Variation in origin

At 6th week of embryo development, when the embryo is about 10 mm long, the lymphatic system begins to form in the human embryo. At the end of the embryonic stage, 6 primary lymphatic sacs are developed in the lymphatic system including 2 cervical lymphatic sacs, 2 iliac lymphatic sacs, 1 retroperitoneal lymphatic sac and 1 cisterna chyli. Lymphatic vessels develop in a similar way to blood vessels. Lymphatic sacs are fused and reconstructed to form the original lymphatic vessels, which further develop into structures such as lymphatic vessels, lymph nodes and cisterna chyli. The primal cisterna chyli is a bilateral lymphatic system in which the lymphatic sac of the jugular vein and the cisterna chyli are interlinked by a number of collateral anastomoses. Further fusion and reconstruction of primal cisterna chyli form mature cisterna chyli. The selective expression of genes determines the diversity of the structure and morphology of cisterna chyli as well as the complexity of thoracic duct structure (1,3). According to the report, the fusions of lymphatic vessels in this study existed in different structures including simple single tubular, double tubular, triple tubular, or plexus which were showed in 53% of lymphangiography, 50% of autopsies and 15% of abdominal magnetic resonance imaging. However, in most individuals, cisterna chyli still exist in the form of fusiform or cystic lymphangiectasia (4-8). When cisterna chyli is absent, TD is formed by a confluent lymphatic plexus (4-7).

Variation of thoracic duct trunk

In 1915, Davis first proposed nine types of anatomical...
variations of the thoracic duct (9,10). The most common types are type VI (63%) and type II (27%). These changes depend on the apoptosis of the lymphatic sacs and the selective expression of genes for further development during embryonic development (8). In Davis’ study, based on autopsies of 22 cadavers, found that the most common type of thoracic duct was the right main type (63%), and the most common anatomic variation was the coexisting of the left and right thoracic duct main type (27%). Combined with subsequent studies, the incidence of the left and right thoracic duct main type was reported to be between 39% and 47%. In 2015, Oren w. Johnson proposed that variations in the thoracic duct can occur at any point in its path. The variations included the presence or absence of chylum cistern, the morphology of the intrathoracic trunk, the number of ducts, the location of branches and the terminal position. The chylous cistern and thoracic duct were associated with the descending aorta, azygos vein, subclavian vein and spine (11). On the basis of nine-classification, six-classification of thoracic duct variation types was proposed. According to the presence or absence of cisterna chyli, the cisterna chyli were divided into 2 categories. The first category contained complete cisterna chyli, which could be further subdivided into 5 types. Unilateral left trunk injected into right jugular venous angle; unilateral right trunk injected into right jugular venous angle; he thoracic duct was partially replicated near its origin, leaving the chylous cistern, and then connected to form a single vessel that extended to the left jugular venous angle; the thoracic duct was partially replicated at the distal end and then connected to form a single vessel that terminated in the left jugular vein corner, and the type 5 was plexus variation. The second category was the type without cisterna chyli, which could be subdivided. This study performed external validation by magnetic resonance imaging and traditional lymphangiography (3,12). It was concluded that the most common type was unilateral right trunk injected into right jugular venous angle, which was similar to the thoracic duct anatomic variation proposed by Davis in 1915 (4,13,14).

**Variation of termination**

The termination pattern of thoracic duct varies greatly. Combined with different autopsy and thoracic duct imaging data (15,16), TD most often terminates at the internal jugular vein, followed by the jugular venous angle, and then the subclavian vein. The ends of the jugular vein and subclavian vein are usually located within 2 cm of the jugular vein angle (3,17). Less than 5% of cases had other terminations including the external jugular vein, vertebral vein, transverse jugular vein, brachiocephalic vein, and suprascapular vein (8,17-20). The thoracic duct was injected into the left jugular horn in 92% to 95% of cases, into the right venous system in 2% to 3% of cases, and into the bilateral venous system in about 1.0% to 1.5% of cases (3). In all cases where the left jugular venous angle was injected, 68% to 87.5% of the cases were injected as a single thoracic duct, 8.33% to 25% of the cases were differentiated into 2 thoracic ducts, and 4.2% to 7% of the cases were differentiated into 3 thoracic ducts (17,18). In about 20% of the cases, thoracic ducts showed branching and reanastomosis patterns prior to termination (18).

Japanese scholars (17) further proposed subclassification on this basis (17,21). The main terminating points of the thoracic duct were divided into four categories: left jugular venous angle (38%; type A), internal jugular vein (27%; type B), external jugular vein (28%; type C) and complex form (7%; type D). It should be noted that the most common termination point reported by Japanese scholars was not the internal jugular vein but the left jugular venous angle (16,22-25). This may be related to the small number of autopsy samples, bias, and systematic errors caused by the single race. Further verification is needed.

TD is usually striated below or dorsal to the left brachiocephalic vein and divides into two or three branches (26-29). Type A was further subdivided into three subtypes. In type A-1 (36.8%, 14 of 38 cases), the duct was directly injected into the venous angle. In type A-2 (36.8%, 14 of 38 cases), the duct ran under the left brachiocephalic vein and branched into two or three branches, and finally formed a single trunk into the vein angle. In type A-3 type (26.3%, 10 of 38 cases), the duct was divided into two or three branches, one of which terminated in the left subclavian vein, and the other branches were injected into the venous angle. Type B could be divided into two subtypes: type B-1 (59.3%, 16 cases) and type B-2 (40.7%, 11 of 27 cases). The duct ran under the left brachiocephalic vein and divided into two or three branches, and finally formed a single trunk and is injected into the internal jugular vein in type B-1. In type B-2, the duct ran under the left brachiocephalic vein and was divided into two or three branches, one of which terminated in the internal jugular vein and the other branches were injected into the subclavian vein. Type C could be divided into two subtypes: C-1 (42.9%, 12 of 28 cases). One branch is injected into the external jugular
vein, while the other branch is injected into the subclavian vein. C-2 (57.1%, 16 of 28 cases), with one branch into the external jugular vein and the other into the internal jugular vein. Type D was a complex classification with branches terminating in the internal and external jugular veins, as well as the subclavian vein.

**Imaging technology**

**Intraoperative fluorescence imaging (FI) technology**

Intraoperative FI is an emerging technology that injects a small amount of fluorescent dye into specific sites of patients at a specific time during the operation (the injection sites refer to iodine-oil imaging location) (30-32). The FI light source stimulates the fluorescent dye, releasing a specific wavelength of light to be received by the FI sensor. The images generated by the sensor can be viewed individually or superimposed on a standard laparoscopic or thoracoscopic display screen, providing sensitive, continuous, real-time thoracic duct anatomy and functional imaging (33-35).

The most common fluorescent dye used in esophageal surgery is ICG. ICG has been widely used in ophthalmology, vascular surgery, orthopedics, oncology and cardiac surgery (36-39). Until now, FI light sources and sensors that trigger and receive ICG have been widely cited in the market, including the SPY and Pinpoint systems from Novadaq (Novadaq, Ontario, Canada) and HyperEye Medical System (Mizuho ikako-gyo Co, Tokyo, Japan). Both are widely used in standard laparoscopy/thoracoscope and Da Vinci Robotic Surgical System (Intuitive Surgical, Sunnyvale, CA), both of which have built-in ICG imaging capabilities (40,41). ICG fluorescent agent is safe and reliable, but technical difficulties remain. The successful intubation or puncture of target lymphatic vessels or lymph nodes, as well as the operator’s experience and proficiency are the key to the success of imaging, which directly affect the imaging results.

**Radionuclide imaging technique**

Patients are given oral iodine-123-labeled beta methyl branched chain fatty acid (I-123 BMIPP), which is absorbed from the intestinal tract and entered venous circulation through the thoracic duct (42,43). It is important to note that long-chain fatty acids and fat-soluble vitamins are absorbed in the intestinal tract and reach the systemic circulation only through the thoracic duct. BMIPP, a long-chain fatty acid, is directly absorbed into lymphatic channels. This is in contrast to short-chain fatty acids, which are mainly absorbed into the blood through the portal vein system. Long-chain fatty acids are wrapped in bile salts in the duodenum, and their physicochemical property of the lipid solubility is that they can easily enter epithelial cells. Inside the cell, they turn into chylomicrons and then turn into chyle. The chylum passes through the intestinal wall, the mesentery and the chylum cistern; and eventually enters the venous system through the thoracic duct (44).

Patients are placed on a gamma camera immediately after I-123 BMIPP administration (Medic rc-1500i; Hitachi, Tokyo, Japan). Take films in the front and rear views at 20, 30, 60, 90 minutes and 2, 3, 4, 5 and 6 hours respectively. In addition, films should be taken at 24 hours. Each image takes 300 seconds in a 256x256 matrix. The field of view should include the upper abdomen and the entire chest. Continuous radiographic tracing of the circulation of the radioactive tracer from the intestine to the veins throughout the body reveals the disorientation of the thoracic duct (45,46).

Oral I-123 BMIPP for chest catheter imaging is safe, non-toxic, easy to use and noninvasive (45). I-123 BMIPP gives less radiation and provides more detail and better resolution than other radioactive drugs (45,47). I-131 glyceryl trioleate has been shown to accumulate in pericardial effusion, but no related studies have reported that I-123 BMIPP can accumulate in pericardium or show cardiac profile, which may be attributed to short imaging time or the addition of triglycerides and lipoproteins in I-123 BMIPP (48,49). It can reduce the influence of imaging of heart or pericardium on image reading of thoracic duct and increase the image accuracy. The technology is mature, reliable and high feasibility.

**Ultrasonic imaging technology**

Grayscale US, b-flow imaging and color doppler imaging were performed on all subjects using the doppler ultrasonic imaging instrument (LOGIQ S6, LOGIQ 7 or LOGIQ 9; GE Healthcare). The patient is in the supine position, with the head slightly overextended, turning 45° to the right, breathing calmly. The flow signals in the thoracic duct have low intensity and differ from arterial and venous blood flow patterns in adjacent vessels. Different probes (7, 9 and 12 MHz) are used based on the anatomy and patient
Characteristics (15). The anatomical location of the thoracic duct is determined using grayscale US (50). Adjacent veins (with perfusion) are further defined and distinguished by the use of b-flow and color doppler imaging (51).

Ultrasound imaging can be used to understand the local anatomical structure of the cervical segment of thoracic duct and its relationship with adjacent tissues and blood vessels under non-invasive conditions (50). Using tissue harmonic imaging, composite scanning, and speckle imaging to improve resolution and reduce artifacts. Studies have shown that cervical thoracic ducts were observed used by Ultrasound imaging in 96% of subjects, a rate significantly higher than reported by CT and conventional doppler ultrasound (55% to 79%) (52-54). It is important to note that the signal strength of chyle differs between fasting and after meals. After the 24-hour fasting period, the chyloacoustic signal intensity was significantly reduced, which indicates that the amount of fat in the chyle will affect the ultrasound signal intensity. This imaging technology can be applied to postoperative follow-up of patients with chylothorax and chylomelia, which is noninvasive, economical and easy to operate (51,53).

Ultrasound imaging can only show the neck of the thoracic duct, which is a big limitation and defect compared with lymphangiography, CT or MR tomography (52-55). The difficulty of ultrasonography depends on the complexity of the local anatomy of the neck (bone, blood vessels, thyroid gland, and thoracic duct) (15,53,56). For example, in the case of injury or severe swelling after surgery, the examination can be complex and time-consuming. And the data may be distorted. Therefore, ultrasound imaging cannot replace CT or MR imaging of thoracic duct (for example, excluding mediastinal tumor, lung tumor or thoracic aortic aneurysm). However, the immediacy and excellent resolution of ultrasound imaging are incomparable by CT or MR imaging. In addition, there is no need to use contrast agents, and various serious complications caused by contrast agents are avoided. It should be noted that ultrasound imaging can also use a contrast-enhancing agent (SonoVue) to achieve a clear distinction between the cervical thoracic duct and adjacent blood vessels, which can help clarify the diagnosis in the presence of complex anatomical variations or difficult examination conditions (15,51,57).

**Magnetic resonance technology**

The principle of MR hydrography is to obtain heavy T2 weighted image (T2WI), namely long repetition time (TR) plus long echo time (TE), according to the characteristics of long T2 relaxation time of static liquid in human body and comprehensive application of magnetic resonance scanning sequences and parameters, and make use of the effect of heavy T2W to develop water-containing organs (58,59). This technique is very sensitive to slow and stagnant fluid flow (such as cerebrospinal fluid, bile, urine, venous blood, etc.), which show high signal. While the substantive organs and flowing fluid (such as arterial blood) show low signal. Hence it can achieve water imaging effect. MR is a radiation-free, non-invasive, safe and reliable imaging examination method that does not require intubation and injection of contrast agents (60).

At present, there are two main methods of MR water imaging: using the heavy T2-weighted 2D or 3D FSE sequence (FSE T2WI) and using the semi-fourier acquisition (single shot FSE, SS-FSE; Toshiba called fast advanced spine echo, FASE; Siemens calls it half-fourier acquisition single-shot turbo spin-echo). SS-FSE is a T2-weighted image obtained by further extending the time of TR and TE on the basis of FSE T2WI, which is an improved FSE sequence. Compared with ordinary FSE sequences, SS-FSE has the many advantages. Firstly, conventional FSE sequences need multiple 90-degree RF pulse excitation to complete the filling of k-space, while SS-FSE can complete the filling of all k-space with a single 90-degree RF pulse excitation. Secondly, SS-FSE has fast imaging speed, which can reach sub-second imaging speed. Thirdly, with high signal-to-noise ratio and contrast noise ratio, thin-layer imaging can be performed using SS-FSE, and spatial resolution can be improved. SS-FSE has 2D and 3D image acquisition methods. 2D-SS-FSE requires a layer thickness of at least 3 mm, and the patient's movement and breathing can cause artifacts. 3D-SS-FSE can be used with a thinner layer thickness (<1 mm), which does not reduce the image quality in any reconstructed plane and further improve the spatial resolution. 3D-SS-FSE adopts the principle of semi-fourier acquisition. Three-dimensional reconstruction of images is conducted through multiple intensity projection (MIP) after coronal scanning. During scanning, electrocardiographic gate control technology or respiratory gate control technology are often used to reduce artifacts caused by the large blood vessels of the heart or respiratory movement. 3D-SS-FSE is the most ideal thoracic duct imaging method (59,61,62).

MR imaging has the advantages of safety, convenience, non-invasive, no need of contrast agent, relatively short
examination time, and high display rate of large lymphatic vessels such as cisterna chyli and lower thoracic duct, among which the display rate of cisterna chyli is significantly higher than that of angiography (61). However, it also has limitations. The spatial resolution of MR images is limited, and the display of small anatomical structures and details is not ideal. Under physiological conditions, the thoracic duct is in the state of segmental contraction, and it is difficult to show the parts with tapered contraction, leading to discontinuous display of the thoracic duct (58). Thin-layer scanning not only improves the display rate but also reduces the signal-to-noise ratio and image quality. When respiratory gating technique is used, the inconsistency of some cases' image acquisition interval with uneven breathing depth will lead to the decrease of image quality. The fallibility of intestinal fluid and movement also interfered with the display of thoracic duct and chylous cisterna. Moreover, magnetic resonance cannot be quantitatively analyzed, and T1, T2 and proton density measurements are complex and not comparable (62).

Discussion

In recent decades, various classification systems have been proposed to enrich the types of changes in the representation of thoracic duct, which is also a more intuitive and systematic understanding of the complexity of anatomical variation of thoracic duct. However, combined with different research results, we can find the commonness in different classification types, that is, TD is formed by chylous cistern in the hiatus area of diaphragmatic muscle. Except for the head area, right upper limb and half thorax, lymph nodes in all the remaining areas are collected and injected into the venous system. TD is a single channel from the chylous cistern to the level of the ninth vertebra (4), ascending along the mediastinum and crossing from right to left at the T5 level (4,5,18,51) and in most cases traveled as a single pipeline (76%). According to comprehensive data from the published literature, 46% of catheters enter the circulatory system through the internal jugular vein. Before entering the circulation behind the internal jugular vein, the catheter passes to the right, arching obliquely on the caudal and ventral sides (3,6,8,17,19,20,55,56).

Most anatomical studies of TD were performed on cadavers with collapsed catheters, and there were structural changes associated with the use of preservatives. The development and innovation of medical imaging technology make TD easier to identify and closer to its original anatomical and physiological changes. Recent research advances include ICG (approved by FDA for other indications) chest catheter fluorescence developed on the basis of traditional lipiodol angiography, which realize real-time thoracic duct visualization for surgeons during open and minimally invasive procedures. However, this technique still has the systematic defects of traditional lipiodol imaging technology: invasive operation, infection, pain and contrast agent extravasation. And there are no reports about the optimal dose and injection site. The key to imaging is the successful intubation or puncture of the target lymphatic vessel or lymph node and the full visualization of ICG, as well as the tradeoff between the contrast agent concentration at the injection site and the dilution of tracer as it flows through the lymphatic canal. The higher of the concentration injected, the lower of the total fluorescence displayed after quenching. The higher the injection concentration, the lower the total fluorescence after quenching. Preoperative preparation time is long, and the requirements of operator’s experience and technical are high. The imaging quality is limited by lymphatic dispersion, and the imaging effect is poor, so the clinical utilization rate is low. Visualization of TD using magnetic resonance imaging (MRI) varies from 50% to 100% (12,58,60,61). However, computed tomography (CT) scanning, especially the application of multi-slice spiral CT, can achieve almost 100% TD visualization (35). Although MRI and CT can accurately display the entire TD image, they are not portable technologies, and MRI is sensitive to ferromagnetic metals. For those patients in critical condition who need close monitoring and continuous care in intensive care environment, there may still be many inconvenient and urgent problems to be solved. High-resolution ultrasound imaging using a linear probe has a high success rate (96%) in displaying the cervical segment of TD (51), and in some cases is superior to MRI. Ultrasound can be used in real time and is portable, for example ultrasound could be used in patients with chylous fistula during embolization. It is also cost-effective, has short scan times and minimizes patients pain to, and may be more suitable for critically ill patients. The use of ultrasound is limited by trauma or severe swelling after surgery, and the quality of imaging is more dependent on the operator’s experience and technical level. Oral I-123 BMIPP thoracic catheterization is safe, non-toxic, easy to use and noninvasive. I-123 BMIPP gives less radiation and provides more detail and better resolution than other radioactive drugs. As a complement to other thoracic catheterization techniques, the I-123 BMIPP...
provides physiological and metabolic information that is unmatched by other examinations. However, because the I-123 BMIPP tastes slightly bitter, it is often difficult for patients to swallow. This can be overcome by adding other sweeteners.

**Summary**

The thoracic duct is the largest lymphatic vessel in the body. Its anatomical position is hidden and not easy to be exposed, which is difficult to be distinguished during operation, and the complications after injury are serious. Therefore, it is particularly important to know the anatomy of the thoracic duct well in surgery. In recent decades, the development of thoracic catheterization and interventional techniques has opened a new door for us to further expand our understanding of the lymphatic system in the course of disease, offering new hope and new methods for the treatment of many diseases.

**Acknowledgments**

*Funding:* None.

**Footnote**

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm.2020.03.10). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

*Open Access Statement:* This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

**References**


