Central Lymphatic Imaging in Adults with Spontaneous Chyluria

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Purpose: Chyluria is a rare condition primarily prevalent in developing countries in tropical regions. In chyluria, there exists the communication between lymphatic vessels and the urinary tract, but the specific mechanism of this communication remains undocumented. The objective of this study was to assess the morphology of the main lymphatic vessels including the uro-lymphatic fistula, the thoracic duct using Magnetic Resonance Lymphangiography (MRL) and Intranodal Lymphangiography (IL).

Materials and Methods: A retrospective study spanning five years, from January 2020 to January 2024, included 43 patients diagnosed with chyluria through cystoscopy and quantitative urine testing for triglycerides. These patients underwent MRL and then IL for uro-lymphatic fistula embolization.

Results: The study involved 43 patients with an average age of 66.1 ± 19.5 years, with a male-to-female ratio of 1:2. Uro-lymphatic fistula occurred predominantly in the left kidney (72.1%), followed by the right kidney (20.9%), and both sides (7%). MRL imaging showed the thoracic duct in 100% of cases but visualized only 84.5% of the uro-lymphatic fistulas. In contrast, IL imaging showed the thoracic duct in 51.5% of patients but visualized uro-lymphatic fistulas in 100% of cases. In the procedure of IL, the average visualization time of the thoracic duct was 45 minutes, with a range of 35 to 69 minutes.

Conclusion: MRL and IL complement each other in diagnosing the main lymphatic vessels in chyluria patients. The observed circulatory stasis in the thoracic duct supports the hypothesis that it contributes to increased pressure in the thoracic duct and the formation uro-lymphatic fistula as collateral circulations.

Keywords: chyluria, MR lymphangiography, intranodal lymphangiography, uro-lymphatic fistula

Introduction

Chyluria is a condition characterized by the presence of chylous fluid in the urine, specifically the presence of triglycerides with a concentration greater than 100 mg/dL. The triglyceride concentration depends on the patient’s dietary intake of fats. Diagnosis of this condition is often straightforward, as it causes the urine to become cloudy or milky, and the detection of chylomicrons or triglyceride in the urine is a key diagnostic criterion. Clinically, the severity of chyluria can vary, with urine appearing either mildly cloudy or intensely milky, and fat particles may obstruct the urinary tract, necessitating urgent catheterization.

Spontaneous chyluria is a rare condition, and its etiology and pathophysiology remain poorly understood. This condition is more prevalent in hot and humid tropical countries such as Southeast Asia and India, and it is notably rare in developed countries in Europe, North America, and Northeast Asia. Epidemiological studies suggest that chyluria may arise from parasitic infections causing damage to lymphatic vessels, leading to leakage of chylous fluid into the urinary tract, forming uro-lymphatic fistulas.

In the majority of cases, the thoracic duct drains into the venous system at the left internal jugular vein, the subclavian vein, or the angle between the two. The thoracic duct drains the volume of lymphatic fluid from the lower legs, the liver, and the intestine. This anatomical component is relevant to chyluria. In this condition, abnormal communication occurs between lymphatic branches and the urinary tract, but the specific details regarding the quantity, location, and morphology of the
lymphatic branches entering the urinary tract remain unexplored. Therefore, previous treatment methods, including silver nitrate instillation into the kidneys and soft tissue surgery ligation around the renal hilum, have been based on empirical experience rather than addressing the underlying nature of the damage.\textsuperscript{5,6}

With recent advancements in imaging diagnostics of the lymphatic system, a more in-depth study of the lymphatic circulation in chyluria patients has become possible. This allows for accurate visualization of the lymphatic branches entering the renal hilum, providing valuable insights for surgeons to focus on suturing or interventional radiologist for embolization of uro-lymphatic fistulas.\textsuperscript{7} Two imaging methods revealing the lymphatic system, Magnetic Resonance Lymphangiography (MRL), and Intranodal Lymphangiography, complement each other. On both methods of lymphangiography, contrast material was injected into the lymphatic system from the lymph node at the inguinal region. Then, under MRI or fluoroscopy, the contrast depicts the abnormal lymphatic branches that connect with the urologic system.\textsuperscript{8,9} So far, there have been few studies of the central lymphatic system in patients with chyluria. This study, with the largest number of patients, focuses on analyzing images of the major lymphatic vessels in patients with spontaneous chyluria.

**Patients and Methods**

A retrospective descriptive study was conducted on chyluria patients at Hanoi Medical University Hospital from January 2020 to January 2024.

**Patient Selection Criteria**

- Clinically diagnosed chyluria and confirmed by urine tests: urine appearing milky or cloudy, triglyceride concentration in urine > 100 mg/dL.
- Cystoscopy showing the flow of chylous fluid from the ureteral orifice.
- Underwent MR lymphangiography.
- Underwent intranodal lymphangiography.
- Complete medical records with clinical, epidemiological, and imaging information stored in the picture archiving and communication systems (PACS).

**Patient Exclusion Criteria**

- Inadequate MRL images due to patient movement or insufficient information in IL images to calculate the time intervals of contrast agent movement in the lymphatic vessels.
- Patients with any surgical history related to the kidneys, such as kidney stone removal, kidney biopsy, kidney transplantation, lymph node dissection.

**MR Imaging Techniques for Major Lymphatic Vessels**

The patients were punctured with a 25-gauge needle in both inguinal lymph nodes under the guidance of ultrasound outside the magnetic resonance imaging (MRI) room, on a detachable table of the MRI machine (1.5 Tesla, GE Signa HDxt, USA). The needles were secured, and then the detachable table was moved into the MRI room to reattach it to the MRI machine. Through the needles, the contrast agent (Gadovist, Bayer Pharma, Germany) was injected at a rate of 1 mL/minute, with a total volume of 10 mL for each side. During the contrast agent injection, T1 fat saturation sequences were performed in the coronal and axial planes.

**Intranodal Lymphangiography Techniques**

Under a digital subtraction angiography (DSA) system, patients were punctured in the bilateral inguinal nodes under ultrasound guidance. Then, an oil-based contrast agent (lipiodol, Guerbet, France) was slowly injected at a rate of 1 mL/3 minutes. Fluoroscopy was used during the injection of the contrast agent to observe its flow in the central lymphatic system.

**Criteria of Dilatation and Obstruction of TD on MRL and IL**

The entire length of the thoracic duct was visualized, with a diameter exceeding 3 mm (Typically, the thoracic duct is observed in segmented portions due to the fragmentation of the oiled contrast flowing into the subclavian vein). MRL and IL images were blindly analyzed by a single experienced radiologist with 10 years of experience in lymphatic imaging.
Study Variables
Study variables included patient demographics (age, gender, clinical features), morphological characteristics of the main lymphatic vessels on MRL and IL, and criteria for the appearance time of the lymphatic vessels (in minutes).

Statistical Analyses
These data were analyzed using standard statistical techniques, including medians and ranges for continuous data and counts and percentages for categorical data. Differences between groups were explored using the McNemar’s test. A P-value < 0.05 was considered statistically significant. The statistical analysis was done using SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA).

Ethical Considerations
The study received ethical approval from the Ethics Committee of Hanoi medical university, Ha Noi, Vietnam. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, informed consent is not required.

Results
During a 5-year period, a total of 43 chyluria patients underwent intervention for uro-lymphatic fistula embolization using IL. All these patients had undergone MRL within one week prior to the intervention.

Clinical Characteristics
Average age: 66.1 ± 19.5 years (ranging from 38 to 82 years).
- Onset of symptoms: 5.6 ± 3.2 months (ranging from 0.5 to 54 months).
Baseline demographics and MRL characteristics are presented in Table 1 and Table 2.

Magnetic Resonance Lymphangiography Characteristics

Intranodal Lymphangiography Characteristics
Time from the injection of contrast into the inguinal lymph node to its ascent to the level of the L1 vertebra: 45 ± 17 (ranging from 35 to 69 minutes).
- Visualization of the thoracic duct: 22/43 patients (51.5%).
- Visualization of uro-lymphatic fistula: 43/43 patients (100%).
- Obstruction of the thoracic duct at the junction thoracic duct subclavian vein: 43/43 patients (100%).
Comparison of MRL and IL.

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<tr>
<th>Table 1</th>
<th>Gender and Affected Kidney Observed Through Cystoscopy</th>
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Discussion

Population of the Study

Chyluria can be readily recognized by the milky color of urine. Its presentation may vary from intermittent episodes to continuous persistence, depending on the severity experienced by each individual patient. Our patients are typically of middle and old age (average age 66), indicating that this is an acquired condition. Epidemiological research indicates that chyluria is prevalent in hot and humid tropical nations like India, Brazil, and Vietnam, as documented in multiple studies.4,9,10

Regarding renal involvement, currently, there is no study reporting the specific side of the kidney where the uro-lymphatic fistula lesion is present. Our study indicates a significant predominance of left renal involvement, accounting for over 70% of patients. To confirm the uro-lymphatic fistula, we rely on at least one of the following three criteria: visual confirmation of chylous effusion flowing into the ureteral orifice during cystoscopy, identification of dilated lymphatic branches entering the renal hilum on MRL, or visualization of oiled contrast agent entering into the kidney on IL. The reason for the frequent occurrence of chylous reflux into the left renal pelvis is not yet clear and needs to be substantiated through future anatomical and lymphatic circulation studies. Additionally, there is a notable gender difference, with a higher prevalence of chyluria in females compared to males.

MRL Imaging Characteristics

MRL of the main lymphatic vessels is widely applied for the diagnosis of lymphatic disorders, capitalizing on its advantages of being minimally invasive, offering high resolution, and utilizing a contrast agent with low viscosity for rapid movement within the lymphatic system. This enables a much swifter visualization of lymphatic branches compared to imaging with oil-based contrast agents.8 In our study, all patients undergoing MRL exhibited a clear visualization of the thoracic duct without anatomical variations. Dilatation of the thoracic duct was observed in 76.7% of patients (n=33), and uro-lymphatic fistula was seen in 83.7% (n=36) of patients as lymphatic branches entering the renal hilum (Figure 1). These findings are consistent with recent studies on MRL imaging in chyluria.7,8,11

In terms of MRL techniques, there are currently two main approaches: one utilizing contrast agents injected into the inguinal lymph node (MR lymphangiography) and the other employing non-enhanced magnetic resonance lymphography. Both methods aim to reveal the communication between the lymphatic and urinary systems. Sabbah et al conducted MR lymphography on a 3Tesla machine, demonstrating a clear depiction of communication between the lymphatic and urinary systems, accompanied by the consistent dilation of lymphatic vessels at the fistula site.8

The advantages of MRL are evident in the higher number of patients with TD visualization compared to IL using oil-based contrast agent. The group of patients using oil-based contrast agent only had 51% TD visualization compared to 100% in the MRL group (Table 3). This can be explained by the fact that the contrast agent has lower viscosity than oil, allowing for better movement within the lymphatic vessels. Even in non-enhanced MR lymphography using the 3D magnetic resonance cholangiopancreatography (MRCP) sequences, TD is also easily seen.8 Thanks to this advantage of MRL, this diagnostic imaging modality is commonly employed for all patients with suspicion of lymphatic leakage, and specifically for patients with chyluria.

The disadvantage of MRL lies in the low viscosity of the contrast agent, leading to rapid and easy forward flow in lymphatic vessels, making it difficult to visualize uro-lymphatic fistula branches related to the retrograde flow of chyle.

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<th>Table 2 MRI Characteristics</th>
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<td>MRL Imaging</td>
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into the kidney. This is demonstrated in the results showing uro-lymphatic fistula in 83.7% of patients on MRL, compared to 100% visualization of uro-lymphatic fistula on IL with oil-based contrast material (Figure 2 and Table 3).

**Intranodal Lymphangiography**

In the early 2010s, Maxim Itkin introduced a revolutionary technique for imaging the main lymphatic vessels through intranodal lymphangiography (IL), using an oil-based contrast agent injected into the inguinal lymph nodes on both sides. This method represented a major advancement in the diagnosis of disorders within the lymphatic system. The use of IL in chyluria provided insights into the pathogenesis of these conditions, particularly the theory suggesting that obstruction of the thoracic duct increases pressure in the lumbar lymphatic branches, and subsequently creating a pathway into the renal pelvis. In our patients, all individuals with spontaneous chyluria exhibited delayed contrast agent transit time, with an average of 45 minutes from the initiation of contrast injection into the inguinal lymph nodes to its arrival in the cisterna chyli. The hypothesis of thoracic duct obstruction had been previously reported in other studies. M. Itkin et al reported three cases of spontaneous chyluria resulting from compression at the thoracic duct. Cuong et al documented the placement of stents to treat obstructions at the distal thoracic duct, reducing symptoms of chyluria. Conversely, the recurrence of chyluria was observed when the stent became obstructed. This study represents the largest cohort reported on the application of MRL and IL in patients with chyluria.

Other imaging findings included TD dilation, stasis and dilatation of lumbar lymphatic branches, providing additional supportive evidence for the hypothesis of TD obstruction and increased pressure in peripheral lymphatic branches (Figure 3).

| Table 3 Comparison of MRL and IL in Visualizing the Main Lymphatic System |
|-------------------------------|-------------|-----------|-----------|
|                               | MRI         | IL        | P value   |
| Visualisation of TD           | 43/43 (100%)| 22/43 (51.1%)| < 0.001  |
| Visualization of uro-lymphatic fistula | 36/43 (83.7%)| 43/43 (100%)| < 0.001  |
Limitations and Future Directions
The limitation of the study is that it did not measure the pressure within the thoracic duct. Further researches are needed to assess the role of thoracic duct recanalization in the treatment of chyluria and to investigate the causes of narrowing and obstruction at the distal segments of the thoracic duct.

Conclusion
Spontaneous chyluria predominantly affected the left kidney. MR lymphangiography and intranodal lymphangiography revealed consistent findings across all patients, including reduced flow in the thoracic duct, dilation of lumbar branches, and presence of uro-lymphatic fistula branches.
Abbreviation
TD, Thoracic duct; MRL, Magnetic resonance lymphangiography; IL, Intranodal lymphangiography.

Informed Consent
Informed consent was obtained from patient in the study.

Disclosure
The authors report no conflicts of interest in this work.

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