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LYMPHOSCINTIGRAPHIC FINDINGS THAT PREDICT FAVORABLE OUTCOME AFTER LYMPHATICOVENOUS ANASTOMOSIS

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ABSTRACT

Radionuclide lymphoscintigraphy is an imaging technique used to radiologically evaluate the lymphatic system which can be utilized to evaluate signs of lymphatic obstruction that could be indication for lymphaticovenous anastomosis (LVA) operations. Our objective was to investigate and identify the radiographic signs in lymphoscinigraphy that predict favorable outcome after LVA. We retrospectively reviewed the medical charts of 80 patients with upper or lower-limb lymphedema who underwent initial lymphoscintigraphy before LVA during the 2011 to 2014 study period to evaluate statistical association between lymphoscintigraphic findings and the clinical result after LVA. Following LVA, clinical improvement was observed in 50 patients (48 female and 2 male) with no clinical improvement evident in the remaining 1 male and 29 females. Dilated lymph vessels and dermal backflow were identified as the abnormal finding in lymphoscintigraphy that were significantly correlated with improved clinical result after LVA. Our conclusion is that radionuclide lymphoscintigraphy prior to LVA is helpful in identifying patients for whom LVA is of benefit. Based on our findings, presence of dilated lymph vessels and presence of dermal backflow are significantly correlated with improved clinical result after LVA.

Keywords: Radionuclide lymphoscintigraphy, lymphaticovenous anastomosis, LVA, lymphatic obstruction, success predictors

Radionuclide lymphoscintigraphy is an imaging technique used to radiologically evaluate the lymphatic system. This functional test is a minimally invasive procedure requiring a simple intradermal or subcutaneous injection of a radiolabeled tracer. The safety and ease-of-performance of this method has largely replaced the more invasive and technically more difficult technique of lymphangiography. Although image resolution is generally low in lymphoscintigraphy, patients with normal lymphatic anatomy and function will exhibit symmetrical transport of radiotracer through 3-5 discrete lymph vessels per calf, 1-2 vessels per thigh, and symmetrical uptake within proximal lymph nodes bilaterally within 30 minutes. When lymphatic obstruction is detected by lymphoscintigraphy, changes including delayed or asymmetric isotope distribution in lymphatic vessels, delayed lymph node visualization, and/or reduced number or absent lymph nodes. Interruptions in lymph flow, dilated lymph vessels, presence of collateral circulation, and sites of abnormal accumulation (e.g., dermal back flow) can also be visible. In cases of severe damage, the lymphatic system may not be visualized at all on lymphoscintigraphy (1,2).

Lymphaticovenous anastomosis (LVA) aims to alleviate lymphedema by delivering lymphatic fluid directly into the venous system. The main objectives of treatment in patients with lymphedema are to prevent progression of the disease, to achieve mechanical reduction and maintenance of limb size, to alleviate symptoms arising from lymphedema, and to prevent skin infection. Indications for LVA include insufficient lymphedema reduction by well-performed medical and physical therapy, recurrent episodes of lymphangitis, intractable pain, worsening limb function, patient dissatisfaction with the results obtained by non-operative methods, and willingness to proceed with surgical options. Few studies have clearly examined the imaging finding criteria that could define indications for lymphaticovenous anastomosis.

The aim of this study was to investigate and identify the radiographic signs on lymphoscintigraphy that predict favorable outcome after LVA.

MATERIALS AND METHODS

This retrospectively study reviewed the medical chart of 102 consecutive patients with upper or lower limb lymphedema who underwent initial lymphoscintigraphy before LVA during the 2011 to 2014 study peroid. Twenty two of those patients were excluded due to loss to follow up, incomplete medical records, or LVA performed at another hospital. The remaining 80 patients were included. Mean age of patients was 59.5 years (range, 12-72) and the vast majority were female (77/80). Female patients exceeded males due to most being secondary to breast and gynecological cancer leading to upper and lower extremity edema respectfully. All included patients underwent LVA at Siriraj Hospital-Thailand's largest university-base tertiary referral center and the study was approved by the Siriraj Institutional Review Board.

The radiopharmaceutical used in this study was Tc-99m dextran (in-house preparation). All patients were subcutaneously injected in the bilateral webs between the first and second fingers or toes with 37 MBq (1 mCi) of Tc-99m dextran per site, After injection, patients were asked to exercise or massage the site of injection to accelerate uptake of particles into the lymphatic system. Whole body imaging acquisition were obtained at early, 15-minute, 30-minute, 45-minute, 1- hour and 4-hours following administration of the tracer.

The following normal and abnormal features of the lymphatic system were recorded in each qualitative lymphoscintigraphic study:

1. Presence or absence of collateral lymph vessels
2. Presence or absence of dilated lymph vessels
3. Presence or absence of lymph node activity on 4-hour image (reflecting lower limb lymphatic transport capacity)
4. Presence or absence of "dermal backflow" or dermal collateral flow (reflecting the degree of lymphostasis)
5. Presence or absence of normal main lymphatic channel

Postoperative LVA evaluation criteria indicating improvement included softer extremity, decreased circumference, change from heavy to dull feeling of the limb, and absence of cellulitis.

Statistical Analysis

Correlation between abnormal finding by lymphoscintigraphy and clinical improvement after LVA were analyzed using the Pearson's Chi-Square test. Data were analyzed using SPSS statistics version 16.0 (SPSS, Inc., Chicago, IL, USA). A p-value less than 0.05 was considered statistically significant.

RESULTS

TABLE 1
Association Between Lymphoscintigraphic Findings (Collateral Lymph Vessels, Dilated Lymph Vessels, Lymph Node Activity, Dermal Backflow, Main Lymph Vessel) and Clinical Result

Lymphoscintigraphic finding		Clinical result		Total
		Improved	Not improved	
Collateral lymph vessels	Yes	12	4	16
	No	38	26	64
Dilated lymph vessels	Yes	17	4	21
	No	33	26	59
Lymph node activity	Yes	3	4	7
	No	47	26	73
Dermal backflow	Yes	42	19	61
	No	8	11	19
Main lymph vessel	Yes	44	27	71
	No	6	3	9

TABLE 2
Statistical Associations Between Lymphoscintigraphic Findings and Clinical Result

Lymphoscintigraphy finding	p-value for improved clinical result
Collateral lymph vessels	0.248
Dilated lymph vessels	0.042
Lymph node activity	1.0
Dermal backflow	0.035
Present of main lymph vessel	0.784

After LVA, clinical improvement was observed in 50 patients (48 female and 2 male patients). Associations between collateral lymph vessels, dilated lymph vessels, lymph node activity, dermal backflow, and presence of main lymph vessel with clinical outcome after LVA are described individually and collectively in *Table 1*. Statistical association between lymphoscintigraphy findings and clinical result is presented in *Table 2*.

Dilated lymph vessels and dermal backflow were the abnormal findings on lymphoscintigraphy that were significantly correlated with improved clinical result after LVA. Examples of lymphoscintigraphic images in lower and upper extremity lymphatic obstruction before and after LVA with clinical results are presented in *Figs. 1-4.*

DISCUSSION

Lymphoscintigraphy was shown to be a suitable method for identifying patent lymph channels before surgery and for determining function of LVA after operation (3).

There are few studies of lymphoscintigraphic findings used to predict the clinical outcome of subsequent LVA results. Vaqueiro et al (4) reported the value of lymphoscintigraphy in the selection of patients for LVA by demonstrating the patency of major lymph channels suitable for anastomoses, which could not be predicted on clinical grounds. A study by Mikami et al (5) revealed that type II and type III lymphedema are the most likely indications for microscope-assisted LVA. Type II is characterized by mild lymphatic obstruction, and signs of dermal back flow appear in the upper arm on images taken 30 min and/or 120 min after injection. Type III is characterized by significant lymphatic obstruction, and signs of dermal backflow appear in the upper arm and forearm on images taken 30 min and/or 120 min after injection.

Lee and Bergan (6) reported the utility

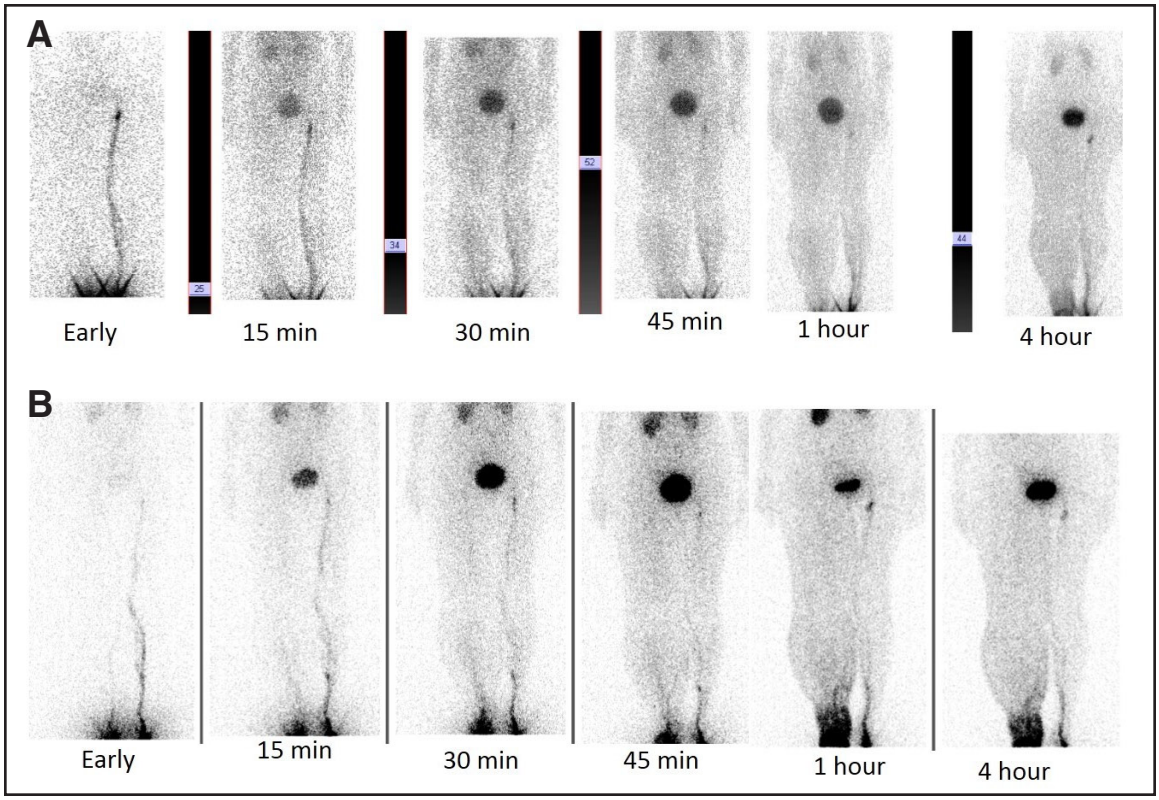

Fig. 1. A 62-year-old female who underwent surgery and radiotherapy for cervical cancer 10 years earlier presented with lymphedema of right leg. Before LVA: (A) non-visualization of main lymph vessel, dilated lymph vessel, collateral lymph vessel, inguinal lymph node, and dermal backflow of the right leg. The left leg demonstrates normal lymphatic drainage. After LVA: (B) no change in the right leg relative to pre-LVA, indicating no improvement.

of lymphoscintigraphy for prediction of the outcome of treatment. They devised a staging system based on lymphoscintigraphic findings in relation to clinical staging, which includes a simple quality-of-life measure to predict treatment outcome and to help decide when additional medical or surgical therapy is indicated. Some cases in this current study were not graded by Lee and Bergan staging so we decided to study the association between presence or absence of lymphoscintigraphic findings and outcome of LVA. The specific findings studied were presence or absence of collateral lymph vessels, dilated lymph vessels, lymph node activity, dermal backflow, and main lymphatic vessel. Based on our findings, presence of dilated lymph vessels and presence of dermal backflow are significantly correlation with improved clinical result after LVA.

A study in quantitative lymphoscintigraphy by Vaqueiro et al (7) reported that the rate of dispersion of colloid from the injection site varied between normal and abnormal limbs and showed significant overlap with the normal range. The results of their quantitative studies were not helpful in the diagnosis of lymphedema nor in the selection of patients for operation.

Lymph is propagated in the extremities by muscle movement, with backflow prevented by valves, similar to the backflow mechanism in the venous system. Quantification of lymphatic flow is therefore extremely sensitive to muscle movement during lymphoscintigraphic study. If muscle

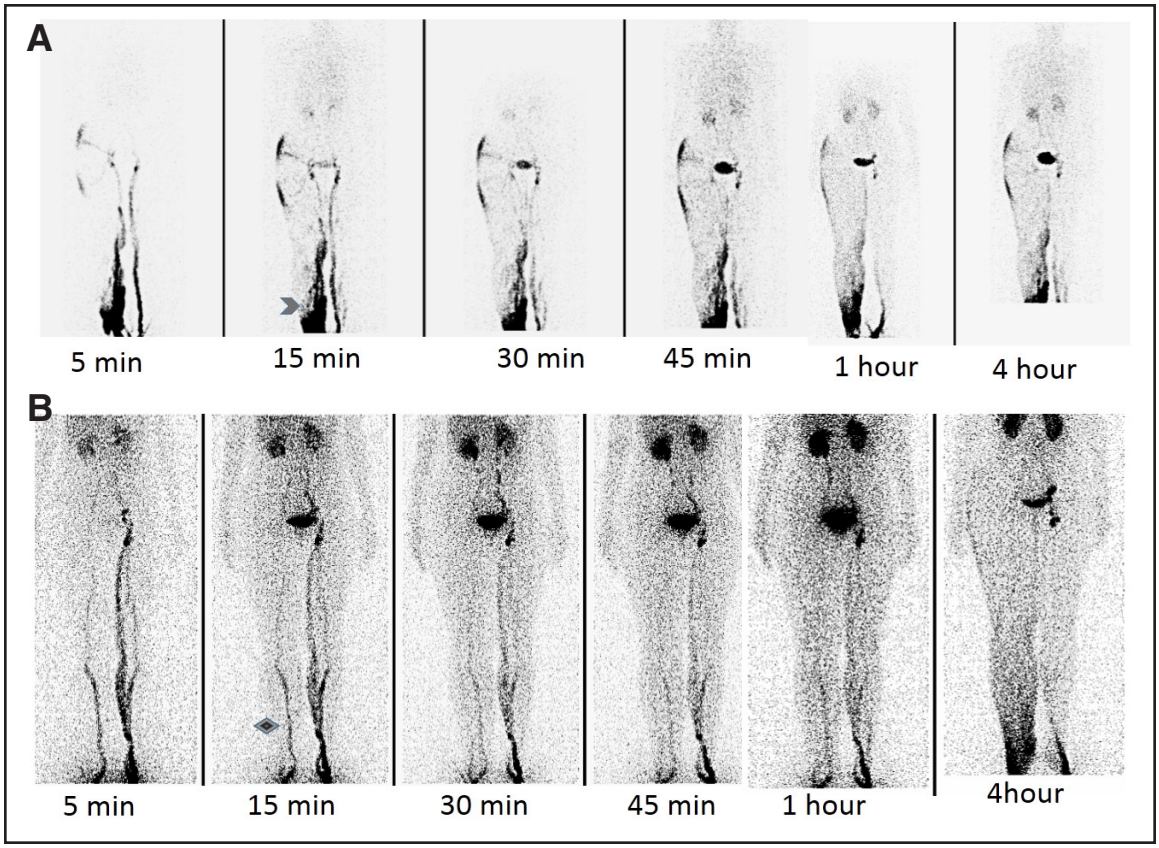

Fig. 2. A 55-year-old female who underwent radical hysterectomy for cervical cancer 19 years earlier who developed chronic progressive edema of right leg was evaluated for lymphedema. Before LVA: (A) reveals lymph vessel dilatation (arrow head) in right leg. After LVA: (B) presence of main lymph vessel (diamond) and improvement in lymph vessel dilatation, both of which indicated improvement.

movement is not controlled and managed according to a standardized guideline, it is difficult to quantitatively and reliably interpret clearance data (2,7). A previous study (8) in ten healthy volunteers who were examined by lymphoscintigraphy without standardized muscular exercise found an uptake range of 83 to 731 count per second. When studied using standardized exercise, the range of colloid uptake in the same volunteers decreased to 273-417 count per second.

Lymphofluoroscopic imaging is a relatively new, mainly two-dimensional imaging technique that provides information on the superficial lymphatic system. Three abnormal dermal backflow patterns are splash, stardust, or diffuse pattern indication of lymphedema (9-12). The most important finding for diagnosis of lymphedema is dermal backflow of lymph from collecting lymph vessels to the skin surface and tissue. A definitive diagnosis may be made by ICG lymphography and lymphoscintigraphy because dermal backflow is observed as an abnormality of the lymph vascular system (13).

A study (14) comparing the utility of lymphofluoroscopic with gold standard lymphoscintigraphy for patients with suspected extremity lymphedema revealed sensitivity and negative predictive value of

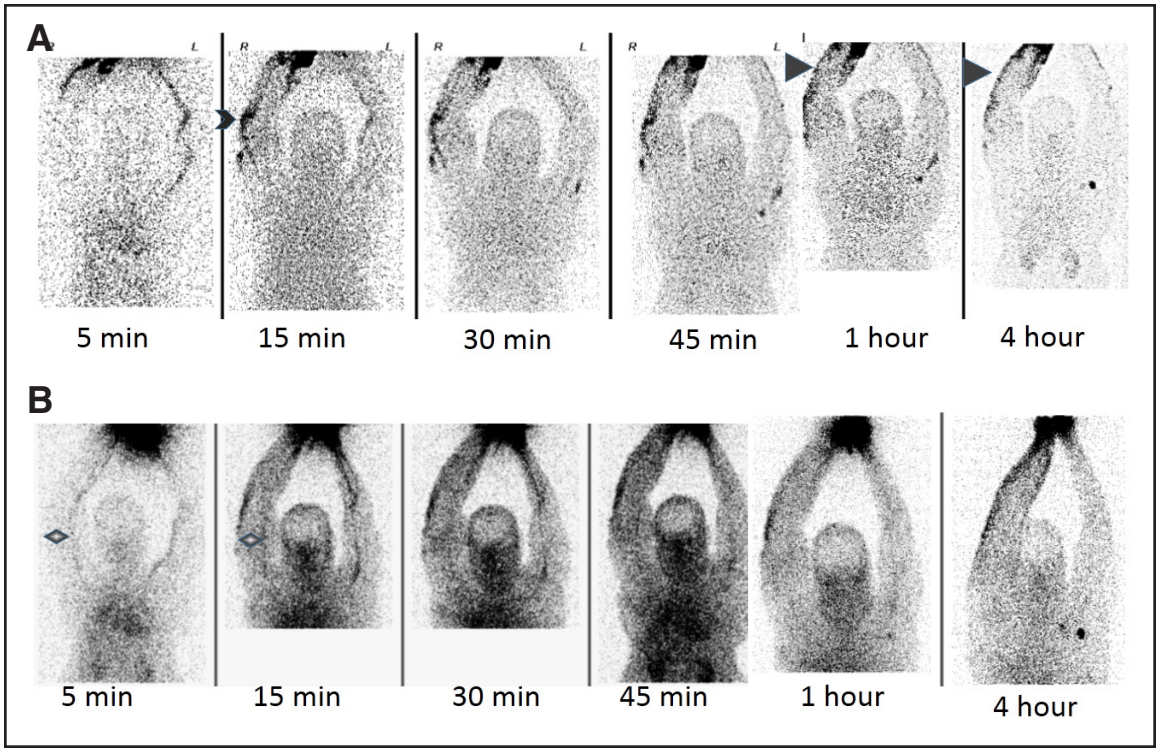

Fig. 3. A 65 year-old female who underwent surgery for cancer of right breast and presented with lymphatic obstruction in the right arm. Before LVA: (A) reveals lymph vessel dilatation (arrow head) and delayed dermal backflow (triangle) of right arm. After LVA: (B) shows faint main lymph vessel (diamond) and improvement in lymph vessel dilatation and dermal backflow indicating improvement in lymphatic obstruction.

lymphofluoroscopy were very high. However, the specificity and positive predictor value were not very high, as a number of limbs were positive by lymphofluoroscopy but negative by lymphoscintigraphy. This is likely due to the superficial characteristics of lymphofluoroscopy compared to images of the deeper system in lymphoscintigraphy.

In patients with secondary lymphedema, earlier and less severe dysfunction may be detected by lymphofluoroscopy than by the lymphoscintigraphy as a splash pattern; however, both examinations are equally useful in determining disease severity and whether patients are suitable for surgical treatment. Lymphofluoroscopy has some advantages over lymphoscintigraphy, including its lack of radiation exposure, less invasive nature, and lower cost potential for real-time observation of lymph vessels during surgery. One disadvantage is that morbidly obese patients cannot be evaluated well by this method because it is impossible to observe lymphatic vessels located more than 2 cm deep in the subcutaneous tissue. Lymphoscintigraphy is more useful to determine the location of lymphatics more than 2 cm deep and to confirm the existence and location of a lymphocyst in the deep subcutaneous tissue or the pelvic cavity. In addition, the combination of lymphoscintigraphy with single-photon emission computed tomography (SPECT-CT) can provide more detailed information about the location of the lymphatic vessels and of the existence and location of lymphocysts not available to lymphofluoroscopy.

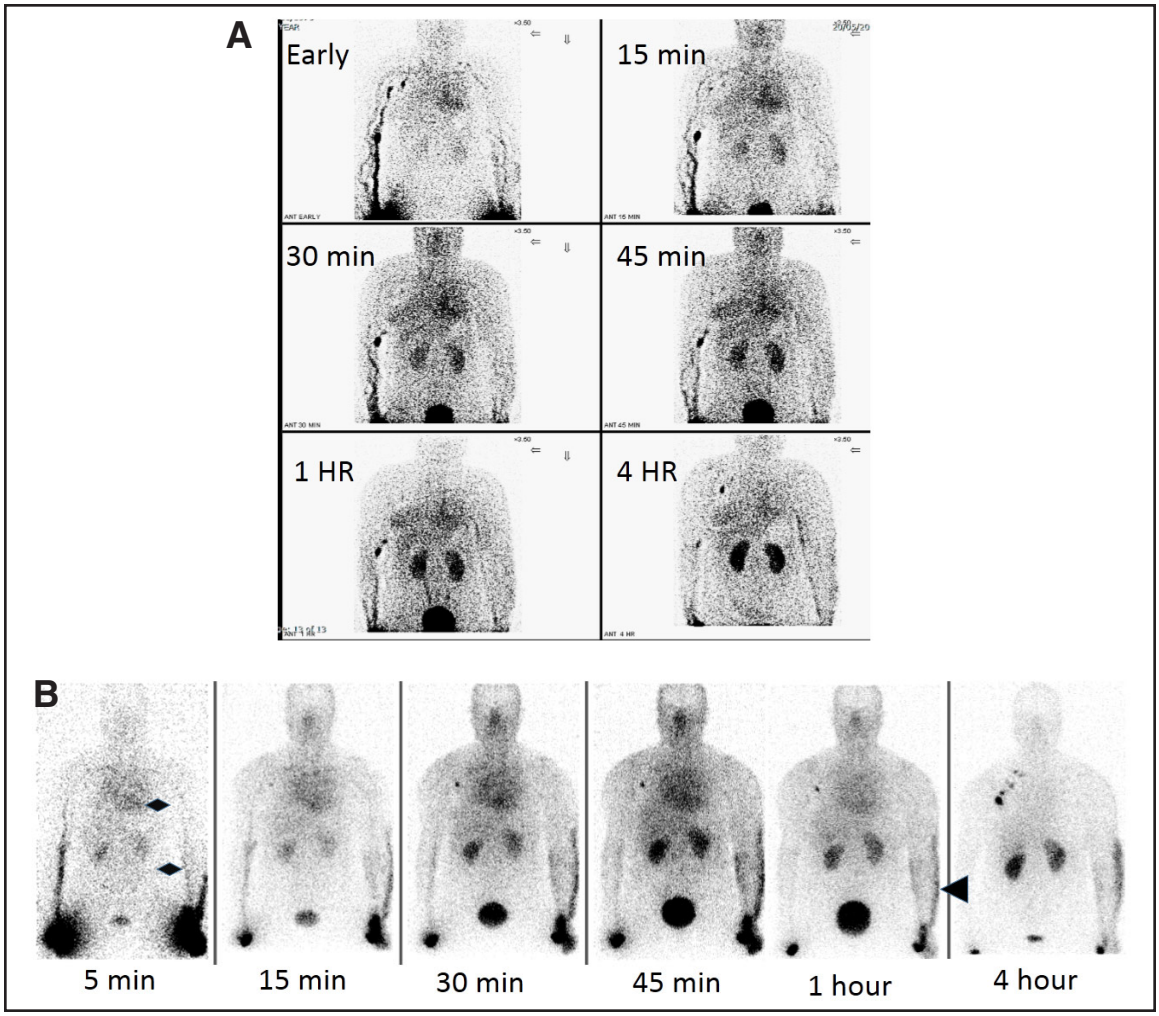

Fig. 4. A 48-year-old female who underwent modified radical mastectomy and complete systemic chemotherapy for cancer of left breast presented with swelling of her left arm. Lymphoscintigraphy before LVA: (A) reveals no activity in main lymph vessel in the left upper arm without dilated lymph vessel, collateral lymph vessel, activity in lymph node and delayed dermal backflow in the left arm. After LVA: (B) left arm shows faint activity in main lymph vessel in the lower arm and no activity in upper arm (diamond) without dilated lymph vessels, collateral lymph vessels or activity in lymph node. Presence of dermal backflow activity after LVA in lateral lower arm (triangle) indicates no improvement in lymphatic obstruction.

CONCLUSION

Radionuclide lymphoscintigraphy prior to LVA is helpful in identifying patients for whom LVA is indicated. Based on our findings, presence of dilated lymph vessels and presence of dermal backflow are significantly correlated with improved clinical result after LVA.

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