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ROLE OF MR LYMPHANGIOGRAPHY FOR EVALUATION OF LOWER LIMB LYMPHEDEMA

Radiology

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ABSTRACT

Aims and Objective - This study aimed to evaluate the feasibility of MR Lymphangiography in the visualization of the lymphatic system of the lower limbs in patients with lymphedema and to know the exact cause and extent of lymphedema for the treatment planning. **Materials and methods -** A total of 7 patients were included in the study. With strict aseptic precautions, a mixture of 10 ml gadolinium-based contrast agent (gadopentate dimeglumine) and 1ml lidocaine (1%), equally divided into 4 parts and injected intradermally into the dorsum of each interdigital web space. The T1 VIBE sequence and heavily T2 weighted 3D TSE sequences were used for the examination. The whole lower limb scanned in 3-4 parts and subsequently, all the parts were composed and viewed as a single image. **Results -** The cause of lymphedema was lymph nodal in two patients, lymphatic vessel origin in one patient, and both lymph nodal and lymphatic vessel origin in four patients. The lymph nodes not showing contrast enhancement were classified as non functional. The dermal backflow was seen in five patients **Conclusion** - MR Lymphangiography provides good morphological and functional information of both lymphatic vessels & lymph nodes. Therefore, it can be considered as a baseline investigation for the evaluation of lymphedema of the lower limb.

KEYWORDS

MR Lymphangiography, MIP, VRT, lymphedema, subcutaneous thickness, lymphatic vessels diameter

Introduction

Lower extremity lymphedema is one of the most common chronic diseases. It is estimated that up to 300 million people around the world are suffering from lymphedema [1]. Lymphatic filariasis, a major cause of lymphedema, is an important public health problem in India. Filariasis is endemic in 17 States and six Union Territories, with about 553 million people at risk of infection [2].

Lymphedema is a pathological condition of the lymphatic system that impedes and diminishes the lymphatic return which leads to interstitial accumulation of lymphatic fluid. Subsequently, there is inflammation, hypertrophy of adipose tissue, and finally fibrosis [3]. It causes significant physical and psychosocial morbidity in patients. Despite its epidemiological relevance, only a few professionals specialized in the management of lymphatic diseases [3][4].

Lymphedema can be classified as primary or secondary. Primary lymphedema is caused by defects in vascular morphogenesis during the embryogenesis and develops in lymphedema syndromes. Primary lymphedema syndromes almost exclusively involves the lower limbs [5][6]

Secondary lymphedema is caused by an acquired defect in the lymphatic system, frequently associated with malignancy, infection, obesity, and trauma. The most common cause of secondary lymphedema worldwide and in developing countries is filariasis. However, in developed countries, the most common causes of secondary lymphedema are neoplasms orsequelaeto treatment of neoplasm. In these cases, the disease can be secondary to obstruction from primary lymphoma or cancer metastases or develop after lymph node dissection and excision [4][7].
Magnetic Resonance Lymphangiography (MRL) is a less utilized diagnostic imaging method. Thus, we evaluated the feasibility of MR Lymphangiography in the visualization of the lymphatic system of lower limbs in patients with lymphedema.

Materials and methods

With due permission from the institutional ethics committee and after taking informed consent, 7 patients of both primary (idiopathic) and secondary lymphedema were included in the study. Those patients who had any ferromagnetic metallic implants, renal insufficiency, known allergic for MRI contrast agents and unwilling to participate refrained from the study.

MRI sequences

The study was conducted in a 3 tesla MRI machine equipped with high-performance gradient coils (Magnetom Skyra, Siemens). The 3D T1 VIBE sequence in the coronal (TR/TE- 10.5/4.9 ; FOV -360 x 688 ; matrix size -256 x 256) and axial plane (TR/TE- 3500/194-198 ; FOV - 351 x 351 ; matrix size -243 x 256), the 3D T2 TSE sequence in the coronal (TR/TE-3500/194-198 ; FOV -351 x 351 ; matrix size-243 x 256) and axial plane (TR/TE -3500/198 ; FOV- 351 x 351 matrix size - 243 x 256) in the pre-contrast phase and subsequently 3D T1 VIBE sequence with same settings was used for post-contrast and delayed phase.

Technique

First, the extent and distribution of the lymphedema were evaluated by plain MR scan in coronal and axial plane using a heavily T2 weighted 3D TSE sequence. 10 ml of MR contrast agent was mixed with 1ml lidocaine (1%). 2 ml of the mixture was injected intradermally in the dorsum of each interdigital webspace of foot, if both limbs were involved then the injection was given bilaterally followed by an immediate massage for 1-2 minutes (**Figure 1**). The technique of contrast injection in MRL is less invasive in comparison to lymphography as lymphatic vessels need not be cannulated, only blind intradermal injection is sufficient. Also, there is no exposure to ionizing radiation. Immediately after the massage, post-contrast scans were done using the T1 VIBE sequence starting from the foot upto the inguinal region divided into 3-4 parts, e.g. foot-ankle, calf-knee, knee-thigh, and thigh-hip. Subsequently, all parts were composed and viewed as a single image.

The maximum intensity projection (MIP) reconstruction and volume rendering techniques (VRT) applied to visualize lymphatic vessels, the extent of lymphedema, and subcutaneous thickness. The maximum value of subcutaneous thickness and diameter of lymphatic vessels was measured in each patient.

Image analysis

The qualitative assessment of the enhancement of lymphatic vessels, inguinal lymph nodes, and subcutaneous veins was done by using the source image, MIP, and VR techniques. Lymphatic vessels are characterized by their beaded appearance, size, and collaterals (Figure 2C,). An area of progressive dispersion of the contrast medium into the soft tissue was recognized as dermal backflow. The dermal backflow indicates the proximal obstruction of the draining lymphatic vessels (Figure 2C, 3A).

Results

A total of 7 patients (73.33% females, mean age 31 years; range 21-62

years) were included in the study. The number of primary and secondary lymphedema subjects was 5 (71.4%) and 2 (28.5%) respectively. The clinical staging was done based on the international society of lymphology [8]; According to which the subjects were categorised, one (14.2%) in stage 0; two (28.5%) in each stage I, stage II, and stage III. Most of our subjects had disease duration 5-10 years (42.8%) then 0-5 years (28.5%) duration groups. The mean duration of the disease was 10.7 years; however, subjects suffering from the disease varied from 1-30 years.Four (57.1%) subjects were having unilateral and three (42.8%) subjects were having bilateral lymphedema. The subcutaneous thickness and diameter of lymphatic vessels were examined in each patient. The mean subcutaneous thickness inlymphoedematous and normal limbs was 29.15 (SD 7.62) mm and 20.03 mm (SD 4.75) respectively. The statistical analysis of mean subcutaneous thickness between lymphedematous and normal limbs was done using the paired t-test and it was found that there was a significant difference (*P value <0.001*) and moderate positive correlation (r = 0.75) found between the two parameters. (Table No. 1) Mean transverse diameter of lymphatic vessels in lymphedematous limb and normal limbs were 3.67 (SD 1.55) mm and 2.17 (SD 0.18) mm respectively and compared using the paired t-test. It was found that there was a significant difference (*P value = 0.001*) and a positive correlation (r = 0.47) was found between the two parameters. (Table No. 2)

Our study demonstrated all 4 types of lymphatic drainage patterns; Type I was seen in one subjects (14.2%) (Figure 3); and Type II was seen in one subjects (14.2%), Type III was seen in two subjects (28.5%) (Figure 2) and Type IV was seen in one subjects (14.2%).

MRL depicted the extent of lymphedema at the level of the foot in one (14.2%) subjects, at the level of foot & leg in three (42.8%) subjects and the level of foot, leg & thigh in three (42.8%) subjects.

Apart from lymphatic vessels, MRL also provided detail morphological and physiological details of inguinal lymph nodes. The cause of lymphedema secondary to involvement of lymph node alone was seen in one (14.2%) subjects, the involvement of lymphatics alone in two (28.5 %) subjects and involvement of both lymph node and lymphatics in four (57.1%) subjects. Among the study subjects; two subjects had filariasis (Figure 3) and one subject had undergone bilateral inguinal lymph node dissection (Figure 2). Dilated lymphatic vessels were visualized up to the mid-leg level in one (14.2%) subjects; upto knee level in two (28.5%) subjects; upto mid-thigh level in one (14.2%) subjects and upto groin level in one (14.2%) subjects. The pattern of dermal backflow seen in five (71.4%) subjects; however two (28.5%) subjects did not show any dermal backflow.

Mild pain at the time of contrast injection was perceived by all patients. Concomitant venous enhancement was detected in all patients. In our study, it was found that 3D MIP and VRT reconstruction images of different angles provide a detailed outline of the lymphatic pathways and help in differentiation from subcutaneous veins.

Figure 1A – Position of the patient into MRI gantry. Figure 1B, 1C - Technique of intradermal contrast injection into dorsal interdigital web space of foot.

Figure no. 2 - Patient of endometrial carcinoma operated with total hysterectomy and B/L inguinal lymph node dissection presented with both lower limbs swelling. Figure 2A - showing absent lymph nodes in bilateral inguinal region. Figure 2B - MIP image showing dermal back flow upto mid leg level. Figure 2C - enlarged MIP image showing dermal backflow (white arrow) and enlarged beaded shaped lymphatic vessels (black arrow).

Figure no. 3 MIP images showing enlargement of right lower limb and enlarged beaded shaped lymphatic vessels (white arrow in 3A) over lateral aspect of right leg. Concomitant venous enhancement also seen (red arrow in 3A &3B)

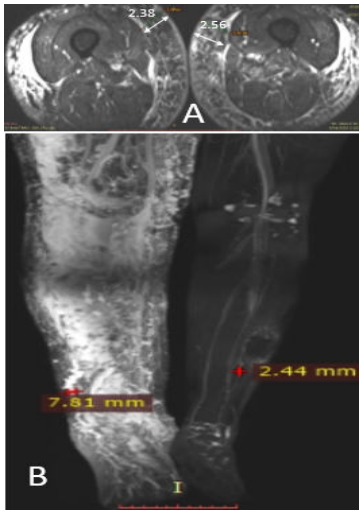

Figure no. 4 Technique of measurement of subcutaneous thickness (4A). Technique of measurement of diameter of lymphatic vessels (4B).

Table no. 1 Comparison of subcutaneous thickness in lymphedematous and normal limb by paired t-test.

	In lymphedematous limb (mm)	In normal limb (mm)
Mean	29.15	20.03
Variance	7.62	4.70
Pearson correlation	0.7450	
P value	<0.0001	

Table no. 2 Comparison of diameter of lymphatic vessels in lymphedematous and normal limb by paired t-test.

	In lymphedematous limb (mm)	In normal limb (mm)
Mean	3.67	2.17
Variance	1.55	0.18
Pearson correlation	0.475	
P value	<0.001	

Discussion

On MRL study of 7 subjects, we found the detailed anatomical and functional information about lymphatic vessels and inguinal lymph nodes. We measured the subcutaneous thickness at the point of

maximum subcutaneous thickness and the MR lymphangiography showed a significant difference between the mean subcutaneous thickness of normal and lymphedematous limb. Similarly on MRL study of 26 subjects, Lohrmann-et-al revealed an increased subcutaneous thickness at the level of the lower leg, whereby the mean subcutaneous thickness was 44 mm [5] [9].

The mean transverse diameter of lymphatic vessels in the lymphedematous limb and normal limbs shows a significant difference. Similar results were found in the study of Qing Lu-et-al; the mean transverse diameter of the lymphatic vessels in the normal and swollen calf was 2.49 mm and 3.41 mm, respectively, and the mean diameter of the lymphatic vessels in swollen calf was significantly larger than that of the contralateral calf (P value = 0.05) [6] [10].

Zhou-et-al has classified the lymphatic drainage patterns into four subtypes: (1) type I: single or multiple mildly dilated lymphatic vessels (number<5); (2) type II: only multiple moderate or severely dilated lymphatic vessels; (3) type III: numerous dilated lymphatic vessels with collateral dermal backflow; (4) type IV: numerous dilated lymphatic vessels with the presence of honeycomb structures. He demonstrated all types of lymphatic drainage patterns, as the frequency of type I–IV pattern was 25% (16/64), 45.31% (29/64), 17.19% (11/64), and 12.5% (8/64), respectively [7] [11]. Our study demonstrated Type I pattern in one subjects ; and Type II pattern in one subjects, Type III pattern in two subjects and Type IV in one subjects.

MRL also demonstrates the cause of lymphedema secondary to lymph node involvement, lymphatic vessel involvement, and both lymph node and lymphatic vessel involvement. A similar result was found in the study of N.F. Liu et al. Who also have classified the cause of lymphedema in his study of 272 subjects, as the lymph node affected only subjects were 63/272; Lymph node with lymphatic vessel abnormality were 105/272 subjects and Lymphatic affected had only been 106/272 subjects [9] [12].

The pattern of dermal backflow seen in five subjects; however, two subjects do not show any dermal backflow. Similar results were observed in the study of Lohrmann-et-al; who demonstrated the dermal backflow pattern in 70% (7/10) subjects [10] [13].

Conclusion

The present study of MR lymphangiography found to be a minimally invasive and safe technique. Due to multiplanar imaging and better spatial resolution, it provides good morphological and functional information of both lymphatic vessels & lymph nodes. 3D MIP reconstruction and VR techniques of different angles of view provides a detailed outlining of the lymphatic pathways andcan differentiate lymphatics from subcutaneous veins. The extent and severity of lymphedema, site, and the level of dilated lymphatic vessels are well delineated by MR lymphangiography. MR lymphangiography can trace the probable aetiology of lymphedema. The diameter of lymphatic vessels and subcutaneous thickness can be measured and a good correlation is noted between the parameters. Additionally, good details of lymph nodal morphology can be obtained. Thus, MR Lymphangiography can be considered as a baseline investigation for the treatment planning and follow-up of the patients suffering from lymphedema.

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