

# Evaluation of Cervical Thoracic Duct Exploration in Idiopathic Chyluria: A Retrospective Comparative Study

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**Purpose:** The purpose of this study is to evaluate a novel surgical method for idiopathic chyluria.

**Methods:** Data from 63 patients with idiopathic chyluria who underwent direct lymphangiography (DLG) were retrospectively analyzed. Of these, 50 patients received cervical thoracic duct exploration (CTDE) as a treatment, while 13 were managed with a low-fat diet. The treatment efficacy of the two groups was compared, and a univariate analysis of the CTDE treatment effect was performed.

**Results:** DLG revealed that the contrast agent passed upwards and outwards through paravertebral lymphatics into the region of the renal hilum and pelvis (left: 38.10%; right: 33.33%; bilateral: 28.57%). Dilatation of retroperitoneal lymphatics was found in 90.47% of cases. Additionally, 47.6% of patients demonstrated contrast agent reflux into lymphatic trunks in the neck (the percentage of contrast agent reflux to the jugular trunk, subclavian trunk, and broncho-mediastinal trunk being 28.57%, 38.09%, and 6.34%, respectively). The effective rate in the CTDE group was higher than in the low-fat diet group ( $\chi^2 = 5.893$ ,  $p=0.015$ ). Univariate analysis of the patients who underwent CTDE demonstrated that younger age ( $p=0.036$ ) and Grade III chyluria were risk factors for ineffective treatment, while patients with Grade I had better treatment outcomes ( $p=0.029$ ).

**Conclusion:** Obstruction of the cervical thoracic duct may be a significant cause of idiopathic chyluria. Alleviating this obstruction may be an effective treatment strategy for idiopathic chyluria.

**Plain Language Summary:** Dr Xin's team wanted to find a better way to help patients with idiopathic chyluria—a condition where milky fluid (called chyle) leaks into urine for unknown reasons. Current treatments like low-fat diets often do not fully solve the problem. The team suspected blockages in lymph vessels might be the cause, especially in the neck area. First, they used a special X-ray technique (Direct Lymphangiography) to examine the lymphatic system of the patients. They found that almost all people in the study had dilated retroperitoneal lymphatics (90.47%) and about half (47.6%) had contrast agent reflux to cervical lymphatic trunks. Then, they compared two treatments: A low-fat diet (the usual approach) and Cervical Thoracic Duct Exploration (CTDE), a surgery to find and fix blockages in key lymph vessels in the neck. Finally, they found that the surgery (CTDE) was significantly more effective at stopping the idiopathic chyluria than the low-fat diet management. They also found that people with milder symptoms (Grade I) especially benefited from the surgery, and younger people and those with more severe symptoms (Grade III) generally had a harder time getting better, regardless of treatment. These Results Mean: 1. Blockages in Cervical Thoracic Duct are a key cause of the idiopathic chyluria. 2. Surgery (CTDE) to alleviate these blockages is a promising new treatment, offering better results than just low-fat diet control. 3. This surgery could be especially helpful for people with milder symptoms. 4. The findings give doctors a clearer target for treatment and offer new hope to people who have not found relief with diets alone.

**Keywords:** chyluria, idiopathic, thoracic duct, direct lymphangiography, DLG, lymphovenous anastomosis, LVA

## Introduction

Chyluria is a rare condition marked by the presence of chyle in the urine. The exact incidence of this disorder remains unknown, as the existing literature primarily comprises case reports and small case series.<sup>1</sup>

The etiology is the parasitic infection by *Wuchereria bancrofti* in 95% of the cases found in tropical and subtropical areas.<sup>2</sup> Non-parasitic causes, by contrast, are extremely rare. Trauma, surgery, malignancy, radiation, pregnancy, and renal or bladder lymphangioma have been reported as non-parasitic causes of chyluria.<sup>3</sup>

Currently, management of chyluria consists of conservative treatments and surgical measures. Conservative treatments, including rest, low-fat diet, extracorporeal ultrasound-guided high intensity focused ultrasound, and medication, can be used for mild chyluria.<sup>4,5</sup> Goyal et al reported success rate of 70.3% at mean follow-up of 25-months for conservative management of chyluria.<sup>6</sup> On the contrary, Okamoto observed a cure rate of only 15% and partial improvement in 23% for conservatively treated patients of chyluria.<sup>7</sup>

Surgical management is indicated for patients with refractory or severe chyluria who have failed to respond to conservative treatment. Currently, a variety of surgical options are available, including sclerotherapy,<sup>2</sup> nephrectomy,<sup>8</sup> lymphovenous anastomosis (LVA), and renal pedicle lymphatic ligation.<sup>9</sup>

Sclerotherapy entails the instillation of sclerosing agents, such as silver nitrate, povidone-iodine, or radiographic contrast media, into the renal pelvis. This minimally invasive technique attains an initial success rate of around 70–80%.<sup>1</sup> Nevertheless, the long-term recurrence rate remains high, nearing 50%.

LVA is a microsurgical technique aimed at redirecting lymphatic drainage and reducing intralymphatic pressure. The long-term success of this procedure largely depends on the maintenance of anastomotic patency, with reported failure rates reaching approximately 14%.<sup>10</sup> Despite its theoretical advantages, the clinical application of LVA in the treatment of chyluria has declined in recent years. This trend is largely attributable to the relatively high rate of postoperative recurrence and the growing adoption of laparoscopic and robotic approaches, which provide better outcomes and less invasiveness.

A treatment modality analogous to LVA is thoracic duct stenting, although this approach has primarily been described in isolated case reports. Cuong et al<sup>11</sup> reported a case of chyluria caused by stenosis or obstruction at the junction between the thoracic duct and the subclavian vein. The patient was successfully treated with percutaneous thoracic duct stent placement, which restored lymphatic drainage and resolved the chyluria. Similarly, Hoa et al<sup>12</sup> initially achieved remission of chyluria with thoracic duct stenting; however, recurrence occurred four months later due to in-stent occlusion, underscoring the potential limitations of this technique.

In addition to endolymphatic procedures, renal pedicle lymphatic vessel ligation has emerged as a more commonly applied therapeutic approach. Early reports by Hemal and Gupta et al<sup>13</sup> demonstrated that retroperitoneoscopic renal pedicle lymphatic disconnection achieved complete resolution of chyluria in all treated ipsilateral renal units. Nevertheless, recurrence from the contralateral renal unit was observed in two patients at 1 and 9 months postoperatively. More recently, Wang et al<sup>9</sup> reported a series of 52 patients who underwent renal pedicle lymphatic ligation; of these, 49 experienced long-term remission during a follow-up period ranging from 3 to 152 months, whereas 3 patients showed no therapeutic response. Although this surgical method appears effective, it carries inherent risks of injury to adjacent anatomical structures, including the ureter, renal artery, and renal vein.

Previous research has predominantly concentrated on parasitic chyluria, whereas investigations focusing specifically on idiopathic chyluria remain relatively limited.<sup>14,15</sup>

Idiopathic chyluria, a type of non-parasitic chyluria, is attributed to congenital or acquired anatomical abnormalities of the urinary lymphatic system.

In this study, we detail our surgical procedure—The Cervical Thoracic Duct Exploration (CTDE)—and report on our 15 years of experience using this method to treat idiopathic chyluria.

## Materials and Methods

### Patients

The data of patients with idiopathic chyluria who received DLG in our department from June 2007 to December 2018 were reviewed. The inclusion criteria were as follows: a diagnosis of chyluria or recurrent chyluria based on urinary tests

positive for chylomicrons and triglycerides ( $>15\text{mg/dl}$  or  $0.169\text{mmol/L}$ )<sup>2</sup>, negative filarial antigen testing, and patients who underwent DLG. The exclusion criteria were the diagnosis of any primary renal diseases, such as tumors, nephrotic syndrome, active renal tuberculosis, and inflammatory renal diseases; any secondary chyluria, such as post-nephrectomy chyluria, iatrogenic chyluria, and parasitic chyluria; and any other lymphatic disorders, such as lymphedema, chylothorax, and chylous ascites.

A total of 63 patients (36 females and 27 males; median age: 53 years; age range: 9–77 years) were enrolled in the study. The duration of chyluria ranged from 1 month to approximately 50 years, with the age at onset varying between 4 and 65 years. According to the established grading system for chyluria,<sup>16</sup> 25 patients were classified as Grade I, 20 as Grade II, and 18 as Grade III.

Some patients already received treatment prior to hospitalization: 7 patients underwent laparoscopic ligation of renal hilar lymphatics, 2 patients underwent LVA in the inguinal region, 4 patients received silver nitrate instillation, and 9 patients were put on a long low-fat diet. The remaining 41 patients did not have any pre-hospitalization treatment.

This retrospective study was approved by the Ethics Committee of Beijing Shijitan Hospital (approval number: sjtky11-1x-2022(047)). The requirement for informed consent was waived due to the retrospective nature of the study and the use of anonymized data, in accordance with institutional and national ethical guidelines. The study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments.

## DLG

One foot was selected as the injection site of the contrast agent—lipiodol (Guerbet, France). With Innova 2100-IQ digital flat-panel angiography system (GE, United States), the cardiac mode was selected to dynamically collect images. A total of 8–20 mL of lipiodol was infused into the lymphatic vessel at a rate of 4–6 mL/h. The following images were obtained: the structure of retroperitoneal lymphatic vessels, abnormal reflux pathways, and compensatory pathways. All images were reviewed by two surgeons with more than 10 years of experience independently.

## CTDE

CTDE is a novel procedure performed based on a preoperative diagnosis of thoracic duct obstruction, as confirmed by DLG. The primary objective of this technique is to improve chyle return at the cervical thoracic duct, hereby reducing pressure within the retroperitoneal lymphatic system and preventing chyle reflux into the kidneys.

The operation typically lasts approximately one hour, with an estimated blood loss of 5–10 mL. Potential complications include injury to the recurrent laryngeal nerve, damage to the internal jugular vein or common carotid artery, and postoperative venous thrombosis.

The surgical procedure is performed as follows: A transverse incision was made above the clavicle to reveal the internal jugular vein and the venous angle, where the thoracic duct or right lymphatic duct was identified.

## Treatment Effectiveness Evaluation

If the triglyceride in three random urine tests exceeds  $1.25\text{ mmol/L}$ , the treatment is deemed ineffective. Conversely, if the triglyceride in three random urine tests falls below  $1.25\text{ mmol/L}$ , or if the patient reports the absence of cloudy urine or white clumps, the treatment is considered effective.

## Statistical Analysis

Data were described by absolute (n) and relative (%) frequencies, median (IQR), mean, and standard deviation. Continuous variables were compared using a two-tailed *t*-test. Nominal variables were compared using the Fisher's exact test or Likelihood Ratio Chi-Square test. All statistical analyses were conducted with SPSS (IBM SPSS Statistics Version 20). A *p*-value  $< 0.05$  was considered statistically significant.

## Results

### DLG

DLG was successfully performed in all patients. The lymphatic system was visualized from the iliac to the cervical portion of the thoracic duct either continuously or discontinuously. Sixty-two patients had a thoracic duct in the left chest, whereas one patient had a right-sided thoracic duct.

### Retroperitoneal Lymphatic Vessels

Contrast agent reflux into renal lymphatics was found in all 63 cases (Figures 1 and 2), of which 24 were left renal reflux, 21 were right renal reflux and 18 were double renal reflux.

Fifty-seven patients (90.5%) were found to have dilatation of retroperitoneal lymphatic vessels in which contrast agent flowed in both directions (Figure 1). Six patients (9.5%) had no dilatation of retroperitoneal lymphatics (Figure 2).

### Lymphatic Reflux

Contrast agent reflux into the lymphatic trunks in the left neck was observed in 30 patients (47.6%), with the percentages of contrast agent reflux to the jugular trunk, subclavian trunk, and broncho-mediastinal trunk being 28.57%, 38.09%, and 6.34%, respectively. (Figures 3 and 4, Table 1). Retroperitoneal lymphatic vessels were dilated in all these 30 patients. The number of patients with Grade III chyluria was significantly higher among those with lymphatic trunk reflux in the neck compared to those without reflux, while the number of patients with Grade I chyluria was significantly lower among those with lymphatic trunk reflux in the neck ( $p=0.029$ ). (Table 2).

### Compensatory Pathways

Eight patients (12.7%) were found to have contrast agent influx into the right neck via compensatory pathways of the thoracic duct (Figure 5). Among these cases, one demonstrated a compensatory pathway originating from Level T3, two from Level T5, and five from Level T6.

### CTDE

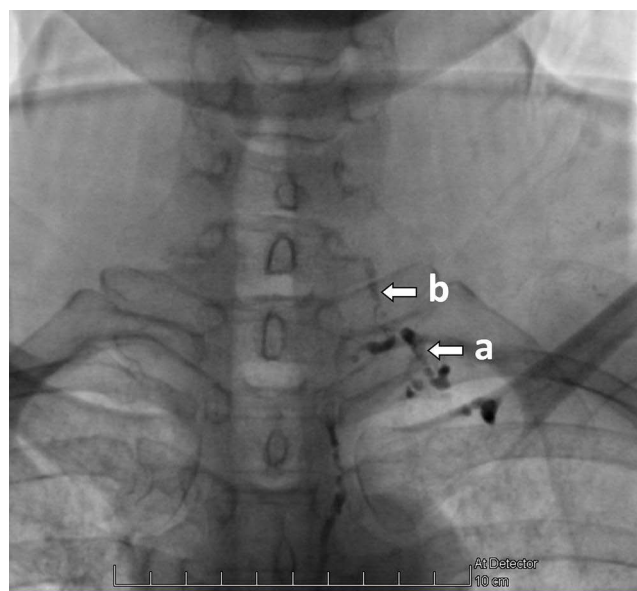
Fifty patients with retroperitoneal lymphangiectasia and/or contrast agent regurgitation in the cervical lymphatic trunks underwent CTDE. Additionally, 13 patients were managed conservatively with a low-fat diet due to limited willingness to comply with physician-recommended interventions. Various degrees of obstruction were observed in the cervical



**Figure 1** A 55-year-old female patient with chyluria for 6 months. Tortuosity and dilatation of abnormal retroperitoneal lymphatic vessels (a). Lipiodol refluxes into the renal lymphatics on the left side (b).



**Figure 2** A 66-year-old female patient with chyluria for 30 years. Lipiodol refluxes into the renal lymphatics on the right side (a) and left side (b). Non-dilation of retroperitoneal lymphatic vessels (c).

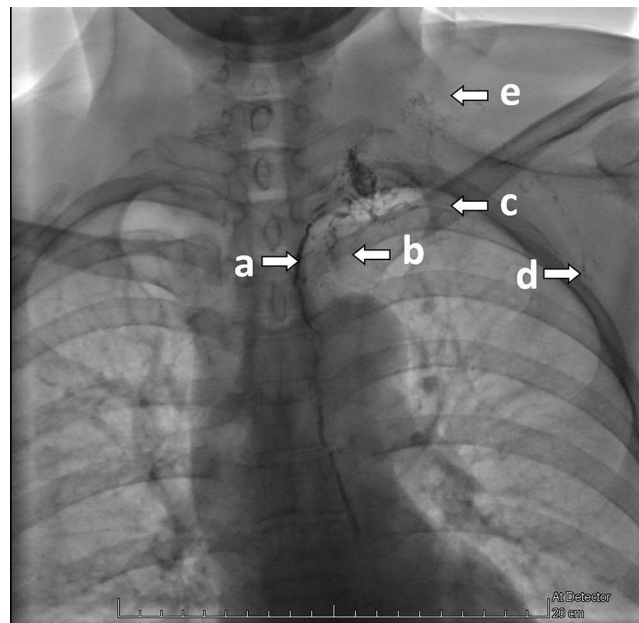


**Figure 3** A 58-year-old female patient with chyluria for 2 months. The cervical portion of the thoracic duct (a). Lipiodol refluxes through the left jugular trunk (b).

thoracic duct and the right lymphatic duct. The causes of obstruction include compression on the cervical thoracic duct by surrounding dense fibrous connective tissue, carotid artery sheath, lymphocele, hemangioma, blood vessels (including transverse cervical vein, vertebral vein, internal jugular vein, communicating veins, suprascapular artery), and abnormal development of the cervical thoracic duct (Figure 6 and Table 3). These factors impeded the return of chyle to the venous stream. We excised the obstructive tissues to restore and enhance the flow of chylous fluid into the veins.

### Follow-Up Result

A median follow-up period of 8 years (mean: 6.75 years; range: 5–15 years) was conducted for 55 out of 63 patients through outpatient visits, inpatient reviews, or telephone follow-ups. Among these, 44 patients received CTDE treatment, while 11 were treated with a low-fat diet. Among the 11 patients treated with the conservative low-fat diet, 2 (18.2%) achieved clinical improvement. In contrast, of the 44 patients treated with CTDE, 26 (59.1%)



**Figure 4** A 61-year-old female patient with chyluria for 40 years. Thoracic duct(a). Lipiodol refluxes through the left broncho-mediastinal trunk (b). Lipiodol refluxes through the left subclavian trunk (c). Lipiodol refluxes through the left subclavian trunk to the axillary region (d). Lipiodol diffuses in the lymphatics of the left neck (e).

demonstrated positive outcomes, with the difference being statistically significant ( $\chi^2 = 5.893, p = 0.015$ ). Table 4 presents the factors affecting the therapeutic effect of CTDE. Age and grade are key factors influencing prognosis, with p-values of 0.036 and 0.029, respectively.

**Table 1** Characteristics of Lymphatic Reflux on Direct Lymphangiography

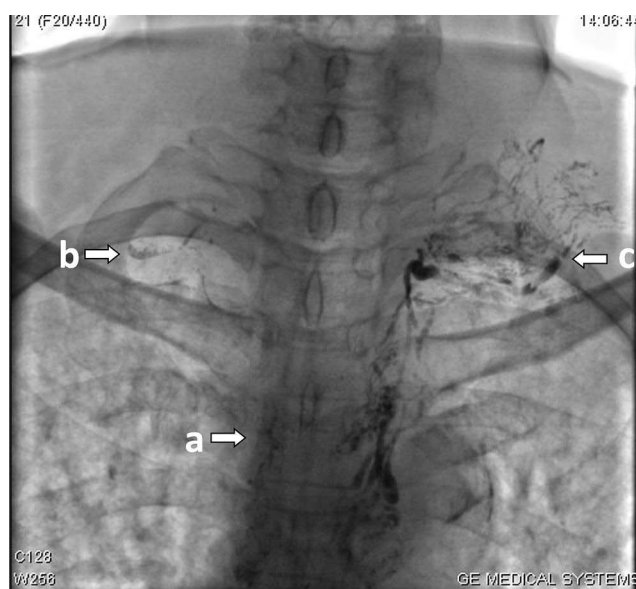
The site of Lymphatic Reflux	Number (%) of Patients
Lymphatic trunks in the neck	30(47.6)
Jugular trunk	4(6.3)
Subclavian trunk	8(12.7)
Broncho-mediastinal trunk	1(1.6)
Jugular trunk and Subclavian trunk	14(22.2)
Subclavian trunk and Broncho-mediastinal trunk	2(3.2)
Jugular trunk and Subclavian trunk and Broncho-mediastinal trunk	1(1.6)

**Table 2** Comparison of Clinical Manifestations and Chyluria Severity Between Patients With and Without Lymphatic Trunk Reflux

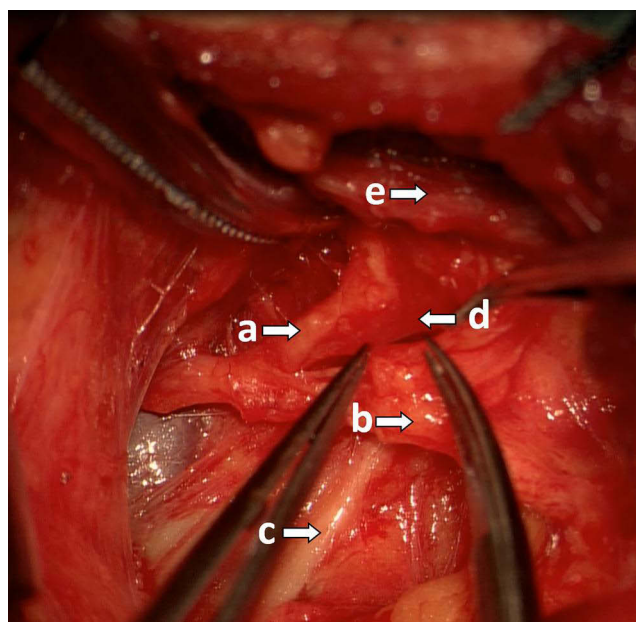
	Lymphatic Trunk Reflux (n=30)	Non-Lymphatic Trunk Reflux (n=33)	P value
Gender ratio (M/F)	13/17	14/19	1.000*
Age (years)	53.70±16.30	49.27±19.95	0.342**
Disease course (months)	159.56±164.67	188.24±186.03	0.521**
Grade			0.029***
Grade I	8(26.7)	17(51.5)	
Grade II	9(30.0)	11(33.3)	
Grade III	13(43.3)	5(15.2)	

**Notes:** Data are presented as mean ± standard deviation or number of patients (%). \*P value calculated using Fisher's exact test. \*\*P value calculated using independent-sample t-test. \*\*\*P value calculated using likelihood ratio chi-Square test.

**Abbreviations:** M, male; F, female.



**Figure 5** A 74-year-old male patient with chyluria for 50 years. The compensatory pathways starting from Level T6(a). Lipiodol diffuses through compensatory lymphatics to the right neck (b). Lipiodol diffuses in the left neck (c).



**Figure 6** A 50-year-old female patient with chyluria for 10 years. Thoracic duct (a). The left jugular trunk containing refluxed chyle (b). The left subclavian trunk containing refluxed chyle (c). The dense fibrous connective tissue that has been dissected (d). Internal jugular vein (e).

## Discussion

The etiology of chyluria can be parasitic or non-parasitic. The majority of parasitic causes are lymphatic filariasis, with the nematode *Wuchereria bancrofti* contributing to more than 90% of cases.<sup>16</sup> Non-parasitic causes are relatively uncommon and are mainly described in case reports. Idiopathic chyluria due to lymphatic structural anomalies is even rarer in non-parasitic chyluria.<sup>14</sup>

The pathogenesis of chyluria is not well understood. Lymphangiography, with a sensitivity of 90%, is the most critical pre-operative imaging as it provides information on location, caliber, and the number of fistulous communications.<sup>17,18</sup> It may also help discover developmental dysplasia of lymphatic vessels, which can facilitate the investigation of the etiology of idiopathic chyluria.

**Table 3** Intraoperative Findings of Obstruction During Cervical Thoracic Duct Exploration

Cause of Obstruction	Number	Percentage (%)
Fibrous connective tissue	37	74.00
Carotid artery sheath	26	52.00
Peripheral vessels*	11	22.00
Peripheral lymphatic vessels	8	16.00
Congenital anomaly	5	10.00
Valve malformation	2	4.00

**Note:** \*Peripheral vessels included transverse jugular vein (6 cases), internal jugular vein (2 cases), external jugular vein (1 case), communicating vein (1 case) and suprascapular artery (1 case).

**Table 4** Univariate Analysis of Variables Associated with Treatment Success in Cervical Lymphatic Duct Exploration

Factor	Effective Treatment (n=26)	Ineffective Treatment (n=18)	p value
Gender ratio (M/F)	13/13	8/10	0.767*
Age (years)	56.03±16.67	45.11±16.22	0.036**
Disease course (months)	167.00±173.38	179.38±148.96	0.807**
Reflux site			0.455***
Left kidney	12(46.15)	5(27.78)	
Right kidney	8(30.77)	7(38.89)	
Bilateral kidneys	6(23.08)	6(33.33)	
Grading			0.029***
Grade I	11(42.31)	2(11.11)	
Grade II	10(38.46)	7(38.89)	
Grade III	5(19.23)	9(50.00)	

**Notes:** Data are presented as mean ± standard deviation or number of patients (%). \*P value calculated using Fisher's exact test. \*\*P value calculated using independent-sample t-test. \*\*\*P value calculated using likelihood ratio chi-Square test.

**Abbreviations:** M, male; F, female.

Although the pathogenesis of chyluria is unclear, two theories have been postulated—the obstruction mechanism and the reflux mechanism—to explain the presence of chyle in urine.<sup>2,3,19</sup> However, the existing theories mainly focus on filarial chyluria, proposing that lymphatic vessel obstruction is mostly attributable to parasitic inflammation and that chyle reflux into the urinary tract can result from lymphatic valve insufficiency. Lymphangiography demonstrates diffuse dilatation of retroperitoneal lymphatics.<sup>20</sup> Theories on the pathogenesis of idiopathic chyluria are currently lacking due to its rare occurrence and limited documentation.<sup>5,21</sup>

In our study, tortuous dilatation of retroperitoneal lymphatics was evident in 90.5% of the patients. Such finding was similar to that seen in filarial chyluria. The retroperitoneal lymphangiectasia could result from abnormal congenital lymphangiogenesis, increased pressure in retroperitoneal lymphatics caused by obstruction of chylous flow, or both. The aforementioned postulation requires further investigation. Nonetheless, we found that 47.6% of the patients had contrast agent reflux to the jugular trunk, subclavian trunk, and/or broncho-mediastinal trunk, all of whom demonstrated dilatations of retroperitoneal lymphatics.

Hence, we propose that the obstruction and reflux theory, which has been used to explain filarial chyluria, can also explain some idiopathic chyluria. The distinction lies in the location of the obstruction, which may be the end of the thoracic duct for idiopathic chyluria. Obstruction of the distal thoracic duct makes it difficult for chyle to return to the venous system, leading to elevated pressure in retroperitoneal lymphatics, which in turn can result in dilatation and tortuosity of retroperitoneal lymphatics as manifested on DLG. As the pressure for chyle returning to the venous system rises, chyle will reflux to the lymphatic trunks in the neck. Such a hypothesis is supported when we found that there are significantly more cases of Grade III chyluria in patients with lymphatic trunk reflux in the neck. When the pressure

increases further, chyle will flow to the right neck via compensatory pathways of the thoracic duct or reflux into the lower pressure system such as the renal system. Takeno A and Hoa TQ also supported this theory in the diagnosis of chyluria after thoracic duct ligation.<sup>12,22</sup>

Nevertheless, the obstruction of the thoracic duct may not be the only factor in the development of idiopathic chyluria. A study in dogs has demonstrated the formation of collateral circulation between the lymphatic and systemic venous systems after thoracic duct ligation.<sup>23</sup> Thus, we postulate that the development of idiopathic chyluria may be the result of a combination of thoracic duct obstruction and decompensation of collateral lymphatic branches, which leads to gradual elevation of pressure in the thoracic duct and subsequent chyle reflux into the lower-pressured renal system through reflux lymphatics. It should be noted that 6 patients did not show retroperitoneal lymphatic dilatations, which cannot be explained by the theory of thoracic duct obstruction. The problem in these cases may lie in intra-renal capillary lymphatics, the disorder of which may cause chyluria in the presence of normal appearance of renal hilar lymphatics. Such speculation necessitates further investigation.

Operations to treat chyluria include ligation of reflux lymphatics and LVA.<sup>3,24,25</sup> Although the former can block chylous reflux to the kidneys, it does not improve the circulation of chyle. If obstruction of the thoracic duct persists, chyle may reflux to another body cavity, such as thoracic and/or abdominal cavities, which has been reported in some literature.<sup>26,27</sup> There have also been cases of chyluria complicated by lower extremity chylous reflux, chylothorax, chylous ascites, and vaginal chylous fistula in our institution. Hence, for patients with lymphatic trunk reflux in the neck, surgery to relieve the obstruction in the cervical portion of the thoracic duct to improve chyle circulation may be helpful.

CTDE differs significantly from conventional surgical approaches for the treatment of chyluria, which primarily aim to block the reflux of chyle into the kidneys or to divert lymphatic fluid via LVA. In contrast, CTDE targets the underlying pathophysiological mechanisms of chyluria by enhancing chyle drainage and reducing retrograde lymphatic pressure toward the kidneys, thereby preventing both the formation and recurrence of chyluria. Moreover, unlike thoracic duct stenting, CTDE carries no risk of stent occlusion.

During follow-up, 59.1% of patients in the surgery group with CTDE were cured of chyluria, a rate significantly higher than the 18.2% observed in the conservative group.

Single-factor analysis showed that the effective rate of chyluria in the Grade I group was significantly higher than that in the Grade III group within the CTDE group. We believe this is due to long-term retrograde lymphatic fluid causing secondary lymphangiectasia and lymphatic valve insufficiency, which were also confirmed in animal experiments.<sup>28</sup> Even when the obstruction is relieved, chyle fluid continues to flow to the lower pressure kidneys due to the structural changes described above. In this group of patients, further renal pedicle lymphatic vessel ligation or sclerotherapy is required. This work has been carried out and will be summarized in future follow-up studies.

## Conclusion

The idiopathic chyluria is very rare, with cervical obstruction of the thoracic duct being a significant cause. CTDE is an effective intervention for the treatment of idiopathic chyluria, but further studies are needed to determine its long-term patency and effectiveness.

## Abbreviations

DLG, direct lymphangiography; CTDE, cervical thoracic duct exploration; LVA, lymphovenous anastomosis.

## Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare that they have no competing interests in this work.

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