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Primary lower limb lymphedema: classification with non-contrast MR lymphography

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Abstract

Purpose

The purpose of the present study was to analyze the performances of non-contrast MR lymphography for the classification of primary lower limb lymphedema in 121 consecutive patients with 187 primary lower limb lymphedemas.

Materials and methods

121 consecutive patients with clinically diagnosed primary lower limb lymphedema underwent non-contrast MR lymphography with a free-breathing 3D fast spin-echo sequence with a very long TR/TE (4000/884 ms). MR examinations were retrospectively reviewed for severity of lymphedema (absent, mild, moderate, severe) and characteristics of inguinal lymph nodes and iliac and inguinal lymphatic trunks graded as aplasic (no lymph nodes or lymphatic trunks), hypoplastic (less lymph nodes or lymphatic trunks), normal and hyperplasic (more lymph nodes or more and/or dilated trunks).

Results

There was an excellent correlation between clinical stage and severity of lymphedema (Cramer's V of 0,73 ($p < 0.001$)). Differentiation was feasible between inguinal lymphatic vessel aplasia (21%), hypoplasia (15%), normal pattern (53%) and hyperplasia (11%). Severe lymphedema was observed in 46% of aplasic patterns and in 37% of hyperplasic patterns, but in only 15% of hypoplastic patterns and never observed in normal patterns ($p < 0.001$).

Conclusion

Non-contrast MR lymphography is able to classify primary lower limb lymphedemas into hyperplasic, aplasic, hypoplastic and normal patterns.

Keywords

Lower limb lymphedema

Non-contrast MR lymphography

MR lymphography

Lymphatic vessels

Lymphedema

Key points

Non-contrast MR lymphography is able to classify primary lower limb lymphedemas

Lymphedema can be classified in hyperplastic, aplastic, hypoplastic and normal patterns

Non-contrast MR lymphography can optimize clinical management of primary lower limb lymphedemas

Introduction

Lymphedema is a progressive condition characterized by gross swelling of the affected limb, which leads to chronic inflammation, fibrosis, and susceptibility to infection (1).

In 1934, Allen introduced a classification of lymphedema into primary and secondary.

Secondary lymphedema follows obstruction to the lymphatic pathways by causes such as surgery, radiation therapy, and involvement of lymph nodes by malignant disease and other conditions (2). Although primary lymphedema is sometimes congenital, in most cases it appears early in life with a predilection for the female sex: lymphedema precox. Late onset of the disease (after age 35), known as lymphedema tarda, is uncommon (2). Primary

lymphedema is an important medical issue that occurs in 1 out of every 10,000 people in the general population (3). Previous studies using conventional oil-contrast lymphography have demonstrated in primary lower limb lymphedema different patterns of lymphatic vessel abnormalities, which are designated as follows: aplasia, where there are no formed lymph trunks in the areas investigated; hypoplasia, where the lymph trunks are smaller or fewer in number than normal; and hyperplasia, where the lymph trunks of the lower limb are more numerous or greater in diameter than normal (4).

Primary lower limb lymphedema is a chronic, debilitating condition that has traditionally been seen as a refractory or incurable disorder. The conventional treatment for chronic lymphedema aims at alleviating symptoms, and is mainly based on physiotherapy and/or controlled compression therapy. However, with advances in our understanding of lymphedema pathophysiology, as well as new diagnostic and therapeutic tools, this perspective has changed. New surgical approaches include free lymph node autologous transplantation for lymphatic reconstruction and multiple lymphaticovenular anastomoses to derive the excess fluid component (5-7). In essence, lymph node transplantation could be more appropriate for aplasic or hypoplastic primary lymphedema, and lymphaticovenular

anastomoses for hyperplastic primary lymphedema (5-7). In addition, in animal models, it has been demonstrated that vascular endothelial growth factor C (VEGF-C) or VEGF-D may induce growth of the lymphatic capillaries (8, 9).

Patients with primary lymphedema should undergo proper imaging to evaluate the variety and characteristics of lymphedema and to allow for optimal clinical management and appropriate selection of treatment. However, the ideal imaging technique for the evaluation of patients with primary lymphedema has been elusive. The invasiveness and the morbidity of conventional oil-contrast lymphangiography have resulted in a dramatic decrease of examinations (10). The current primary imaging modality for the investigation of peripheral lymphedema is lymphoscintigraphy performed with ^{99m}Tc -labeled nanocolloids.

Lymphoscintigraphy provides insights into lymph flow dynamics. However, it is also hampered by low spatial resolution (11). The principle of contrast-enhanced MR lymphangiography is to subcutaneously inject paramagnetic macromolecules that enter the lymphatic vessels, resulting in contrast enhancement on T1-weighted MR sequences (12, 13). The spatial resolution is far higher than that of lymphoscintigraphy (14). Enhancement of lymphatic vessels is optimal near the contrast media site. On the other hand, visualization of larger lymphatic vessels may be suboptimal, and venous enhancement which is frequently observed may be confusing (15, 16).

Non-contrast heavily T2-weighted 3D MRI, which was introduced in the early 1990s, is a non-invasive imaging technique that can accurately depict the morphological features of the biliary and pancreatic ducts. By using heavily T2-weighted sequences without intravenous administration of any contrast agent, the signal of static or slow-moving fluid-filled structures, such as the lymphatic vessels, results in unique lymphatic vessels to background contrast. Though MR imaging with heavily T2-weighted MR images has already been used for the

morphological diagnosis of lymphedema, analysis of lymphatic vessels has not yet been performed (10, 17-19).

The purpose of the present study was to analyze the performance of non-contrast MR lymphography for the classification of primary lower limb lymphedema in 121 consecutive patients clinically suspected to have lymphedema.

Materials and methods

A. Patients

From March 2011 to March 2015, 121 consecutive patients with clinically diagnosed primary lower limb lymphedema were referred to our institution for non-contrast MR lymphography. Our local institutional review board approved this study. Informed consent from patients was not required for this observational retrospective study. In 14 patients, no lymphedema was demonstrated with non-contrast MR lymphography. In these 14 patients MR lymphography only demonstrated excessive subcutaneous deposition of fat related to lipedema or morbid obesity without any lymphedema. These 14 patients were therefore excluded from further analysis. The remaining 107 patients (90 female and 17 male patients) had a mean age of 37.6 +/- 15.2 years. The mean duration of limb swelling was 20.1 +/- 17.4 years. There were 84 lymphedema precox (onset before age 35) and 23 lymphedema tarda (onset after age 35) patients. Clinical diagnosis and clinical staging were established by a lymphologist surgeon (CB) with more than 20 years of experience.

Clinical staging was based upon the criteria established by the International Society of Lymphology in 2009 (20) (Table 1). All possible secondary causes of lymphatic disease had been excluded by a complete work up before considering the diagnosis of primary lymphedema. Furthermore, in all cases primary lower limb lymphedema was solitary and not

as part of a generalized lymphatic anomaly. All patients had conservative management including physiotherapy and compression therapy but no patient had previous surgery.

B. MR examination

All MR examinations were performed with a 1.5 Tesla General Electric Signa HDxt (GE Medical System, Wisconsin, USA). Five hundred ml of pineapple juice, used as a negative oral contrast agent to decrease bowel content signal intensity, was given 30 minutes before MR examination. The patients were placed in a supine position with their feet first. Three successive acquisitions were performed on the lower leg and foot (first station), thigh (second station), and the pelvic areas (third station), with six-element phased-array coils.

- a) A T1-weighted three-plane localizer was performed for orientation purposes for each station.
- b) Two stacks of T2-weighted MR images using IDEAL (Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation) (fat/water separation technique providing four different contrasts: water, fat, in phase and out phase) T2 FSE (TR/TE; 4233/76 ms) sequences (slice thickness: 6 mm; matrix: 320x192; FOV: 380x380; scan time 3 minutes 30 seconds) were performed in the axial plane. The first stack of images was obtained on the pelvic area for inguinal nodes analysis and the second stack of images was obtained on the legs for lymphedema characteristics analysis.
- c) Non-contrast MR lymphography was obtained with a free-breathing 3D high spatial resolution fast spin-echo sequence similar to that used for 3D MR cholangiopancreatography, with a very long TR/TE (4000/884 ms; flip angle 90°) in the coronal plane. A 90° radiofrequency pulse was applied at the end of the echo train to flip the transverse magnetization to the longitudinal direction. The matrix was 512 × 288 with a field of view of 400 x 400. The section thickness varied from 0.8 to 1.4 mm. A stack of

124 to 316 sections was acquired to cover the entire region of interest. Scan time varied from 3 to 5 minutes depending of the number of native slices. Post-processing of the data was performed to obtain maximum intensity projection (MIP) images and multiplanar reformatted images.

C. Image analysis

All MR examinations were retrospectively reviewed in conference by two radiologists (LA with 10 years of experience and SD with seven years of experience in non-contrast MR lymphography). Agreement was reached by consensus. MR images were analyzed on a PACS system (Carestream version 11.32, Carestream Health, Rochester, NY). For 3D MR lymphography thin source images, 10-mm MIP and volume MIP reconstructed images were evaluated. Observers were blinded to clinical lymphedema staging.

Criteria of analysis included:

- a) Severity of lymphedema graded as absent, mild, moderate and severe.

Lymphedema was graded as mild when: a) superior margin of subcutaneous infiltration was below the knee; and b) fluid infiltration of subcutaneous fat was mild without increase of the dimensions of subcutaneous fat; and c) epifascial fluid collection was minimal (less than 5 mm of thickness).

Lymphedema was graded as severe when: a) subcutaneous infiltration involved the entire lower limb; and b) fluid infiltration was severe with marked increase of the dimension of subcutaneous fat; and c) epifascial fluid collection was severe (more than 15 mm of thickness).

Lymphedema was graded as moderate for all intermediate situations between mild and severe.

- b) Presence or absence of the “so-called” honeycomb pattern corresponding to trabecular structure with enlarged fat pockets surrounded by thick lines (21).
- c) Presence or absence of increased thickness of dermis (dermis thickness greater than 2 mm).
- d) Presence or absence of involvement of muscular compartment (fluid infiltration, fatty muscular involution, or atrophy).
- e) Number of inguinal lymph nodes graded as: no nodes; decreased number: fewer than 3 nodes; normal: 3 to 6 nodes; increased number: 7 or more nodes.
- f) and g) Characteristics of iliac (f) and inguinal (g) lymphatic trunks graded as aplasic when no lymphatic trunks were demonstrated; hypoplastic when fewer than 3 lymphatic trunks were demonstrated; normal when 3 to 6 lymphatic trunks were demonstrated; and hyperplasic when more than 6 lymphatic trunks were demonstrated, or when lymphatic trunks were abnormally increased in diameter (lymphatic trunk diameter ≥ 3 mm).
- h) Presence or absence of distal dilated lymphatic vessels (lymphatic vessel diameter superior to 1 mm) in the leg.

D. Statistical analysis

We reported continuous variables as means (+/- SD) and categorical variables as proportions. We used Student's t-test to analyze between-group differences as appropriate. A chi-square test was used for categorical variables with expected values more than 5, and Fisher's exact test was used for categorical variables with expected values less than 5. We used Cramer's V coefficient to measure the correlation between two nominal variables. All analyses were performed with the use of SAS software, version 9.3 (SAS Institute). A two-sided p value of 0.05 or less was considered to indicate statistical significance.

Results

All 121 patients completed the MR examination successfully. For the 107 patients with lymphedema demonstrated with MR imaging, inguinal lymph nodes and inguinal lymphatic vessels could not accurately be analyzed in four patients, and iliac lymphatic vessels in another six patients, due to suboptimal positioning of the phase-array coil in the third station of the examination.

Lymphedema was bilateral in 80 patients and unilateral in the other 27, resulting in 187 lower limb lymphedemas (Table 2). Clinical stages were I in 85 lower limbs (45%), II in 78 (42%), and III in the other 24 (13%) (Figure 1a) (Table 3). Familial history of lymphedema was reported in 13 patients. History of erysipelas was reported in 12 patients (18 lower limbs). With non-contrast MR lymphography, lymphedema was mild in 110 (59%) lower limbs, moderate in 44 (23%), and severe in the other 33 (18%) (Figures 1–5) (Table 3). There was an excellent correlation between the clinical stage and the severity of lymphedema, with a Cramer's V of 0.73 ($p < 0.001$) (Table 3).

A so-called honeycomb pattern was present in 120 lower limbs and absent in the other 67 (Figure 2d). It was more common in severe lymphedema ($p < 0.001$). Increased thickness of dermis was present in only 35 lower limbs (19%) (Figure 2d). Involvement of the muscular compartment was never observed. Inguinal lymph nodes were absent in 11 (6%) lower limbs, decreased in 19 (11%), normal in 144 (80%), and increased in six (3%) (Figure 4c). Iliac and inguinal lymph trunks, respectively, were absent (aplastic pattern) in 36 (22%) and 37 (21%) (Figure 4a), decreased (hypoplastic pattern) in 25 (15%) and 27 (15%) (Figure 1b), normal in 94 (56%) and 96 (53%) (Figure 5a), and increased in size or number (hyperplastic or dysplastic pattern) in 11 (7%) and 19 (11%) (Figures 2a, 3a). There was a positive correlation between number of inguinal lymph nodes and number of both iliac and inguinal lymphatic trunks ($p < 0.001$). The severity of lymphedema was positively correlated with the characteristics of

inguinal lymph nodes, iliac and inguinal lymphatic trunks (i.e; aplasia, hypoplasia, normal and hyperplasia) as demonstrated with non-contrast MR lymphography ($p<0.001$). Severe lymphedema was observed in 46% of aplasic patterns and in 37% of hyperplasic patterns, but in only 15% of hypoplastic patterns and never observed in a normal pattern ($p<0.001$) (Table 4).

Distal dilated lymphatic vessels in the leg were observed in 68 (36%) cases. Dilatation of distal lymphatic vessels in the leg was observed in all cases of hyperplasic patterns, but also in 29% of the other patterns (Figures 2b, 2c, 3b, 3c). In contrast, we did not find a significant correlation between distal lymphatic vessel dilatation and duration of limb swelling.

Similarly, we did not find any significant association between patient age, sex, duration of swelling, history of erysipelas or familial history lymphedema and characteristics of lower limb lymphedema as demonstrated with non-contrast MR lymphography.

Discussion

Lymphedema is defined as accumulation of protein-rich lymph in the interstitial space caused by failure of the lymphatic system to conduct lymph back to the blood circulation. This failure to transport excess interstitial fluid and large molecular substances such as proteins, fat and waste material from the interstitium results in development of fibrosis in the dermis in chronic lymphedema (1, 10, 20). Fibrotic changes with inflammatory cells in the dermis and proliferation of collagen fibers occurring in the subcutaneous compartment which is the site of most of the swelling contribute to the solid tissue consistency (1, 20). With non-contrast MR lymphography, primary lower limb lymphedema is demonstrated as a combination of fluid infiltration of subcutaneous fat and epifascial fluid collection. The fluid infiltration of

subcutaneous fat commonly exhibits the “so-called” honeycomb pattern which corresponds to trabecular structure with enlarged fat pockets surrounded by lines corresponding to fluid or fibrous tissue (fibrous strands due to chronic inflammation are caused by the high protein content of edema fluid) or both (21). These features allow for an obvious differentiation from fatty infiltration related to lipedema or morbid obesity (1, 3).

It is also easy to differentiate lymphedema from phlebedema; in the latter condition, there is an involvement of the subfascial muscular compartment with increase in size with muscle edema or fatty muscular degeneration (21, 22). Such involvement of the subfascial muscular compartment was never observed in our series of 187 lower limb lymphedemas, confirming that lymphedema is primarily a disorder of subcutaneous tissue. In most cases, diagnosis of lymphedema can be made on the basis of medical history and physical examination. However, it is not always easy to clinically distinguish between lymphedema and other types of edema, such as phlebedema or lipedema (23, 24). In our study, lymphedema was not demonstrated with non-contrast MR lymphography in 14 patients clinically diagnosed with lymphedema. Only fatty infiltration related to lipedema or morbid obesity was demonstrated in these 14 patients. However, in the other 107 patients, there was an excellent correlation between the clinical stage and the severity of lymphedema, as demonstrated with non-contrast MR lymphography. The level of detail of soft tissue contrast obtained with non-contrast MR lymphography allows for an excellent delineation of soft tissue edema localization, which may help to optimize mapping of the manual lymphatic drainage.

Iliac and inguinal lymphatic trunks were aplasic in 22% and 21% of cases, hypoplastic in 15% of cases, and hyperplastic in 7% and 11% of cases. They were considered normal in 56% and 53% of cases. We also found a positive correlation between lymphatic trunk characteristics and inguinal lymph node number.

In 1957, Kinmonth et al. found aplasia in 14% of cases, hypoplasia in 55% of cases, and hyperplasia in 24% of cases in a study of 87 patients with primary lymphedema (4). By means of X-ray lymphangiography, lymphatic vessels were only considered normal in 6% of cases. Hypoplasia was more common in their study than in ours. However, lymphatic vessels of the entire upper and lower leg were analyzed by X-ray lymphangiography, whereas in our study, only lymphatic trunks were analyzed. Lymphatic vessels distal to the lymphatic trunks were not analyzed because of limited spatial resolution of non-contrast MR lymphography. In addition, in their 1957 study, Kinmonth et al. classified cases with lymph trunk deficient either in number or in size as hypoplastic (4). Because of limited spatial resolution of non-contrast MR lymphography in comparison with X-ray lymphangiography, we only evaluated the number of lymph trunks or the increase in size. Because X-ray lymphangiography is no longer performed, and because to the best of our knowledge no other imaging technique allows for a reliable analysis of lymphatic trunks, we do not have any means for comparing our results to more recent data. One can imagine that recruitment of patients in 1957 was markedly different from our own recruitment.

We found an excellent positive correlation between the severity of lymphedema and characteristics of lymph trunks. Lymphedema was more severe in case of aplastic and hyperplastic patterns. It was less severe in cases of lymphedema with hypoplastic or normal iliac and inguinal lymphatic trunks. According to us such correlation not previously demonstrated reinforces the interest of the classification allowed by non-contrast MR lymphography. Interestingly, we did not find any correlation between dilatation of distal lymphatic vessels and duration of limb swelling. It is frequently considered that in long-standing lymphedema lymphatic dilatation is no more observed because of marked thickening of lymphatic wall; our study did not confirm this hypothesis (25).

In the past, lymphedema was frequently considered to be a refractory or incurable condition, and treatment was aimed to decrease symptoms with physiotherapy and/or compression therapy. However, new surgical approaches are now available. We assume that a detailed anatomic evaluation of both lymph nodes and lymphatic vessels may be useful for surgical planning. The choice of site for free lymph node autologous transplantation may be optimized by the precise evaluation of the extent of lymphedema and by the characteristics of abnormalities of lymph nodes and lymphatic vessels. Lymph node transplantation appears to be an interesting surgical modality in cases of hypoplastic or aplastic lymphedema (6, 26). On the other hand, lymphaticovenular anastomosis appears to be an interesting surgical modality in cases of dilated lymphatic vessels without hypoplasia. Presurgical evaluation needs a precise delineation of the lymphatic drainage system in the targeted limb, including number, caliber, and location. In contrast, the outcome of lymphaticovenular anastomosis may be weaker for patients with atrophied or sclerotic lymphatic vessels (27).

The optimal imaging modality for evaluation of lower limb lymphedema has not yet been established. Because of its invasiveness compared with new techniques, conventional oil-contrast X-ray lymphangiography is no longer performed in patients with lower limb lymphedema (10, 28). The current primary imaging modality is lymphoscintigraphy.

Lymphoscintigraphy can detect retarded tracer transport even in mild lymphedema and is useful to evaluate the functional lymph flow. Quantitative analysis of lymph transport is performed by obtaining dynamic images or measuring the transit time (10, 11). On the other hand suboptimal resolution of lymphoscintigraphy is not suitable for demonstrating normal size lymphatic vessels (10, 11). Contrast-enhanced MR lymphangiography has a far higher spatial resolution (29), and its evaluation of distal lymphatic vessels near the site of contrast injection is excellent. Both contrast enhanced MR lymphangiography and lymphoscintigraphy provide dynamic information of contrast agent uptake. Notohamiprodjo et al. demonstrated

that the two techniques were strongly correlated for depiction of delayed and diffuse lymphatic drainage in peripheral lymphedema (29). However, the visualization of the larger lymphatic vessels, including the inguinal and iliac lymphatic trunks, is of lower quality than the distal lymphatic trunks, and the enhancement of the pelvic lymphatic vessels is usually poor (30). In addition, a substantial amount of contrast material is eliminated via the circulating system, and enhancement of the venous system may complicate analysis of the lymphatic vessels. To improve differentiation from venous structures, Mitsumori et al. (14) added contrast enhanced MR venography. In addition enhanced lymphatic vessels may not be demonstrated in healthy limbs, probably because of a faster lymphatic flow (14). Finally, in comparing contrast-enhanced MR lymphangiography and heavily T2-weighted MRI, Lu et al. demonstrated that number and diameter of lymphatic vessels were different (31). They postulated that uptake of contrast media may be restricted in dilated lymphatic vessels because of increased lymphatic pressure. On the other hand, contrast-enhanced MR lymphangiography allows a functional assessment of the lymphatic vessels transportation and nodal uptake. In a study published in 2005, Liu et al. reported the results of non-contrast 3D MR imaging for the evaluation of lymph circulation disorders. However, because of the limited spatial resolution, they reported that such imaging was not feasible for the depiction of lymphatic vessels in an intact lymphatic system (32). On the other hand, several studies have demonstrated that larger lymphatic trunks, such as retroperitoneal lymphatic trunks, were easily demonstrated with non-contrast MR lymphography (33-35). Yamamoto and colleagues reported the results of Indocyanine Green (ICG) lymphography in 31 cases of primary lower limb lymphedema (36). They were able to differentiate four different patterns including proximal and distal backflow, less and no enhancement patterns. ICG lymphography allowed for the identification of superficial lymphatic vessels. Therefore, the main advantage of ICG lymphography is the potential for real-time observation of lymphatic vessels during surgery.

Limitations of ICG lymphography include relatively small field of view and markedly limited penetration depth, therefore ICG lymphography cannot be used to analyze deep lymphatic vessels (36). In contrast with these techniques non-contrast MR lymphography does not provide any functional information, however the precise anatomic information can be used to identify sites for lymph node transplantation or suitable sites for lympho-venous anastomosis and to optimize mapping of the manual lymphatic drainage. We believe that it could be very interesting to associate non-contrast MR lymphography with a functional imaging modality such as contrast-enhanced MR lymphangiography as already proposed by Mitsumori et al (14). In addition, contrast-enhanced MR lymphangiography appears to be optimal for evaluation of distal lymphatic vessels whereas non-contrast MR lymphography may be superior for evaluation of proximal lymphatic trunks including inguinal and iliac vessels.

The main limitation of the present study is the lack of a comparative imaging modality and the definite lack of a standard of reference. As a matter of fact, in our retrospective study comparative imaging modality was uncommonly available. However, the results obtained with non-contrast MR lymphography are fundamentally different from those obtained by other imaging modalities except X-ray lymphangiography which is no more performed in patients with primary lymphedema. In addition, since it is a single-center retrospective study, we cannot be certain of the representability of the population evaluated. Several image analysis criteria were only based upon our experience of non-contrast MR lymphography and the reading was only performed in consensus. For example, we considered it to be normal to see between three and six lymphatic trunks in the inguinal area, when it is usually normal to find between five and 15 lymphatic vessels with X-ray lymphangiography, due to its greater spatial resolution (4). Our preliminary results should be externally validated by other centers' experiences. Finally, as non-contrast MR lymphography is a relatively new imaging

technique, its main limitation today is its suboptimal spatial resolution, which may be improved upon in the near future with advances in the software and hardware of MR systems.

In summary we believe that non-contrast MR lymphography, which is a perfectly non-invasive imaging technique, is able to differentiate primary lower limb lymphedema in hyperplastic, aplastic, hypoplastic patterns and can potentially optimize clinical management.

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Table 1: Clinical staging of lymphedema

Stage 0	Latent or sub-clinical condition Swelling is not present
Stage I	Early accumulation of fluid which subsides with limb elevation Pitting may occur
Stage II	Limb elevation alone rarely reduces tissue swelling Pitting is manifest
Stage III	Pitting is absent Trophic skin changes are apparent

Table 2: Flow chart of patients with primary lower limb lymphedema

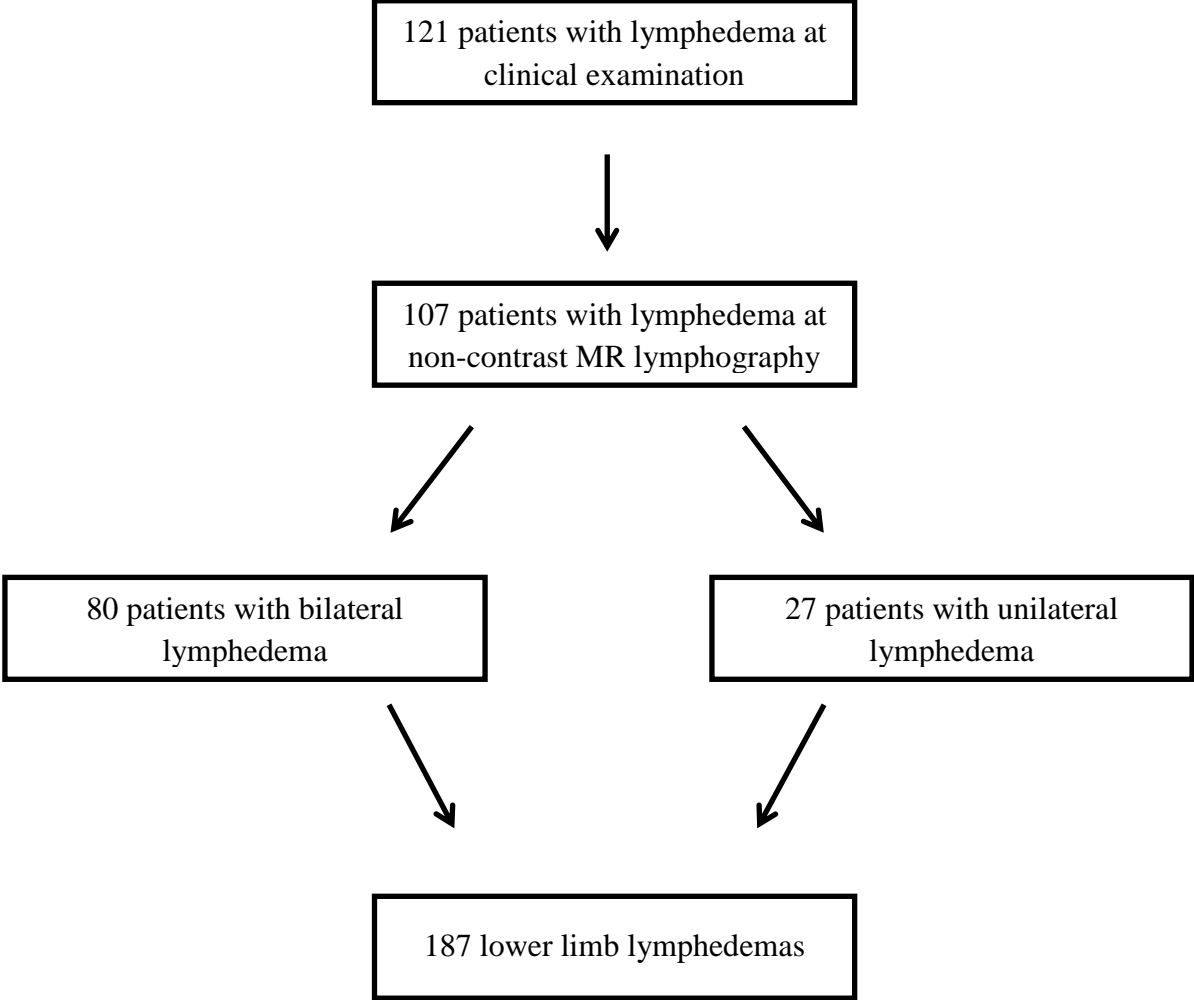


Table 3: Correlation between stage and severity of lymphedema demonstrated by MRI (Cramer's V of 0.73, p<0.001)

		Severity of lymphedema with MRI			
		Mild	Moderate	Severe	
Clinical stage	1	83	0	2	85
	2	27	43	8	78
	3	0	1	23	24
		110	44	33	

Table 4: Correlation between severity of lymphedema and pattern of inguinal lymphatic vessels (Fisher test: $p < 0.001$) (Missing data: 8). Severe lymphedema was more observed in aplasic (46%) and hyperplasic pattern (37%) than in hypoplastic 15% and normal pattern (0%).

		Pattern of inguinal lymphatic vessels				
		Aplasic	Hypoplastic	Normal	Hyperplasic	
Severity of lymphedema	Mild	8 22%	14 52%	83 86%	2 10%	107
	Moderate	12 32%	9 33%	13 14%	10 53%	44
	Severe	17 46%	4 15%	0 0%	7 37%	28
		37	27	96	19	179

Figures legends

Figure 1: 28-year-old female with lower limb lymphedema. Clinical picture of lower limb demonstrates a severe (stage III) left lower limb lymphedema (a). Non-contrast MR lymphography demonstrates only one iliac and inguinal lymphatic trunk on the left side (arrows) and a normal pattern (arrowhead) on the right side (b). A moderate fluid infiltration (I) of subcutaneous fat is demonstrated on the left side. At lower levels (c, d), a severe fluid infiltration (I) of subcutaneous fat is demonstrated on the left side. A mild subcutaneous infiltration (arrow) not clinically detected is demonstrated on the right side. Water IDEAL T2 FSE image (e) demonstrates a severe fluid infiltration (I) of subcutaneous fat and an epifascial fluid collection (C) on the left side.

Figure 2: 54-year-old man with moderate hyperplastic bilateral lower limb lymphedema. Non-contrast MR lymphography demonstrates an increased number of dilated lymphatic iliac and inguinal trunks (arrows) (a). (Note the presence of bilateral hydrocele (H) testis). Dilated lymphatic vessels (arrows) are demonstrated at lower levels (b, c). Fluid infiltration (I) of subcutaneous fat is also well demonstrated (b, c). Water IDEAL T2 FSE image (d) demonstrates a bilateral fluid infiltration (I) of subcutaneous fat with a so-called honeycomb pattern, moderate epifascial fluid collection (C), and an increased thickness of dermis (arrow).

Figure 3: 26-year-old man with left mild hyperplastic lower limb lymphedema. Non-contrast MR lymphography demonstrates an increased number of dilated left lymphatic iliac and inguinal trunks (arrows) (a). Dilated lymphatic vessels are demonstrated at lower levels (arrows) (b, c). Mild fluid infiltration of subcutaneous fat is demonstrated within the leg maximal above the medial side of ankle (arrowhead) (c). Marked dilatation of lymphatic

vessels is demonstrated around the popliteal lymph node (short arrow) (b). Neither lymphatic abnormality nor lymphedema were observed on the right side.

Figure 4: 18-year-old man with left moderate aplastic lower limb lymphedema. Non-contrast MR lymphography demonstrates the absence of iliac and inguinal lymphatic trunks. Normal appearance of right iliac and inguinal lymphatic trunks (arrows). Mild fluid infiltration (I) of medial part of left thigh is also demonstrated (a). Moderate fluid infiltration (I) of left leg is also demonstrated (b). Small superficial lymphatic vessels (arrow) are demonstrated on the medial side of left knee (b). Water IDEAL T2 FSE image demonstrates absence of left inguinal lymph node (c) whereas right inguinal lymph nodes (arrows) are normal and a moderate fluid infiltration (I) of lower limb without epifascial fluid collection of left lower limb (d).

Figure 5: 52-year-old female with mild lower limb lymphedema. Non-contrast MR lymphography demonstrates a normal pattern of iliac and inguinal lymphatic trunks (arrows) at both sides (a). At lower levels (b, c), a bilateral mild fluid infiltration (I) of subcutaneous fat is demonstrated.