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Morphology of the cisterna chyli in nine dogs with idiopathic chylothorax and in six healthy dogs assessed by computed tomographic lymphangiography

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Abstract

Objective: To describe the morphology of the lymphatics in the region of the cisterna chyli in healthy dogs and in dogs with idiopathic chylothorax by using computed tomographic lymphangiography.

Study Design: Retrospective study.

Animals: Nine dogs with idiopathic chylothorax and six healthy dogs.

Methods: Computed tomographic lymphangiograms were reviewed to evaluate the number of cisterna chyli branches, total cross-sectional area of the branches normalized to the cross-sectional area of the aorta, number of branches with cross-sectional area greater than 25% of the aorta cross-sectional area, and ratio of the total perimeter to the total cross-sectional area of the branches. Data (mean ± SD) were compared between unaffected dogs and dogs with idiopathic chylothorax.

Results: The cisterna chyli included more branches in dogs with chylothorax (4.30 ± 1.57) than in unaffected dogs (1.67 ± 0.56, $P = .02$), occupying a relative perimeter approximately double that in unaffected dogs ($P < .001$). The relative cross-sectional area of the cisterna chyli was approximately twofold smaller in affected (0.73 ± 0.35) than in unaffected (1.63 ± 0.91, $P = .02$) dogs. The fraction of dogs with branches greater than 25% of the cross-sectional area of the aorta tended to be larger in unaffected dogs ($P = .07$). Most larger branches were located dorsal or to the right of the aorta.

Conclusion: The cisterna chyli of dogs with idiopathic chylothorax contained smaller and more numerous branches compared with that of unaffected dogs.

Clinical significance: Altered cisterna chyli morphology may impact the surgical approach for cisterna chyli ablation in dogs with idiopathic chylothorax.

1 | INTRODUCTION

Chylothorax is the accumulation of chyle in the pleural space, which can result in respiratory distress, malnutrition, and chronically restrictive pleuritis.[1,2] Causes of chylothorax include trauma, cardiac disease, cranial mediastinal masses, heartworm disease, fungal granulomas, cranial vena caval thrombosis, and congenital abnormalities.[1,2] When an underlying cause for the accumulation of chyle cannot be found, the disease is considered idiopathic.

Medical management of idiopathic chylothorax in dogs is rarely successful. Thoracic duct ligation (TDL)

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with or without subphrenic pericardectomy (PC) is commonly employed as surgical management, and the report of the largest case series to date described a response rate of 95% after thoracoscopic treatment.[3] Previous response rates to TDL-PC as low as around 60% have been reported, prompting investigations of treatment methods such as cisterna chyli ablation.[4] Cisterna chyli ablation is a procedure designed to reduce lymphatic hypertension induced by thoracic duct ligation, which has been theorized to promote development of collateral lymphatics and prevent recurrence of chylothorax.[5]

The cisterna chyli is a collection reservoir for lymph from the abdominal viscera prior to travel through the thoracic duct back into venous circulation. The cisterna chyli has been described as a 5- to 9-mm diameter crescent-like to globular structure located dorsolateral to the aorta.[6,7] However, when dogs with idiopathic chylothorax have been examined, anatomical variation has been noted.[8] Cisterna chyli ablation is performed to create a large opening in this reservoir, allowing chyle to be redirected from the thoracic duct back into the abdomen. This theoretically reduces pressure in the lymphatic system caudal to the site of thoracic duct ligation and may promote formation of new lymphaticovenous connections outside the pleural space.[5] Currently recommended techniques for cisterna chyli ablation are celiotomy or minimally invasive surgery for transabdominal retroperitoneal approach to the cisterna chyli dorsal to the left kidney and sharp dissection or traction of the cisternal membranes from the aorta.[4,5,9-11] Currently the extent of ablation required for optimal decompression is not known. However, the configuration of the cisterna chyli may have an impact on the extent and outcome of ablation. Furthermore, the surgical approach may be influenced by the configuration of the cisterna chyli. Lymphangiography is a diagnostic tool performed prior to thoracic duct ligation to delineate the number and location of branches of the thoracic duct because failure to ligate all of the branches may result in failure of the procedure.[12,13] Previous researchers have noted cranial mediastinal lymphangiectasia when evaluating lymphangiography from dogs with chylothorax.[4,14] In the authors' experience, a large number of dogs with idiopathic chylothorax also have abnormal branching of the lymphatics in the region of the cisterna chyli. Complex branching of the lymphatics in the region of the cisterna chyli may make ablation technically more challenging and impair the extent of ablation. The cisterna chyli has more recently been described by using contrast enhanced computerized tomography (CT), but by using intravenous contrast medium rather than by using lymphangiogram.[6] Therefore, we designed a study to investigate possible differences in cisterna chyli configurations between dogs with chylothorax and healthy dogs.

The objective of this study was to describe the morphology of the lymphatics in the region of the cisterna chyli in healthy dogs and in dogs with idiopathic chylothorax by using CT lymphangiography. We hypothesized that dogs with chylothorax would have relatively smaller cisternae, with an increased number of lymphatic ducts in the area of the cisterna.

2 | MATERIALS AND METHODS

2.1 | Case Selection

Medical records of dogs admitted to the Washington State University Veterinary Teaching hospital between April 2014 and January 2019 in which idiopathic chylothorax had been diagnosed were examined. Diagnosis of idiopathic chylothorax was based on paired triglyceride levels from the serum and pleural fluid consistent with chylothorax and ruling out other known underlying etiologies. Dogs that had CT lymphangiography performed with slices extending through the left renal artery were included in the study. Dogs were excluded when the CT data did not extend caudal to the left renal artery or when contrast medium was not seen extending to the level of the jugulocaval angle. DICOM (digital imaging and communications in medicine) data for the healthy control cases were obtained from a previous study in which researchers compared CT and radiographic lymphangiographic imaging of the thoracic duct in unaffected dogs.[15] This previous study was approved by the University of Guelph IACUC in accordance with recommendations of the Canadian Council on Animal Care. Six mature mixed breed hound dogs were used and were considered healthy on the basis of complete physical examination and hematologic evaluation. In the previous investigation, both left and right popliteal lymph nodes were injected on different dates, and the CT study included in the present study was selected randomly via coin toss.

2.2 | Computed tomographic lymphangiogram

Unaffected dogs were premedicated with acepromazine (0.05 mg/kg IM) and hydromorphone (0.05 mg/kg IM). General anesthesia was induced with propofol (3-6 mg/kg IV) and maintained with isoflurane in oxygen (×1.5-2 minimum alveolar concentration). Isotonic crystalloids were administered during imaging, and the dogs were ventilated by using a volume cycled mechanical ventilator with a tidal volume of 10 mL/kg and a respiratory frequency of 10 breaths/minute. The hair along the caudal aspect of the stifle was clipped and aseptically prepared. The popliteal lymph node to be injected first was selected by a coin toss. Twelve milliliters of iodinated nonionic contrast medium (Iohexol, GE Healthcare, Mississauga, Ontario, Canada; Omnipaque 350 mgI/mL) was percutaneously injected into the popliteal lymph node over 4 to 5 minutes. Computed tomography (4-slice GE Lightspeed helical CT scanner; GE, Wauwatosa, Wisconsin) was performed immediately after lymph node injection. The dogs were positioned in right lateral recumbency, and the CT studies were performed with 3.75-mm slice thickness by using a standard and edge-enhanced algorithm. Images were acquired in helical fashion with a pitch of 0.75. The study was repeated by using the contralateral lymph node 48 to 72 hours later.

Dogs with chylothorax were sedated with dexmedetomidine (5-10 mcg/kg IV) and butorphanol (0.2 mg/kg IV). The dogs were positioned in sternal recumbency with the hind limbs extended caudally. Hair along the caudal aspect of the stifle was clipped and aseptically prepared. Local anesthesia was performed by inverted U block caudal to the stifle with 30 mg of lidocaine (1.5 mL) subcutaneously. A 3-cm surgical cut down to the popliteal lymph node was performed, a hemostat was attached to the capsule of the distal pole of the lymph node, and 90 mg/kg of iodine iodinated nonionic contrast medium (Iohexol, GE Healthcare, Marlborough, Massachusetts; Omnipaque 300 mgI/mL) was injected through a 25-g butterfly catheter into the lymph node over 4 to 5 minutes. Care was taken to stabilize the node digitally and by retraction on the hemostat while the viscous contrast medium was injected to avoid dislodging of the needle tip. Computed tomography (16-Slice Aquilion helical CT scanner; Toshiba, Tustin, CA) was performed immediately prior to and after lymph node injection. Data were acquired in helical mode with a pitch of 1.5, and slices were reconstructed at 3- to 5-mm slice thickness by using a standard soft tissue window (level: 40; width: 400).

Transverse plane DICOM data were used as acquired (perpendicular to the long axis of the table) and exported into ImageJ (version 1.52; National Institutes of Health, Bethesda, Maryland). Lymphangiograms were reviewed by one author (R.R.) who was not blinded to the presence of chylothorax. Slices were reviewed at the level of the insertion of the left renal artery into the aorta as well as at the level of the intervertebral disc space and midbody of the vertebra cranial to the insertion of the left renal artery into the aorta (three slices total). This area was chosen because it has been suggested as the target area for cisterna chyli ablation.[4,6,10-12] The perimeter and cross-sectional areas of the cisterna branches and aorta were determined by using free-hand selection and the "Measure" tool in ImageJ. The ImageJ application was used to zoom in on the area of interest for increased accuracy, although no standard zoom factor was used. The number of cisterna chyli branches, total cross-sectional area of the branches divided by the cross-sectional area of the aorta, number of branches with cross-sectional area greater than 25% of the aorta cross sectional area, and total perimeter divided by the cross-sectional area of the branches were determined. The branches greater than 25% of the aorta cross-section were evaluated because these would be the most attractive targets for ablation. Location of larger branches (>25% of aorta area) was determined by the clockwise location of the center of the branch in relation to the aorta. Thus, branches centered at 2 to 4 o'clock in relation to aorta were considered left sided, branches centered at 5 to 7 o'clock in relation to aorta were considered ventral, branches centered at 8 to 10 o'clock in relation to aorta were considered right sided, and branches centered at 11 to 1 o'clock in relation to aorta were considered dorsal. In addition, in an attempt to estimate surgical accessibility from the right or left side, we defined large branches located at 7 to 11 o'clock predominantly right sided (ie, not readily accessible from the left side) and branches located at 1 to 5 o'clock predominantly left sided. When the aorta was obscured by signal from the branches of the cisterna chyli, its area was estimated by using immediately adjacent slices for comparison. Three-dimensional reconstructions were used to avoid inclusion of the mesenteric lymphatics and ureters in the analysis.

2.3 | Statistical analysis

The results from the three slices examined were averaged for each animal. Data were assessed for normality with the Shapiro–Wilk test and were summarized as mean $\pm$ SD for normally distributed data or as median and interquartile range (IQR) for non-Gaussian distributed data. Differences between group means were assessed with Student's t test when data were normally distributed and with a Wilcoxon rank-sum test when data were not normally distributed. The number of dogs with at least one branch greater than 25% of the cross-sectional area of the aorta and the number of left-sided branches was compared between the groups by using Fisher's exact test. All analysis was performed in SAS University Edition (SAS Institute, Cary, North Carolina). $P < .05$ was considered significant.

3 | RESULTS

Nine dogs with idiopathic chylothorax and six unaffected dogs met the inclusion criteria. All unaffected dogs were hound cross breeds, with a mean body weight of 20.6 ± 2.9 kg. Dogs with idiopathic chylothorax included three Labrador retrievers and one each of Anatolian shepherd, standard poodle, Italian spinone, German shepherd, Bouvier Des Flanders, and Great Pyrenees, with a mean weight of 32.3 ± 9.7 kg. The median age of unaffected dogs was 1 year (IQR, 1-1), and the median age of the dogs with idiopathic chylothorax was 4 years (IQR, 3-6). Affected dogs were older (P = .008) and weighed more (P = .014) than unaffected dogs. The amounts of contrast medium administered (mL/kg) did not differ between the two groups (P = .30).

The number of cisterna chyli branches was greater in the dogs with idiopathic chylothorax compared with unaffected dogs (P = .002; Table 1; Figure 1). The total cross-sectional area of the cisterna branches normalized to the cross-sectional area of the aorta was greater in the unaffected dogs than in the dogs with idiopathic chylothorax (P = .018). The ratio of the total perimeter of the cisterna branches to the total area of the cisterna branches was used to evaluate the degree of branching of the cisterna (with more numerous smaller branches, this ratio is expected to increase). The ratio of perimeter to area of the cisterna was greater in dogs with chylothorax than in unaffected dogs (P < .0001). The number of branches >25% of the cross-sectional area of the aorta was not different between unaffected dogs and dogs with chylothorax (P = .068). However, all six unaffected dogs and only three of nine dogs with chylothorax had at least one branch/CT slice with cross-sectional area larger than 25% of the aorta (P = .028).

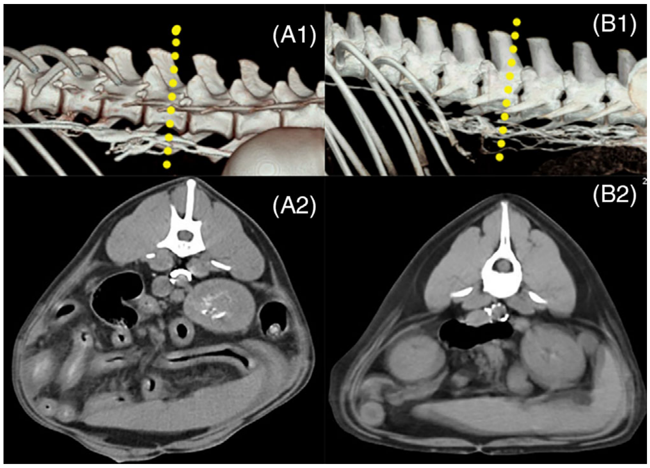

FIGURE 1 Three-dimensional (3D) reconstructions of the computed tomographic lymphangiogram data in an unaffected dog (A1) and in a dog with idiopathic chylothorax (B1), with transverse images at the site of the left renal artery in the unaffected dog (A2) and in the dog with idiopathic chylothorax (B2; window level 40; window width 400; slice thickness 3 mm for unaffected dog and 5 mm for dog with chylothorax). Dotted lines illustrate the location of the transverse slice on the 3D reconstruction

Most branches larger than 25% of the cross-sectional area of the aorta were to the right of or dorsal to the aorta in both groups (Figure 2). Additional large branches were occasionally found to the left of or ventral to the aorta. There was no difference in the number of large predominantly left-sided branches between unaffected dogs and dogs with idiopathic chylothorax (P = .26). In unaffected dogs, 19 of 25 (76%) large branches were predominantly right sided, and three of 25 (12%) large branches were predominantly left sided. In affected dogs, 12 of 22 (55%) branches were predominantly right sided, and seven of 22 (32%) branches were predominantly left sided. Five of nine (56%) affected dogs had no large predominantly left-sided branch at all, whereas seven of nine (78%) dogs had at least one larger branch predominantly right sided.

4 | DISCUSSION

The cisterna chyli of dogs with idiopathic chylothorax contained smaller and more numerous branches than that of unaffected dogs. We therefore accepted our hypothesis. This finding could have implications in the surgical planning for cisterna chyli ablation because appropriate decompression of the cisterna chyli may not be achievable in some dogs with highly tortuous cisternae.

TABLE 1 Summary of morphologic data for unaffected dogs and dogs with chylothorax

Variables	Unaffected, n = 6	Chylothorax, n = 9	*P*-value
Branches, n	1.67 ± 0.56	4.30 ± 1.57	.002
Cisterna total area/aorta area	1.63 ± 0.91	0.73 ± 0.35	.018
Perimeter/area	0.58 ± 0.14	1.06 ± 0.18	<.0001
Branches >25% the area of the aorta, n	1.39 ± 0.53	0.81 ± 0.56	.068

Note: Data are mean ± SD.

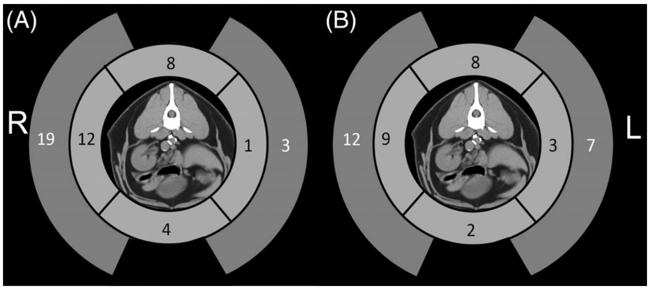

FIGURE 2 Distribution of branches >25% of the cross-sectional area of the aorta in unaffected dogs (A) and dogs with chylothorax (B). The inner shaded circles with black numbers illustrate branch location as dorsal, ventral, left, or right. The outer shaded shapes illustrate the branches that were predominantly left or right sided. The central images are transverse computed tomographic images of a dog with idiopathic chylothorax at the level of L3 illustrating branches to the left (3 o'clock), right (8 o'clock), and dorsal (11 o'clock) to the aorta (window level: 40; window width 400; slice thickness 5 mm)

The cisterna chyli is generally described as an elongated lymphatic sacculation dorsal to the aorta receiving lymph from the lumbar and mesenteric lymphatic trunks before emptying into the thoracic duct.[16] Cisterna typically extend from the level of the origin of the celiac artery to about the level of the left renal hilus.[16] A more caudal plexiform compartment is located on the ventral surface of the aorta, which receives lymphatics from the abdominal viscera and pelvic limbs, and has multiple connections around the aorta to the dorsal saccular compartment.[16] Birch et al[6] retrospectively evaluated abdominal CT data both before and after intravenous contrast medium in 30 dogs and found that the cisterna chyli was most often dorsal or lateral (right sided) to the aorta at the level of the celiac and cranial mesenteric arteries or within a distance equal to two lumbar vertebrae caudal to these arteries. They were unable to identify a cisterna chyli in 13% of cases and speculated that this could have been the result of abnormal morphology individual anatomical variability resulting in absence of a cisterna chyli. Johnson and Seiler[17] retrospectively evaluated the cisterna chyli in 30 dogs undergoing thoracolumbar MRI. They also were unable to identify the cisterna chyli in 13% of cases and found that the cisterna chyli was consistently located at the level of the celiac and cranial mesenteric arteries and commented that the ventral portion of the cisterna chyli was extremely variable and difficult to define. These previous imaging studies focused on dogs without a known pathology of their lymphatic system, and their results provide evidence that, even in the absence of a lymphangiopathy, a certain proportion of dogs may lack a cisterna chyli.

Our results provide evidence that dogs with idiopathic chylothorax may have a more generalized malformation of the lymphatic system. Dogs with idiopathic chylothorax have previously been found to have abnormal lymphatic morphology in other locations, notably cranial mediastinal lymphangiectasia.[4,18] Lymphangiectasia in the cranial mediastinum has been speculated to result from increased venous pressure thus leading to lymphatic hypertension. However, when investigated, central venous pressure levels have not proven abnormal, which contrasts this theory.[4] Mediastinal lymphangiectasia may result from primary rather than secondary lymphangiopathy, which could also result in aberrant cisterna chyli morphology. Several authors have previously commented on the anatomical variation of the cisterna chyli seen in dogs with idiopathic chylothorax. Steffey and Mayhew[8] examined 15 dogs with chylothorax using CT lymphangiography and commented that the location, size, and overall morphology of the cisterna chyli were highly variable. Similarly to many of the dogs in the current study, three of the dogs in the Steffey and Mayhew[8] study did not exhibit a clear regional lymphatic dilation identifiable as the cisterna chyli. These authors recommended that preoperative CT lymphangiograms be performed for surgical planning because of the risk of aberrant lymphatic anatomy in dogs with idiopathic chylothorax. Staiger et al[19] used a single paracostal approach for simultaneous thoracic duct ligation and cisterna chyli ablation. This research group also commented on the inconsistency and variability of the anatomy of the cisterna chyli in dogs with chylothorax. Indeed, one of the dogs required a second surgery because of a large lymphatic plexus draining to two thoracic duct collaterals. At our institution, lymphangiographic studies are considered essential for successful surgical planning in cases of chylothorax.

The cisternae of the unaffected dogs used in our study were all identifiable in the region of the left renal artery. In contrast, a saccular dilatation was not readily apparent in several of the dogs with chylothorax, and, instead, a plexiform network of lymphatics appeared to surround the aorta. The location of the large branches tended to be dorsal or to the right of the aorta in both the unaffected dogs and the dogs with chylothorax. However, there were significantly fewer dogs with chylothorax that had at least one large branch per slice present, and the smaller branches appeared to be more randomly distributed. This could make identification of a target area for ablation difficult in some cases. In addition, when large branches were present, most dogs had the large branches located such that approach from the contralateral side would be very challenging. Early reports described cisterna chyli ablation approached from the left side.[9] In our case series, only four of the nine dogs with chylothorax had a large branch readily accessible from the left side. This finding further illustrates the requirement for imaging of the lymphatic branches to help determine the location and approach for cisterna chyli ablation.

The present study had several limitations in addition to the retrospective nature of data accumulation. The samples in both groups were small. This may have contributed to type II errors in our data analysis. Furthermore, the variance of the estimation of variance made with small sample numbers will in itself be large. Therefore, the likelihood of replication of our result is also lower than it would have been for a similar study with a larger sample and, thus, higher power. We recognize that a small-sample study like this is much more sensitive to experimental circumstances compared with a large-sample study. Therefore, we consider our result somewhat preliminary, and the true number of lymphatic branches and their size must be elucidated by a larger study.

The unaffected dogs were younger and smaller than the dogs with idiopathic chylothorax. Size differences were controlled by normalization of measurements to the aorta, as previously reported by Birch et al,[6] who found a linear positive correlation between absolute body weight and cisterna chyli maximum diameter but no difference in the ratio of aorta to cisterna chyli based on age, sex, or weight category. In addition, they found no effect of weight on the shape of the cisterna chyli. Our study was retrospective in nature, and some data were lost or incomplete in the medical records, including the amount of contrast medium given to one of the dogs. The unaffected dogs and the dogs with idiopathic chylothorax were not imaged by using a uniform protocol, and this could have introduced variability into the data. General anesthesia and forced inspiratory breaths are known to collapse some thoracic duct branches.[20] All of the control dogs were ventilated during imaging, but this did not appear to affect the quality of the lymphangiogram, with contrast medium extending into the mesenteric lymphatic afferents in many dogs. In addition, a single observer who was not blinded to the identification of the dogs reviewed the CT images. This could have predisposed to confirmation bias, and future studies should be performed with a larger cohort of dogs and blinded observers.

In conclusion, dogs with idiopathic chylothorax tended to have smaller, more numerous branches of their cisterna chyli compared with unaffected dogs. The morphologic differences in the lymphatic system of dogs with idiopathic chylothorax lead the authors to recommend preoperative lymphangiography in all dogs undergoing surgical treatment, and imaging should extend caudal enough to include the region of the cisterna chyli. In some dogs with highly tortuous or absent cisternae, adequate decompression of the thoracic duct via cisterna chyli ablation may be challenging.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this report.

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