Abstract: Chylothorax in dogs and cats is a challenging condition to treat, partly because its pathogenesis is poorly understood. When a cause for chylothorax can be established, treatment is directed at correcting this cause. When no cause is identified and a default diagnosis of idiopathic chylothorax is made, treatment can only be directed at reducing the chylous pleural effusion. Current recommendations for treatment of idiopathic chylothorax vary but are based on reported responses to these treatments. Some animals will be refractory to these treatments. This review presents a brief synopsis of the pathophysiology of idiopathic chylothorax and examines the benefit of different treatments based on the current veterinary literature.

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Idiopathic Chylothorax in dogs and cats: Current treatments and future directions

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ABSTRACT

Despite significant recent advances in the understanding of the pathogenesis and treatment of chylothorax in dogs and cats, it remains a challenging and poorly understood condition. When a cause for chylothorax in a patient can be established, treatment decisions are relatively straightforward. However, when a diagnosis of idiopathic chylothorax is made, treatment options are less clear, particularly as the diagnosis likely covers several pathological processes with a common end point: chylous pleural effusion. Treatment recommendations based on reported responses to a number of treatment alternatives are now available to manage idiopathic chylothorax, but a proportion of patients will be refractory to treatment. This review presents current understanding of the pathophysiology of chylothorax and recommends treatments based on the latest literature.

INCIDENCE AND AETIOLOGY

Cats are about four times more likely to present with chylothorax than dogs,[1] but the true incidence in either species is largely unknown. Chylothorax was thought to occur after rupture of the thoracic duct, but this occurrence is considered unlikely because traumatic rupture of the thoracic duct resolves spontaneously within one to two weeks of injury.[2, 3] Two basic mechanisms are considered important in the development of chylous effusion in
the pleural cavity; 1) an increase in resistance to outflow of chyle from the thoracic duct and 2) an increase in the volume of chyle requiring drainage.[4] Combinations of both mechanisms probably occur.

Causes of increased resistance to outflow from the thoracic duct include diseases that increase central venous pressure (CVP)[5, 6] such as dirofilariasis, hypertrophic cardiomyopathy, paroxysmal atrioventricular block, pericardial disease, space occupying mediastinal lesions such as lymphosarcoma and fungal granulomas, lung lobe torsion, diaphragmatic hernia, venous thrombosis and congenital vascular disorders.[7-14] Increased chyle production has been reported in man as a result of hepatic cirrhosis[15] and may occur in animals secondary to portal hypertension or systemic hypertension due to right-sided heart failure.[9, 13, 16]

Despite these findings, the definitive cause of chylothorax is not identified in many animals and a diagnosis of idiopathic chylothorax is made, with one study reporting 7 of 12 chylous effusions to be idiopathic.[17] The diagnosis of idiopathic chylothorax almost certainly covers a variety of pathologic processes that makes development and assessment of treatment options difficult. Reports in the veterinary literature are typically of a low level of evidence and uncontrolled cases series predominate. To date, only one prospective randomised treatment trial has been reported.[18]

TREATMENT

When the cause of the chylothorax is known and addressed, successful resolution of the effusion may occur over a period of weeks to months.[19, 20] Where idiopathic chylothorax
is diagnosed, the treatment strategy is less clear. Medical treatment has been recommended for a period of 4–8 weeks, but if there is no resolution of the effusion, or if medical treatment cannot be initiated or continued, then surgical treatment can be attempted.[20-23] Whether this is the best strategy is not known. Persistent chylothorax (in the face of failed response to treatment) is associated with fibrotic changes to the pleural surfaces and ectasia of lymphatics. In the most severe cases, fibrosing pleuritis may develop, and carries a high mortality rate, with all 7 patients reported in one study dying of the condition.[24] The effect of less severe fibrotic pleural changes on subsequent treatment outcomes is unknown, but may be important, and is unlikely to be positive.

*Medical treatment for idiopathic chylothorax*

Supportive care for animals with idiopathic chylothorax has been advocated as first choice based on observation that spontaneous resolution can occur in some animals. [1, 23, 25] Thoracocentesis or thoracostomy tube drainage of the pleural effusion to reduce respiratory compromise and strategies to reduce the volume of chyle produced such as low fat diets, selective administration of medium chain triglycerides, somatostatin derived drugs,[26] and use of benzopyrone drugs [21] are the mainstay of treatment. [1, 20, 23] It should be noted however, that reports of spontaneous resolution of idiopathic chylothorax are scant and poorly documented.

Low fat diets are recommended to reduce the lipid content of chyle draining through the thoracic duct. Although the volume of chyle is largely unaffected by the dietary fat content, effusions with lower fat concentrations may be more easily resorbed.[27, 28] The replacement of long chain fatty acids in the diet with medium chain fatty acids is no longer recommended. Medium chain fatty acids substantially reduce the palatability of the diet and
medium chain fatty acids do not by-pass the lymphatics to enter the portal vein directly as previously thought.[28]

Octreotide (Sandostatin, Novartis Pharmaceuticals Australia, North Ryde, NSW) is a somatostatin analogue, which has been reported to reduce the volume of chyle flow in the thoracic duct and reduce the time taken for transected thoracic ducts to heal in dogs.[29-31] Several case reports of people with chylothorax noted the condition waxed and waned in step with the use and withdrawal of the drug. [26, 31, 32] There are no controlled veterinary studies reporting use of the drug. Octreotide is thought to reduce visceral blood flow, reduce gastrointestinal secretions and increase gastrointestinal transit time and water absorption, thereby reducing the quantity of chyle produced.[1] A dose of 10 μg/kg SQ three times daily for two to three weeks is recommended.[1]

Rutin is a bioflavonoid nutraceutical. Administration of rutin in a randomised, placebo-controlled double blinded study in 53 people reported a reduction in peripheral lymphoedema.[33] Rutin is thought to reduce lymph leakage from blood vessels, increase protein removal by lymphatics, increase tissue macrophage concentrations and phagocytosis of chyle, and increase proteolysis and removal of protein from tissues.[20, 23, 33, 34] In a case report of four cats with chylothorax which received rutin after thoracic drainage, chylothorax resolved in two cats, partially resolved in one cat and was unchanged in one cat.[23] However spontaneous resolution of chylothorax may have occurred, so no conclusions can be drawn from this case report. The extension of the use of rutin to the treatment of chylothorax is justified by the supposition that the benefits seen in the treatment of lymphoedema will also occur in cases of chylothorax. There is no evidence to support this hypothesis.
Surgical treatment for chylothorax

Surgery may be indicated if supportive treatment is inadequate to manage the clinical signs of chylothorax or the condition fails to improve satisfactorily. The goal of surgery is to resolve chylothorax and prevent sclerosing pleuritis secondary to chronic inflammation in the presence of chyle.

Thoracic duct ligation alone or combined with other procedures has been the mainstay for surgical treatment. Ligation blocks the flow of chyle resulting in an increase in afferent pressure, encouraging the formation of new venous anatomises. These venous anastomoses, in the abdomen or caudal thorax, direct chyle into the systemic circulation and prevent fluid leakage into the pleural space. Most commonly the thoracic duct and any branches are identified and ligated individually or the caudal dorsal mediastinum is ligated en bloc. Experimentally thoracic duct embolisation and thoracic duct sealing with a harmonic scalpel have also been described. The thoracic duct can be visualised after lymphangiography with direct administration of contrast agent into the popliteal lymph node, caecal lymph node, or intestinal lacteals. The injection of methylene blue mixed with contrast agent or the feeding of various digestible oils or cream, three to four hours before surgery has also been recommended to improve visualisation of the duct. Once identified the duct, or ducts, are then ligated and lymphangiography is repeated to ensure complete obstruction. Success rates of around 50% in dogs and less than 40% cats have been reported using ligation alone.

En bloc ligation is achieved when all structures ventral to the vago-sympathetiuc trunk and dorsal to the aorta are ligated in the caudal thorax. En bloc ligation alone was shown to
obstruct the thoracic duct and resolve clinical signs in 6 of 12 dogs and has yielded results comparable with individual duct ligation clinically.[36, 40] En bloc ligation does not require lymphangiography. If thoracic duct ligation is used as a sole procedure it shows only a 50% resolution of chylothorax in dogs and 35% in cats irrespective of the technique used.[25, 35, 41, 42] Additional procedures used in combination with thoracic duct ligation are aimed at improving the percentage of animals responding to surgical intervention.

Pericardiectomy combined with thoracic duct ligation is hypothesised to decreases central venous pressure by allowing the right side of the heart to fully dilate.[16] There is no direct evidence that pericardial constriction is involved with the development of chylothorax. There is only one study that directly measured the effect of pericardiectomy on central venous pressure in dogs,[18] and it did not support the hypothesis as it resulted in a reduction of central venous pressure in only one of eight dogs. Histologic examination of excised pericardial tissue showed surface deposition of fibrin and mild pericarditis but otherwise relatively normal pericardial tissue,[15] again failing to support constrictive pericarditis as a factor in the development of chylothorax. Pericardiectomy appears to have a tenuous link to a logical pathophysiologic mechanism.

Two retrospective studies of partial pericardiectomy combined with thoracic duct ligation showed resolution in 85% (31/37) dogs and 91% (29/32) cats while a randomised prospective study reported resolution in only 60% (6/10) dogs.[18, 43, 44] While these results appear favourable, low case numbers, lack of a control group and a poorly defined diagnosis make interpretation of the results problematic. The recent randomised prospective study of pericardiectomy combined with thoracic duct ligation may be a better indication of likely outcomes, but still suffers from low case numbers and lack of a clear diagnosis.
Cisterna chyle ablation [10] has been combined with thoracic duct ligation to disrupt the flow of chyle within the abdomen and so promote extra-thoracic venous anastomoses.[18, 45, 46] Cisterna chyle ablation in nine healthy beagles showed that abdominal venous anastomoses did form and chyle did not enter into the thoracic duct.[45] Reports of CCA in dogs with chylothorax showed resolution in 10/12 dogs in one randomized trial and resolution in 7/8 dogs in another case series.[18, 46] A recent experimental study and case series describes a single paracostal surgical approach to allow both ductal ligation and cisterna chyli ablation, obviating the need for a separate approach for each procedure. A successful outcome for this procedure was reported in 6 of 7 dogs.[47] The results are comparable to the clinical reports of thoracic duct ligation combined with pericardiectomy but CCA has a demonstrated theoretical mechanism of action and offers a more rational basis for treatment. Cisterna chyli ablation has been reported in cats.[42]

Transcatheter embolisation of the thoracic duct has been reported in two experimental studies in dogs.[5, 6] Cyanoacrylate was injected into the cisterna chyli and thoracic duct via a catheter placed in a jejunal lacteal and resulted in complete obstruction of chylous flow in the thoracic duct in all eight dogs.43 A pyogranulomatous foreign body reaction was noted at six weeks, but this had become quiescent by six months. Percutaneous embolisation of the thoracic duct was attempted in 15 dogs, and successfully performed in four dogs.44 Despite being successful in people,[48] thoracic duct embolisation appears technically difficult in dogs and has not been reported in clinical use.

Thoroscopic approaches have been reported to successfully perform both pericardiectomy and thoracic duct ligation with results similar to open approaches, as 6 of 7 dogs with
idiopathic chylothorax responded in one study.[17] Right sided thorascopic approaches have been reported with the patient in sternal or lateral recumbency, and methods used to seal the thoracic duct including application of vascular clips or a harmonic scalpel.[17, 37]

Thorascopic thoracic duct ligation requires a skilled endoscopist familiar with the regional anatomy.

Ancillary surgical procedures include pleurodesis, omentisation, diaphragmatic fenestration, pleuropitoneal shunts and pleurovenous shunts. These procedures aim to reduce the physiologic impact of the chylous effusion.

Pleurodesis can be successful in people[49] but has had poor results in dogs because of the resistance of the canine pleura to adhesion formation.[50, 51] Clinical reports do not support the use of pleurodesis for management of pleural effusions in the dog and it cannot be recommended.

Omentalisation requires the mobilisation of a leaf of omentum into the thoracic cavity through a surgical defect in the diaphragm or a paracostal incision. Theoretically, the omentum provides a large surface area for absorption of chyle and can adhere to thoracic duct perforations to seal them. Chyle absorbed from the omentum is likely returned to the thoracic duct, which would question the benefit of this procedure. A study of nine dogs and four cats and several case reports show equivocal results.[43, 52, 53] Omentalisation may in fact function because of diaphragm fenestration, allowing movement of chyle from the thoracic cavity to the peritoneal cavity.

Diaphragmatic fenestration creates a defect in the diaphragm, which is covered by a porous
mesh that allows free movement of chyle from the pleural cavity to the peritoneal cavity. It has been reported for the successful management of idiopathic chylothorax in 1 of 2 dogs after primary procedures had failed.[54]

Pleuroperitoneal shunting involves the placement of a Denver type pleurovenous shunt (Denver Biomedical, Colorado, USA) which allows active shunting of chyle from the pleural cavity to the peritoneal cavity.[55, 56] The afferent catheter is placed in the pleural cavity and the efferent catheter empties into the peritoneal space. The pump is placed subcutaneously over a rib to allow manual pumping of fluid by compression of the pump chamber. One millilitre of fluid is pumped per cycle and frequent pumping is required to prevent respiratory signs from developing. The procedure is associated with multiple complications. In a study of 14 dogs, seven of 13 developed short term complications, and eight of 11 developed long term complications.[56] Short term complications included infection, obstruction, kinking and pain on pumping, requiring two pumps to be removed and one dog to be euthanased. Long term complications included obstruction, abdominal distension, pyothorax, peritonitis and pleural compartmentalisation. Owner compliance can be difficult. The mean survival for dogs was 27 months and the mean disease-free interval was 20 months. The technique may be a salvage procedure when all other treatment has failed. Selection of owners capable of complying with the time requirements and willing to tolerate complications is important.

Pleurovenous shunts requires placement of a Denver type shunt with the afferent catheter in the pleural cavity and the efferent catheter in either the azygous vein [54], or the vena cava [54, 57, 58]. In one report, effusion resolved in two dogs and the third dog developed a fibrosing pleuritis and was euthanased.[57] Another dog was euthanased at 10 weeks because of complications related to the venous shunt.[58]
Conclusion

Based on the current literature, recommendations for treatment of chylothorax remain directed at initial medical treatment followed by surgical intervention when there is failure of spontaneous resolution or continued effusion, causing compromise. Surgery is aimed at obstructing the ingress of chyle into the thorax and thereby forcing the establishment of venous anastomoses. This will prevent fibrosing pleuritis secondary to chronic pleural inflammation caused by chyle. Thoracic duct ligation with either cisterna chyle ablation or pericardectomy appears to give the best outcomes although recent work questions the role of pericardectomy. Ancillary procedures such as omentalisation, diaphragmatic fenestration or pleuroperitoneal shunting can be attempted to control clinical signs in refractory animals. The refinement of laparoscopic and thoracoscopic techniques and percutaneous thoracic duct embolisation may reduce the morbidity of surgery.

References


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