BMC Medical Imaging

RESEARCH Open Access

The application of non-enhanced magnetic resonance thoracic ductography combined with magnetic resonance abdominopelvic scanning in the diagnosis of chylous leakage of the female reproductive system

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Abstract

Objective To explore the value of non-enhanced magnetic resonance thoracic ductography (NMRTD) combined with MR abdominopelvic scanning in the diagnosis of chylous leakage of the female reproductive system.

Methods A retrospective analysis was conducted on the multimodal imaging data from non-enhanced magnetic resonance thoracic ductography (NMRTD), direct lymphangiography (DLG), and abdominopelvic magnetic resonance imaging (MRI) for 18 female patients with reproductive system chylous leakage. Among these patients, 7 had vaginal chylous leakage, 10 had vulvar cutaneous chylous leakage, and 1 had both conditions.The rate of successful visualization of the thoracic duct, the consistency of the drainage directions of the outlet of the thoracic duct, and the degree of visualization of each segment of the thoracic duct by NMRTD and DLG were analyzed. A retrospective analysis was performed on the abnormal manifestations of abdominopelvic MR.

Results NMRTD had a significant advantage over DLG in terms of successful visualization of the thoracic duct (94.4% vs. 66.7%, $P=0.035$). The display of the drainage directions in the outlet area of the thoracic duct by the two methods showed excellent consistency (kappa value = 0.815) in 12 patients whose outlet areas were visualized by both methods. The degrees of visualization of the upper, middle, and lower segments of the thoracic duct in the NMRTD group were significantly greater than those in the DLG group (*P* values were 0.02, 0.00 and 0.00, respectively). All 18 patients (100%) showed dilatation of the lymph vessels in the pelvic cavity and retroperitoneum on abdominopelvic MR and DLG as well as pelvic perineal reflux or leakage on DLG. MR revealed multiple-site abnormalities that could not be detected by DLG, including multiple long T1 and long T2 lesions of the spleen in 8 patients (44.4%), of the

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subcutaneous in 7 patients (38.9%), of the bone in 6 patients (33.3%), perineal lymphedema in 18 patients (100%), and abdominopelvic effusion in 10 patients (55.6%).

Conclusion NMRTD combined with abdominopelvic MR has advantages in comprehensively evaluating the thoracic duct and multiple systemic abnormalities in patients with chylous leakage of the female reproductive system.

Keywords Non-enhanced magnetic resonance thoracic ductography, Direct lymphangiography, Vaginal chylous leakage, Vulvar cutaneous chylous leakage, Thoracic duct

Introduction

Chylous leakage of the female reproductive system including vaginal chylous leakage and vulvar cutaneous chylous leakage, is an extremely rare complication of lymphatic disorders. It can be observed in primary lymphatic malformations and may also be secondary to tumors, infections, trauma, surgeries, and other factors. Due to its complexity, rarity, and limitations in lymphatic imaging, only a few case reports currently exist [1–8], and comprehensive imaging studies on lymphatic system abnormalities in such patients, especially of the thoracic duct, are lacking. Moreover, the treatment of this condition is complex and may involve lymph-vein anastomosis and thoracic duct embolization. Therefore, exploring a safe, effective, and high-resolution lymphatic imaging method for the diagnosis and development of treatment regimens is particularly important. This study retrospectively analyzed the multimodal imaging data of 18 patients and aimed to investigate the value of non-enhanced magnetic resonance thoracic ductography (NMRTD) combined with abdominopelvic MR scans in patients with this disease. To the best of our knowledge, this study had the largest sample size and is the only study to simultaneously apply NMRTD and direct lymphangiography (DLG).

Information and methods

Patients

The data of 18 female patients with chylous leakage of the reproductive system who were treated from January 2010 to May 2024 in the Department of Lymph Surgery at Beijing Shijitan Hospital were retrospectively collected (the study was approved by Institutional Ethics Board of Beijing Shijitan Hospital No. IIT2024-059-001,and informed consent has been obtained from the legal guardians of all minor participants under the age of 16).All of these patients underwent NMRTD, DLG, and abdominopelvic MR.

Imaging methods

Nonenhanced magnetic resonance thoracic ductography(NMRTD)

Combined abdominal and pelvic scans were performed using a Philips Ingenia 3.0 T magnetic resonance scanner with a head coil combined with a partial coil with a 3D heavy T2-weighted water imaging sequence. The scanning parameters were as follows: TR 2500 ~ 3000 ms, TE550 ~ 600 ms, echo chain length 85 ~ 105, voxel size: 1.0 × 1.0 × 1.0 mm, and scanning field 36 (FH) × 30 (RL) × 99 (AP) cm. A total of 90 layers were collected, and 100 layers were collected for some obese patients. Two segments were collected covering the area from the root of the neck to the pelvic floor level.Postprocessing used maximum intensity projection MIP to obtain MRTD images.

Direct lymphangiography (DLG)

Three milliliters of methylene blue and 2% lidocaine mixture (ratio of 1:1) was injected between the roots of the dorsal toes of 1 to 3 of one foot, and the skin of the dorsal foot was incised under a microscope to look for blue-stained lymph vessels. After successful puncture, 8–15 ml of iodized oil (10 ml/tube, Guberbet Company, France) was injected at a rate of 4–10 ml/h, and the foot was dynamically observed under DSA for 1.5–4.0 h and selectively photographed.

Abdominopelvic MR

A Philips Ingenia 3.0 T magnetic resonance scanner was used, and a routine sequence of abdominal and pelvic plain scans was performed using body coils.

Image analysis

All the NMRTD, DLG and abdnimoplevic MR imaging data were reviewed by two radiologists with over 10 years of experience. If there was a disagreement, a consensus was reached under the guidance of a senior radiologist with 20 years of experience. The rates of successful visualization of the thoracic duct, the consistency of the drainage directions of the thoracic duct outlet, and the degree of visualization of each segment by the NMRTD and DLG were compared. The degree of visualization of the thoracic duct was evaluated as follows. The main thoracic duct was divided into three segments: lower, middle and upper [9]; the lower segment ranged from the diaphragmatic hiatus to the fifth thoracic vertebral body; the middle segment ranged from the lower border of the fifth thoracic vertebral body to the aortic arch; and the upper segment ranged from the aortic arch to the outlet of the thoracic duct. The scoring criteria for the degree

visualization of the thoracic duct were as follows [10]: 0 = invisible; 1 = partially visible (< 1/3); 2 = moderate visualization (1/3 to 2/3); 3 = good visualization (2/3, but part cannot determine its continuity); and 4 = fully continuously visible. Other observation indicators were as follows: lymphangiectasis; lymphatic reflux; abnormalities of the spleen, bones and subcutaneous soft tissues; lymphedema; and pleural and abdominopelvic effusions.

Statistical analysis

Statistical analysis was conducted using SPSS 26.0 software (IBM Corp., Armonk, NY, USA). The quantitative data are presented as the means ± standard deviations, and the qualitative data are presented as frequencies and percentages.

The chi-square test was used to evaluate the rates of successful visualization of the thoracic duct by NMRTD and DLG. This test is well - suited for comparing categorical data, allowing us to determine if there are significant differences between the two methods in terms of successful visualization rates, $P < 0.05$ indicated a statistically significant difference.

The Kappa test was used to evaluate the consistency of the drainage direction of the thoracic duct outlet shown by NMRTD and DLG.The Kappa value was used to indicate the degree of consistency, with specific ranges defined as extremely low (0-0.2), mild (0.21–0.4), moderate (0.41–0.6), high (0.61–0.8), and excellent (0.81-1). This approach provides a clear and objective measure of the agreement between the two imaging modalities.

Table 1 Patient characteristics

Variable	No. patients
Age (mean ± SD)	25.00 ± 11.62
Primary	17 (94.4%)
Secondary	1 (5.6%)
Location of reproductive system chylous leakage	
Vagina	7 (38.9%)
Vulva	11 (61.1%)
Vagina & Vulva	1 (5.6%)
Chylous vesicles	12 (66.7%)
Vulvar	12 (66.7%)
Left thigh	1 (5.6%)
Right foot	1 (5.6%)
Vulvar mass	1 (5.6%)
Lymphedema	18 (100%)
Perineum	18 (100%)
Lower extremity	8 (44.4%)
Unilateral	5 (27.8%)
Bilateral	3 (16.7%)
Chyluria	3 (16.7%)
Chylothorax	5 (27.7%)
Chylous ascites	10 (55.6%)

The Mann–Whitney test was used to compare differences in the degree of visualization of each segment of the thoracic duct by NMRTD and DLG. This is a non-parametric statistical test used when data doesn't meet parametric assumptions like normal distribution, it helps compare differences between two independent groups by ranking data points and analyzing the sum of ranks to determine if there's a significant difference.We set a significance level of $P < 0.05$, which indicates a statistically significant difference.

Results

Patient characteristics

18 patients were included, their ages ranged from 12 to 48 years, with an average of 25.00 ± 11.62 years. The disease history ranged from 1 to 28 years, with an average of 9.90 ± 5.76 years. Seventeen primary cases (94.4%) were diagnosed with generalized lymphatic anomalies (GLAs) according to the latest classification standard of the International Society for the Study of Vascular Anomalies [11], and in 1 patient (5.6%), the condition was secondary to a cesarean section. There were 7 patients (38.9%) with vaginal chylous leakage, 11 patients (61.1%) with multiple miliary vesicles on the vulva and rupturing with chylous leakage, and 1 patient (5.6%) with both. There were 12 patients (66.7%) with multiple miliary chylous vesicles on the vulva; among them, 1 patient (5.6%) had multiple vesicles on the left thigh, 1 patient (5.6%) had multiple vesicles on the right instep, and 1 patient (5.6%) had a large neoplasm of the vulva. All 18 (100%) patients had reproductive lymphedema, among which 8 (44.4%) had lower extremity lymphedema, 5 (27.7%) had unilateral lymphedema, and 3 (16.7%) had bilateral lymphedema. There were 3 patients (16.7%) with chyluria, 5 patients (27.7%) with chylothorax, and 10 patients (55.6%) with chylous effusion in the abdomen and pelvic cavity. The Patient characteristics are shown in Table 1.

NMRTD

Except for 1 patient with massive pleural effusion, the thoracic duct was successfully visualized in the remaining 17 (94.4%) patients. Significant dilation of the thoracic duct was observed in 6 patients (33.3%) (Fig. 1A and B), with the widest diameter ranging from 0.8 to 1.5 cm. The outlets of the thoracic ducts drained into the left jugulovenous angle in 10 patients and 1 patient had a completely right-sided thoracic duct that drained into the right side (Fig. 1C), and 6 patients had thoracic ducts that drained bilaterally.

DLG

The thoracic duct was successfully visualized in 12 patients (66.7%), all of whom had different degrees of outlet obstruction. The outlets of the thoracic ducts drained

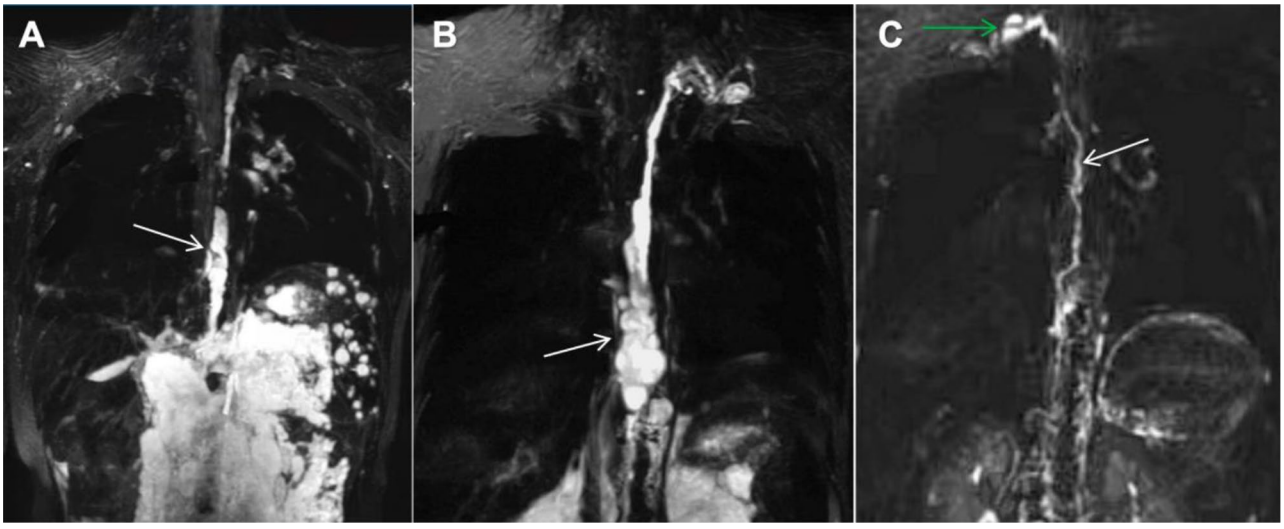

Fig. 1 NMRTD images. **A**-**B**, the thoracic ducts were clearly visualized and dilated (white arrow). **C**, NMRTD showed a completely right-sided thoracic duct (white arrow) that drained into the right venous angle (green arrow)

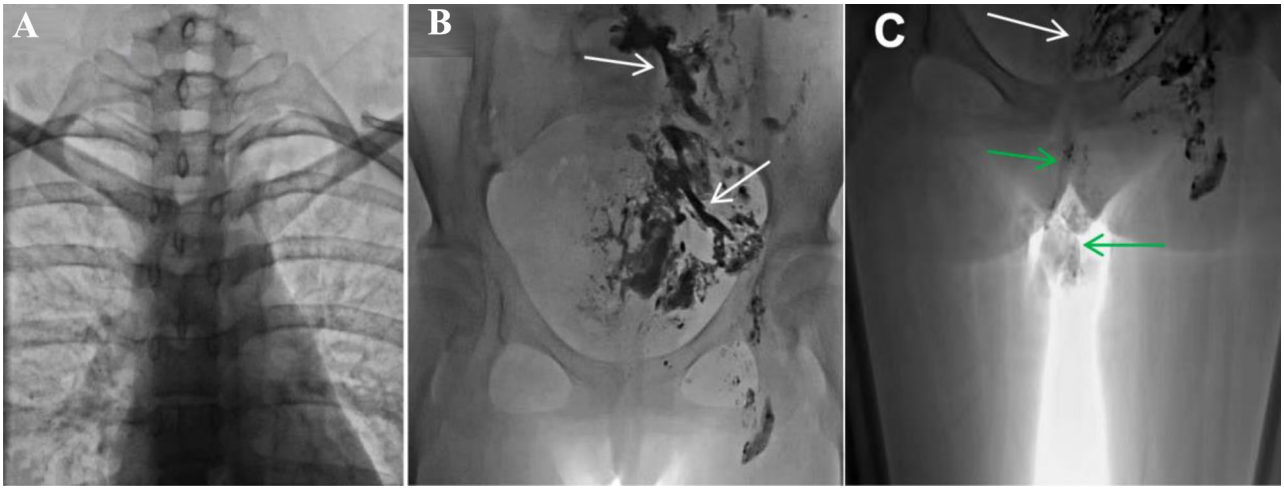

Fig. 2 DLG images. **A**, young woman with vaginal chylous leakage for10 years, who was the same girl of Fig. 1A. A, the thoracic duct was not visualized on DLG; **B**-**C**, a large number of tortuous, dilated and disordered lymphatic vessels were shown in the pelvis (white arrows), and the contrast agent could been seen leaking from the vagina(green arrows)

into the left juglovenous angle in 9 cases; in 2 patients, it drained bilaterally, and 1 patient had a completely right-sided thoracic duct that drained into the right juglovenous angle, which was consistent with NMRTD.

All 18 patients (100%) had pelvic and retroperitoneal lymph vessel dilation and pelvic perineal reflux or leakage,5 patients (27.7%) had difficulty in contrast agent ascending, even after deep breathing, massaging the groin and repeated movement of the lower limbs, it still stopped at the level of the 3rd lumbar vertebra to the 11th thoracic vertebra, which led to failure of visualization of the thoracic duct and its outlet area (Fig. 2). A large amount of reflux was observed in the huge soft tissue mass of the vulva. Renal reflux ocurred in 3 patients (16.7%), and lower limb and abdominal wall reflux occurred in 4 patients (22.2%).

Abdominopelvic MR

The abdominopelvic MR images of 18 patients (100%) revealed pelvic and retroperitoneal lymph vessel dilation, tortuosity, and disorder, among which 8 patients (44.4%) had uterus and vagina involvement (Fig. 3A and B), 1 patient (5.6%) had a very large soft tissue mass in the vulva, and multiple earthworm-like nourishing lymph vessels were connected to the mass from the bilateral iliac regions (Fig. 3C and D). Abnormal signals of circular long T1 and long T2 (multiple lymphangiomas) at multiple sites, including 8 patients (44.4%) with lesions in the spleen),7 patients (38.9%) with lesions in the abdominal

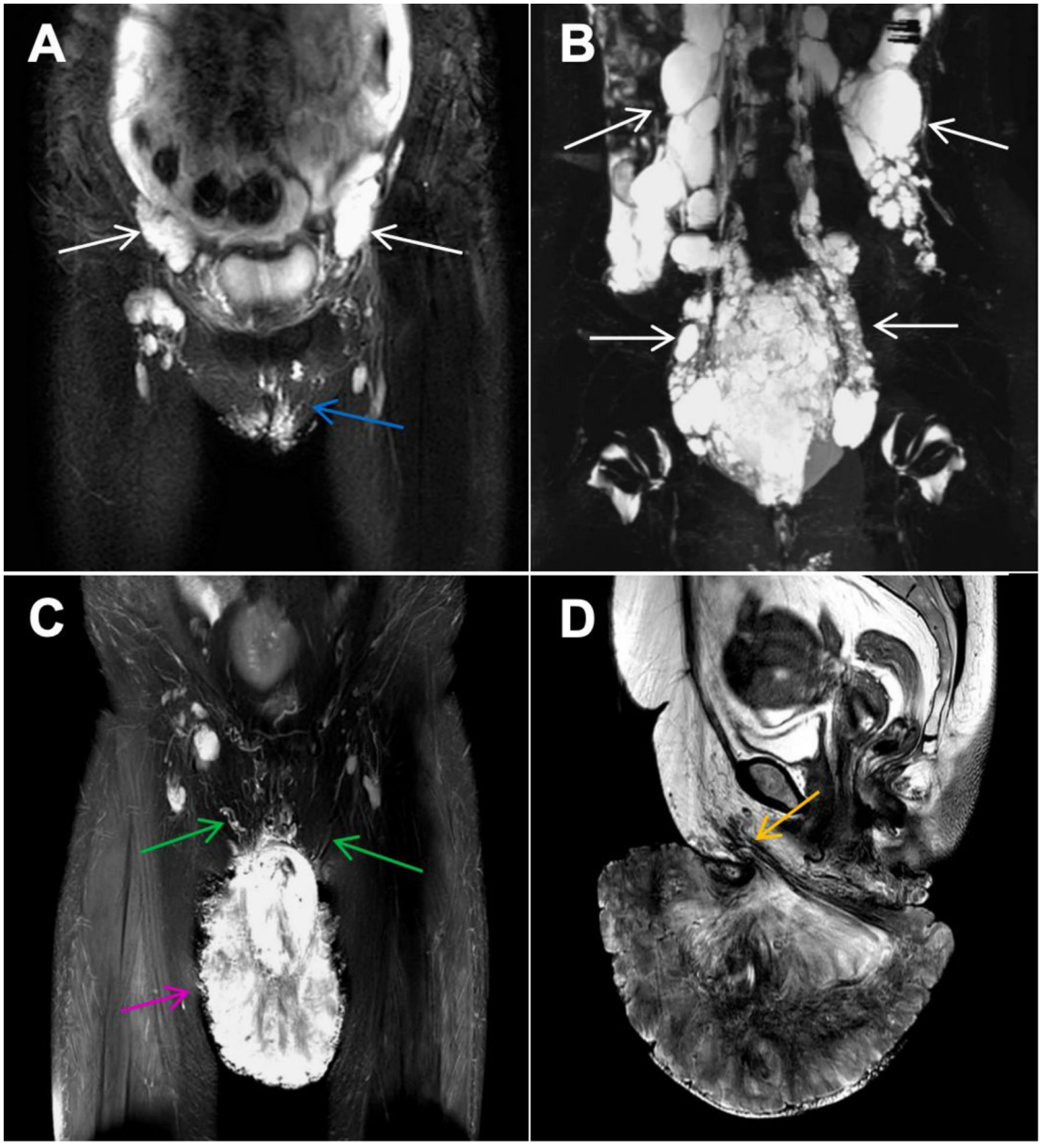

Fig. 3 MRI images. **A**-**B**, MRI coronal views showed multiple cystic dilated lymphatic vessels in the abdominopelvic region (white arrows), tortuous and dilated lymphatic vessels in labia(blue arow). **C**-**D**, a middle-aged woman had a gradually enlarged soft tissue mass in the vulva accompanied by multiple vesicles and chylous leakage for 15 years after cesarean section. MRI coronal view showed a huge soft tissue mass(pink arrow) in the vulva with multiple earthworm-like nourishing lymphatic vessels (green arrows). MRI sagittal view showed the mass originated from the vulva(orange arrow)

wall, 3 patients (16.7%) with lesions in the labia), and 6 patients (33.3%) with lesions in the bone were found (Fig. 4). Perineal lymphedema was observed in 18 (100%) patients, who presented with swelling and thickening of subcutaneous soft tissues with a characteristic grid, patch-like long T2 signal. Pelvic effusion was found in 10 patients (55.6%).

Statistical results

MRTD had a significant advantage over DLG in terms of successful visualization of the thoracic duct (94.4% vs. 66.7%, $P = 0.035$; Table 2). The display of the drainage directions in the outlet area of the thoracic duct by the two imaging methods showed excellent consistency (kappa value = 0.815, Table 3). The degrees of visualization of the upper, middle, and lower segments of the thoracic duct by NMRTD were significantly greater than

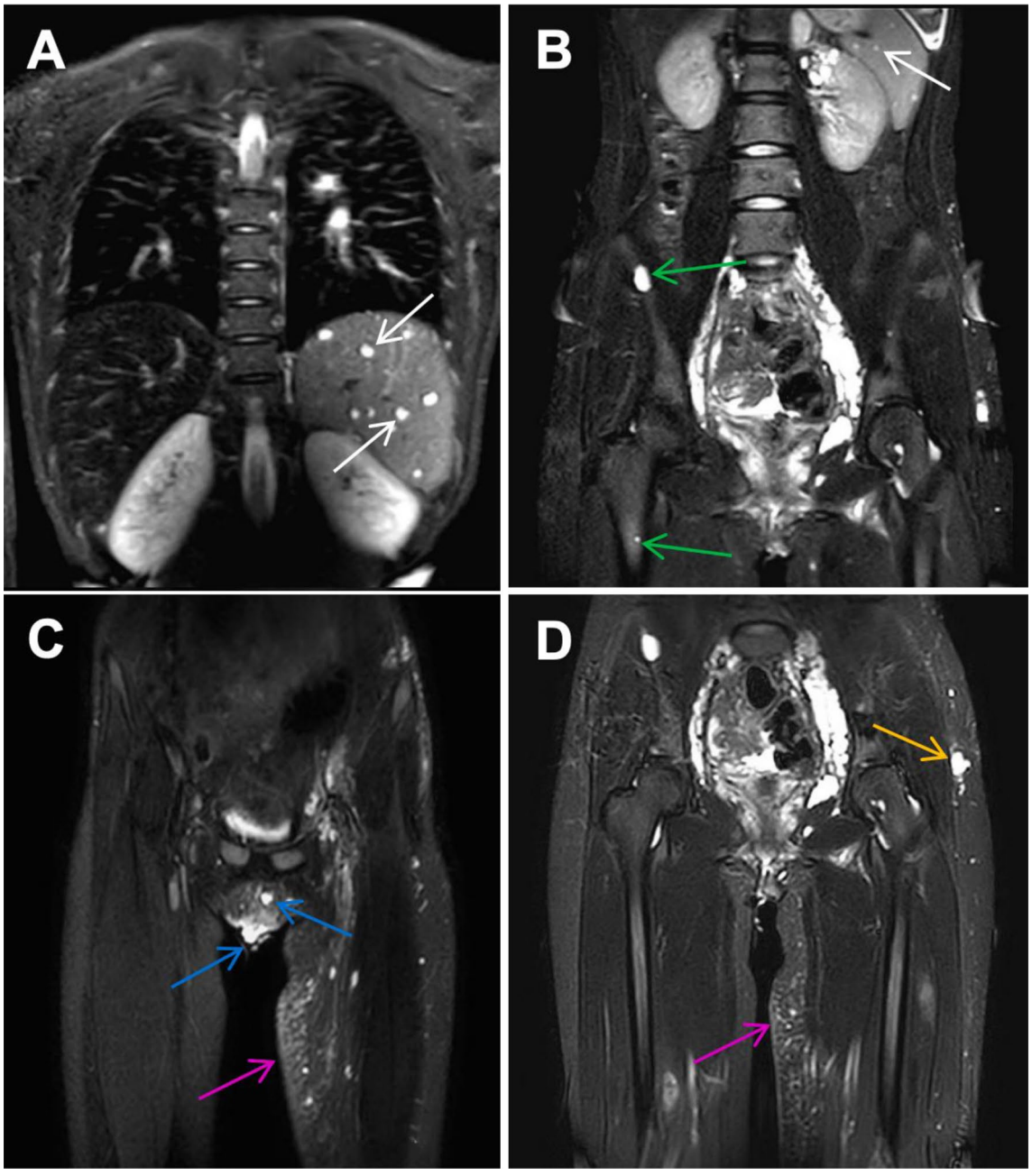

Fig. 4 MRI images. **A**-**D**, MRI coronal view showed multiple lymphangiomas of the spleen(white arrow), right ilium and femur(green arrows), labia(blue arrows), and the left pelvic subcutaneous(orange arrows); **C**-**D**, lymphoedema of the left thighs can be seen(pink arrows)

Table 2 Rates of successful visualization of the thoracic duct by NMRTD and DLG

		Method(%)		Numbers	χ2	*p*
		NMRTD	DLG			
Result	0*	1 (5.56)	6 (33.33)	7 (19.44)	4.433	0.035
	1*	17 (94.44)	12 (66.67)	29 (80.56)		
Total		18	18	36		

0*Failed, 1*Successful

Table 3 Consistency test of the drainage directions of the thoracic duct outlet between the NMRTD and DLG

	NMRTD	DLG	Kappa value	*P*
Left	8	9		
Right	1	1		
Bilateral	3	2	0.815	0.000
Total*	12*	12*		

Total*There were 12 patients whose the outlet area of the thoracic duct were visualized by both imaging methods

Table 4 The score of the degree of visualization of each segment of the thoracic duct by MRTD and DLG

Section of the thoracic duct	Method		The z value of the Mann - Whitney test statistic	*P* value
	MRTD (*n* = 18)	DLG (*n* = 18)		
Upper	4.00 (1.75, 4.00)	1.5. (0.00, 2.00)	-3.051	0.002
Middle	4.00 (3.00, 4.00)	2.00 (0, 3.00)	-3.956	0.000
Lower	4.00 (3.75, 4.00)	3.00 (1.00, 3.00)	-3.741	0.000

those by DLG (P values were 0.02, 0.00 and 0.00, respectively; Table 4).

Discussion

The thoracic duct is the longest central lymph vessel in the whole body, with an average diameter of approximately 1.3 mm (range, 0.5–2.0 mm) [12]. The thoracic duct plays a crucial role in the lymphatic circulation; it collects approximately three-quarters of the lymph fluid from the whole body, with the exception of the right upper limb, right chest, and right head and neck, and it drains into the junction of the left subclavian and internal jugular veins [13]. Accurate evaluation of the thoracic duct is very important for understanding pathological lymphatic abnormalities in patients with chylous leakage of the female reproductive system, making preoperative assessments, and developing treatment plans. However, due to the concealed course and small diameter of the thoracic duct, imaging is challenging.

DLG is a traditional lymphatic imaging technique that is helpful for detecting macroscopic abnormalities such as reflux, dilation, and obstruction [14]. However, DLG relies on contrast agents and is an invasive technique; moreover, it has low resolution and is insufficient to provide a precise evaluation of the central lymph vessels. NMRTD uses heavy T2-weighted water imaging technology, it does not require contrast agents, and it is noninvasive, with high resolution, good repeatability, and a short examination time [15–17]. This method provides the possibility for accurate evaluation of the thoracic duct.

In this group of patients, the rate of visualization of the thoracic duct and the degree of visualization of each segment of the thoracic duct by NMRTD were notably superior group than by DLG. There are some reasons we think explain this difference. First, in this group of patients, there was significant lymphangiectasis, chyle reflux, and chylous leakage in the retroperitoneum and pelvic cavity, as well as lymphedema of the perineum and lower limbs; this led to the dilution and retention of contrast agents, resulting in a relative scarcity of contrast agent, which in turn caused failure to visualize the thoracic duct and its outlet. Multiple MR lymphangiography studies [15, 18–19] employing contrast agents have also revealed failure of thoracic duct visualization due to significant reflux and lymphedema. Second, DLG identified a high proportion of thoracic duct outlet obstruction in this group of patients, and the dilation of the thoracic duct observed by NMRTD may also be related to it, which may lead to high pressure in the thoracic duct, making it difficult for contrast agents to enter. Finally, although the mechanism underlying spontaneous contraction of lymph vessels is not fully understood, the theory that smooth muscle cell contraction of the lymph vessel walls is one of the main driving forces of lymphatic fluid reflux has been widely recognized [20]. Given that most patients in this study had GLA, it is worth further exploring whether there are congenital functional abnormalities of the smooth muscle in the lymph vessel. We believe that the superposition of the above reasons could have led to the failure to visualize the thoracic duct and its outlet area by DLG.

It has been reported that 92–95% of the thoracic ducts in the normal population drain into the left venous angle, approximately 2–3% drain into the right side, and approximately 1.0–1.5% have bilateral drainage [21]. We noticed that in many studies involving abnormal lymphatic circulation, there is a relatively high rate of variation in the thoracic duct [22, 23], which is also consistent with our research. Our study revealed that the evaluation of the drainage direction at the outlet of the thoracic duct by NMRTD was highly consistent with that of DLG, which is recognized as the gold standard. This finding was confirmed by exploring the thoracic duct in all 12 patients. NMRTD plays a vital role in the development of surgical plans, such as lymphatic–venous anastomosis involving the thoracic duct outlet area, and in the prevention of surgical accidents [24, 25].

Most patients in this group had GLA, which often involves multiple lymphatic abnormalities, including lymphangiectasia, chyle reflux in the pelvic cavity and retroperitoneum, lymphangiomas at multiple sites, and obstruction of the thoracic duct [26, 27]. In our study, DLG revealed a relatively high rate of obstruction at the outlet of the thoracic duct. Moreover, the dilation of the thoracic duct observed in multiple cases by NMRTD also suggested a high rate of obstruction. This exacerbates the pressure of the lymphatic circulation in the pelvic

cavity. The pelvic cavity, particularly the uterus, vagina, and perineum, are characterized by extensive lymphatic drainage. Due to the influence of gravity, these regions are subjected to relatively high lymphatic circulation pressure and obstructions of the thoracic duct, which aggravate this pressure, causing lymphatic reflux, dilation and proliferation of lymph vessels in the uterus, vagina and perineum, and eventually leading to chylous leakage.

Multiple chylous vesicles were found in the vulva of 12 patients; these vesicles are called localized lymphangioma circumscriptum (LC), and they are caused by the abnormal proliferation of lymph vessels in the deep dermis and subcutaneous tissue [28]. When they are ulcerated, a lymphocutaneous fistula forms, and repeated local chylous stimulation and lymphoid tissue proliferation can lead to local skin polypoid hyperplasia, which was confirmed by postoperative pathology of patients with vulvar masses in this group.

MR is an important imaging method for evaluating and classifying lymphatic malformations [29]. In our study, abdominopelvic MR revealed multiple lymphatic abnormalities in the uterus, vagina, spleen, subcutaneous and bone, as well as abdominal and pelvic effusion, etc., which could not be visualized by DLG. In patients with a vulvar mass, MR clearly showed the nourishing lymph vessels, which provides an important basis for preoperative diagnosis and surgery. Lymphedema, which is a specific manifestation of lymphatic circulation disorders, was present in 100% of the patients in this group, and MR was able to clearly reveal the scope of lymphedema, which is very important for further research on lymphedema staging and lymphatic reflux function [30–32].

Our study has certain limitations. Firstly, the disease is rare, and the sample size of this study was relatively small. Moreover, as a static morphological imaging technique, NMRTD lacks dynamic information regarding lymphatic reflux. Therefore, in future research, it is necessary to further expand the sample size and enrich the research on multimodal imaging.

NMRTD provides a noninvasive, safe and efficient imaging method for visualizing the thoracic duct and its outlet area [33–36] by using a heavy T2-weighted sequence, independent of contrast agent, independent of retroperitoneal and pelvic lymphatic reflux, lymphangiectasia, chylous leakage, lymphedema of the lower limbs, etc. When it combined with abdominopelvic MR, NMRTD can be used to comprehensively and accurately evaluate the morphological information of lymphatic system abnormalities in patients with chylous leakage of the female reproductive system, and this approach plays a key role in the comprehensive evaluation and management of patients, especially provides important guidance for subsequent surgical treatments those involving the thoracic duct and its outlet area.We recommend that NMRTD combined with abdominopelvic MR should be considered to incorporated into the diagnosis and treatment routines for these patients.The expert consensus of multidisciplinary evaluation of complicated lymphatic anomalies (CLAs) [37] suggested that whole-body MR was the first choice for CLA. We recommend that NMRTD combined with abdominopelvic MR should be included in the diagnosis and treatment of female patients with chylous leakage of the reproductive system.

Abbreviations

NMRTD	Nonenhanced magnetic resonance thoracic ductography
DLG	Direct lymphangiography

Acknowledgements

This work was supported by the National Natural Science Foundation of China (61876216).

Author contributions

(I) Conception and design: M Huo, YL Yue, RG Wang; (II) Administrative support: CY Zhang, L Li, JF Xin; (III) Provision of study materials or patients: XP Li, YM Zhang, MX Zhang, Y Sun; (IV) Collection and assembly of data: L Sun; (V) Data analysis and interpretation: M Huo, YL Yue, CY Zhang, L Li; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Funding

This work was supported by the National Natural Science Foundation of China (61876216).

Data availability

All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and was approved by Institutional Ethics Board of Beijing Shijitan Hospital No. IIT2024-059-001,and informed consent has been obtained from the legal guardians of all minor participants under the age of [16].

Consent for publication

The results/data/figures in this manuscript have not been published elsewhere, nor are they under consideration (from you or one of your Contributing Authors) by another publisher.

Competing interests

The authors declare no competing interests.

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Received: 19 January 2025 / Accepted: 24 April 2025
Published online: 03 May 2025

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