting and visualizing the lymphatics was 12.75 min (range 5–30 min). It took 53.28 min on an average (range 30 to 100 min) to complete the procedure. The time taken was more in the first six cases and it reduced to 30–40 min in the subsequent cases. The suture used was either 8-0 or 9-0 ethilon. The number of lymphatics identified was ranging from 1 to 5 (average 2.67). The total number of lymph nodes removed was 08–47 (average 20.15).

Table 1 Stage distribution of the patients taken up for upfront surgery

	Tx*	T1	T2	T3	T4
N0	3	1	6	2	0
N1	0	1	6	0	0
N2	0	0	2	0	0
N3	0	0	0	0	0

*Tx denotes post-lumpectomy status with no residual tumor seen on final histopathology

Table 2 Stage distribution of the patients who received neo-adjuvant chemotherapy

	T1	T2	T3	T4
N0	0	0	0	0
N1	0	3	0	4
N2	0	2	0	1
N3	1	1	1	1

Twenty four patients out of 35 received or are receiving Taxane-based CT, 2 patients are receiving Herceptin only, and 1 is taking oral hormonal therapy only. Three patients are lost to follow-up. Ten patients are undergoing adjuvant RT.

All patients are under three monthly follow-ups, and treatment is completed for 8 patients. Lymphoscintigraphy is performed for two patients and shows normal lymphatic flow in the ipsilateral arm, absence of ipsilateral axillary lymph nodes, and early visualization of the liver. Two patients had developed transient lymphedema which was managed with compression sleeves (class II) for continuous use, and the swelling subsided in 2 months for the first one and 1 month for the second one. The first patient is compression sleeve free for 5 months and the second one for one month. No other patients developed arm edema till date. Follow-up lymphoscintigraphy scans for the rest of the patients are awaited.

Discussion

The incidence of BCRL varies widely in the literature. The prevalence of breast cancer-related lymphedema in patients undergoing complete axillary lymph node dissection varies from 6 to 50%, and its incidence ranges from 0 to 22% [1, 2, 4, 8–10].

The risk factors for BCRL are not limited to surgery. Radiotherapy, taxane-based chemotherapy, and obesity (BMI ≥ 30 kg/m^2) also predispose the patient to lymphedema. The incidence of BCRL is four times higher in patients undergoing complete axillary clearance when compared with sentinel lymph node biopsy alone (19.9 vs 5.6%) [4]. Hence, it is directly proportional to extent of axillary lymph nodal clearance.

BCRL is one of the most dreaded complications of breast cancer treatment. The cancer survivors suffering from lymphedema have low quality of life, reduced mobility, low self-esteem, and high risk of infections [11–14]. Curing lymphedema is difficult and till date, there is no single widely accepted method to cure lymphedema with complete success. Lymphovenous anastomosis by microsurgery or super-microsurgery, vascular lymph node transfers, stem cell therapy, etc. are newer methods in the armamentarium, but none is able completely bring back the limb volume in all patients [14].

Lymphadenectomy is the single most important risk factor for developing BCRL [3, 4, 9]. Prevention of lymphedema is better as it is known that once occurred, lymphedema is incurable. Boccardo et al. have proposed the method of performing pre-emptive lymphatic by-pass at the time of axillary dissection where the lymphatics draining arm are anastomosed with a vein in axilla [5]. This technique is named LYMPHA (lymphatic microsurgical preventing healing approach). Boccardo et al. performed a randomized controlled trial and was conducted in 49 patients and has a follow-up period of 18 months [6]. The incidence of lymphedema in the study group was 4.34% and that in the control group was 30.43% which was found to be statistically significant. The further 4-years' follow-up was reported by the same investigator in 74 patients where only three patients developed lymphedema. [15]. The same technique was performed by Feldman et al. at another institute and showed similar results as claimed by Boccardo et al. [16].

The advantages of this procedure are its short procedure time, needs no extra incision, performed in same general anesthesia which is given for modified radical mastectomy, and does not add much to the cost. Rescuing divided lymphatics at the site of injury by performing lymphovenous anastomosis is the most physiological way to reconstruct the damage.

In the current study is a pilot project where LYMPHA is performed for lymphedema prevention in Indian patients with a slight modification as originally described by Boccardo et al. The aim of the present report is to assess feasibility of LYMPHA. It was found to be feasible in all patients and early outcome, i.e., 6 months follow-up of patients showed that only one patient developed ongoing lymphedema. One patient developed transient lymphedema which subsided in a 2-month period with compression stocking.

Conclusion

Prevention is better than cure and more so when the disease is considered incurable once occurred. By performing microsurgical multiple lymphovenous anastomosis after axillary dissection, prevention of lymphedema is attempted. This pilot project proves the feasibility of this technique, and the early outcomes are encouraging. More multi-centric randomized controlled trial including more number of patients with longer follow-up is needed to prove its efficacy and to be included as a standard treatment protocol during axillary dissection.

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Compliance with Ethical Standards

The authors declare that they have no conflict of interest.

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