

AFGHAN HOUND CLUB OF AMERICA BREED SYMPOSIUM - OCTOBER 19, 2005

Jonathan F. McAnulty DVM, PH.D.

Chylothorax * Lung Torsion * Hemangiosarcoma

Our Speaker: Dr. Jonathan McAnulty, DVM, MS, Ph.D

Education

- Associate Professor of Surgery
- DVM 1981, University of Georgia
- Internship 1982, Purdue University
- Surgical Residency 1985, University of Pennsylvania
- MS 1989, University of Wisconsin
- PhD 1994, University of Wisconsin

Research

Mechanisms of cellular injury during hypothermia and ischemia. Current focus is on the effects of bioactive peptides on kidneys stored ex vivo at low temperatures. The thrust of this work is to reduce injury to organs stored for transplantation in order to reduce the incidence of delayed function and chronic allograft nephropathy as well as to increase the donor organ supply for human transplantation. Other ongoing research projects include studies targeted at improving the outcomes in clinical feline kidney transplantation and in development of new methods for treatment of chylothorax in dogs and cats.

Responsibilities

Small animal general surgery, lectures, labs, and clinical instruction and research.

Clinical Interests

Organ transplantation, surgical treatment of ear disease, plastic reconstructive surgery, and treatment of chylothorax.

Morris Animal Foundation Funded Study: D03CA-31.

Year 3 of 4: \$23,825

"Comparative Clinical Trial for Surgical Treatment of Chylothorax in the Dog"

Grant Type: Established Investigator

Principal Investigator: Jonathan F. McAnulty, DVM, Ph.D.

Institution: University of Wisconsin-Madison

Chylothorax is the accumulation of free floating fatty fluid in the chest that results in restricted breathing. It occurs in both cats and dogs, but Afghan hounds appear to be

particularly affected. The disease is poorly understood, with no treatment advancements made in the past 20 years. Current treatment involves binding the thoracic duct, which runs alongside the aorta and is part of the lymphatic system. This procedure has a failure rate of 40 to 50 percent. The investigators are testing two new surgical treatments to determine whether either procedure could become the new standard for treating chylothorax in dogs.

2005 AHCA BREED SYMPOSIUM

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Special thanks to the following donors for artwork which will be auctioned off by Darlyn Pfeiffer before the program. Proceeds will go to health studies.

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Violet Skiles
"Garden Diva" afghan painting

Current treatments for chylothorax in the dog

Jonathan F. McAnulty DVM, Ph.D. Associate Professor of Surgery School of Veterinary Medicine University of Wisconsin

What is chylothorax?

Chylothorax is a disease where fatty fluid accumulates within the chest cavity. This fatty fluid, which is called chyle, is the fluid which drains from the abdominal lymphatic channels. In dogs with chylothorax, this fluid accumulates in the chest cavity and causes a gradual collapse of the lung lobes. This progressive accumulation of fluid will eventually cause death due to suffocation unless it is drained off, usually be a needle and syringe.

What is the normal drainage pattern for chyle?

Chyle, the fat-containing lymphatic fluid from the intestines, normally flows into lymphatic vessels in the abdomen. These vessels converge on a structure called the cisterna chyli which can be likened to a large reservoir for the chylous fluid. The cisterna chyli resides above the aorta in the abdomen and narrows down as it approaches the diaphragm. After passing the diaphragm into the chest, the cisterna will have narrowed into a vessel which is called the thoracic duct (this may be a single vessel or several vessels which typically branch out but then rejoin along the pather of the thoracic duct). This vessel will travel through the chest above the aorta and empty into the blood circulation in one of the great veins in front of the heart.

How is chylothorax treated?

Chylothorax is considered to be *idiopathic* when there is no obvious cause such as trauma, surgery, cancer or other notable disease of the chest, circulatory system or thoracic organs. If there is an obvious cause of chylothorax, such as a mass in the chest, then treatment is first directed at this potential cause. If the chylothorax is considered idiopathic, then treatment is symptomatic in that it is targeted at stopping the accumulation of chyle in the chest but does not address the specific cause of the disease.

The cause of idiopathic chylothorax is poorly understood and treatment of this disease can frequently be unsatisfactory. Conservative treatments such as periodic drainage by needle aspiration or medical therapies often constitute a "holding pattern" for many dogs, failing to provide permanent relief. In these dogs, a progressive wasting is often seen as the nutrients contained in the chyle are lost to the dog as the fluid is removed from the chest over time.

In the dog, surgical treatment of chylothorax is most commonly done by ligation (blocking the duct by tying it off with suture material) of the thoracic duct, a procedure best performed when combined with imaging studies (contrast lymphangiography) to outline the duct and all of its channels so that the best chance of identifying all the channels is obtained. This was first described in 1982 and subsequent case series have established that success in resolving chylothorax in dogs is about 50-60% with this method.

Since that time, a wide variety of treatments have been proposed to try to improve upon these results. These methods have often been tested in limited case series and most have generally been abandoned when the success rates were shown to be no better or even worse than that of thoracic duct ligation alone. These treatments have included medical therapy such as with rutin or octreotide (a somatostatin analogue), sclerotherapy (pleurodesis), thoracic duct embolization with cyanoacrylic adhesives, pleural shunting or pumping, diaphragmatic fenestration and omental draping into the pleural space. In our clinical experience at the University of Wisconsin, all of these therapies (with the exception of omental draping) have not provided any improvement in results over surgical ligation of the thoracic duct. Omental draping, for which a single case report has been published, has not been performed at the UW-VMTH. This is because the omental lymphatic

drainage empties into the cisterna chyli and hence the thoracic duct, creating the physiological equivalent of a perpetual motion machine. Thus, the rationale behind trans-diaphragmatic draping of the omentum into the chest as an absorptive drain remains obscure. In the absence of compelling clinical data to show its efficacy, we do not see a basis for use of this procedure. Sporadic use of many of these different treatments, alone or in combination with thoracic duct ligation, continues at referral centers based on various rationales which weigh the costs, familiarity with the various surgical procedures, impacts of surgical trauma and likelihood of a positive long term outcome. No single treatment is universally accepted because the overall prognosis with all methods for treating chylothorax is guarded at best.

There has been a significant lack of improvement in the treatment of chylothorax since 1990. Strategies for treatment of chylothorax up to that time were focused on several principles involving either, 1) obstruction of chyle flow into the chest (thoracic duct ligation or thoracic duct embolization), 2) reduction of chyle volume (dietary or drug treatments such as MCT oil and low fat diets), 3) transport of chyle elsewhere to relieve respiratory distress, such as to the peritoneum for absorption or to the venous system by mechanical aids (shunts, pumps and diaphragmatic fenestration), or 4) obliteration of the pleural space to eliminate a place for chyle to accumulate (pleurodesis). In the last decade, new treatments have been limited to several drug treatments introduced to reduce the volume of chyle formation (rutin and octreotide), which have not proven to be uniformly effective in chylothorax in dogs. The only other innovation in the last decade has been the attempt to use the omentum as a physiologic drain, reported in a single dog. However, as noted above, the rationale behind that approach is difficult to ascertain and no further reports on its efficacy have been forthcoming. Recently, two new approaches to this disease have been presented with encouraging preliminary results. These methods, cisterna chyli ablation and pericardectomy, are the focus of this prospective randomized trial.

Rationale and basis for new surgical treatments for chylothorax in the dog

What new treatments are currently under study for treating chylothorax in the dog?

The recent introduction of two new procedures, cisterna chyli ablation with thoracic duct ligation (CCA-TDL) and pericardectomy with thoracic duct ligation (P-TDL), mark the introduction of two new conceptual approaches to the treatment of chylothorax. CCA-TDL focuses on creating an environment conducive to the formation of lymphatic drainage channels to the venous circulation outside of the chest space. Thus, this approach utilizes the strategy of shunting chyle to the venous system without allowing its transport along the thoracic duct with its attendant risk of leakage into the chest. The destruction of the cisterna chyli does two things; first, it prevents lymphatic hypertension that occurs with thoracic duct ligation. Evidence of this hypertension can be clearly seen in the distension of the cisterna chyli after thoracic duct ligation. Experimental studies have shown that new lymphaticovenous channels that must form to provide new drainage routes for chyle require 5 to 14 days to form. Thus, alleviation of lymphatic hypertension will at least temporarily prevent the formation of collateral lymphatic channels and tilt the balance during healing in favor of successfully forming new channels into the venous circulation rather than developing lymphatics that bypass the thoracic duct ligature. The second effect of CCA is to disrupt the connection of the abdominal lymphatics that carry chyle from the thoracic duct. The effect of this is to stimulate these lymphatic channels to find new lymphaticovenous connections in the area of their disruption. Thus, with CCA, chyle is diverted directly to the venous circulation in the abdomen which eliminates the potential for leakage into the pleural space.

Pericardectomy-TDL is based on the hypothesis that that some degree of venous occlusion or hypertension is responsible for chylothorax. This hypothesis is predicated on experimental models where partial occlusion of the cranial vena cava results in chylothorax in 50% or more of experimental animals so treated. The relationship of this model to the spontaneous idiopathic disease is not clear as there are substantial differences in clinical signs and presentation in the experimental animals versus observations made in animals with spontaneous disease. Nonetheless, this model does provide a plausible hypothesis regarding one potential cause of idiopathic chylothorax. The rationale for P-TDL is to reduce either venous or right heart restriction that

may be causing subtle venous congestion as a cause of chylothorax. Preliminary clinical experiences reported with this procedure suggest that this approach may have merit.

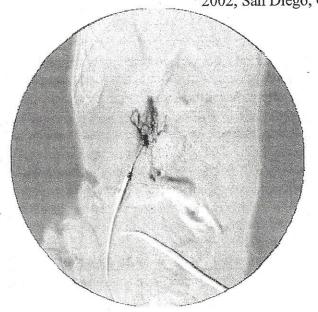
Is there either experimental or clinical evidence that these procedures may be effective?

There is considerable difficulty in modeling chylothorax in the experimental environment. Procedures applied to normal dogs may have little relevance to the spontaneous disease state and thus, although valuable and informative, experimental studies must always be interpreted with caution when applying the results to animals with the spontaneous disease. Laboratory studies can only take the clinician so far in terms of evaluating a specific treatment for chylothorax. After that point, it becomes necessary to examine the impact of the treatment in a controlled rigorous manner in the patient population that presents with the spontaneous disease.

Contrast lymphangiogram showing the direct flow of chyle to the abdominal vena cava (major vein for return of blood from the abdomen) after cisterna chyli ablation with thoracic duct ligation in a dog. In this study, radiographic contrast material is injected into the lymphatic channels to outline the drainage pathways.

However, a recent experimental study conducted at the University of Wisconsin has shown that CCA-TDL does result in a diversion of the abdominal lymphatic drainage into the venous circulation within the abdominal cavity and averts drainage of chyle through the thoracic duct in the majority of dogs so treated. This study confirmed the hypothesis that CCA would promote new lymphatic drainage

channels and provided us with information which has allowed us to further refine the procedure, changes which may enhance its effectiveness even more. Further, a limited clinical case series in dogs treated with this technique has shown resolution of the chylothorax in the majority of dogs so treated. Pericardectomy-TDL has also recently been presented as being effective in dogs with spontaneous idiopathic chylothorax (Dr. T. Fossum, Texas A&M University, clinical case data presented at the American College of Veterinary Surgeons meeting, 2002, San Diego, CA).



An alternate pattern of lymphatic drainage seen after cisterna chyli ablation with thoracic duct ligation. CCA-TDL resulted in development of a diffuse network of lymphaticovenous connections in the abdominal cavity. Injection of contrast material resulted in rapid dilution and loss of detail at the lymphaticovenous connections, even after several injections of contrast, showing a vigorous dispersion of material into the venous circulation within the abdominal cavity.

How are these procedures currently being studied?

There are several approaches to evaluating a new treatment to determine if it is more effective than the current standard therapies. The least rigorous approach is to evaluate small case series. However, in many instances this may be one of the most practical approaches as it may be very difficult to obtain the necessary funding or case numbers to structure an appropriate trial. This approach is most valuable when the current standard therapies have an extremely poor success rate (very short survival times or failure rates of 90% or more). In such instances where success is rare at best, successful outcomes in a small consecutive series of cases (6-10 dogs or more) would be very unlikely to have occurred by chance and would give a fairly high degree of confidence that the new treatment is indeed superior.

It is more difficult to evaluate outcomes in a condition, such as chylothorax, where the success rate hovers around 50%. This is because it is much more likely in this instance that a run of 6-10 successful outcomes is entirely possible purely by random chance. It is equally likely that the next 6-10 may be failures. Thus, this type of clinical problem presents an issue for study related to the statistical power that can be obtained for the study. In simplest terms, the greater number of cases that can be recruited into any study, the greater the power of the study and the greater the likelihood that any differences between treatment groups can be detected. A further issue in any trial is treatment bias. In a nutshell, this involves either conscious or subconscious tracking of cases into different treatment groups based on clinical judgments made by the attending clinician. This tracking can bias results by putting more treatable cases into one particular treatment group. The best means of avoiding bias such as this is to conduct a trial on a prospective randomized basis.

Current trial for treatment of chylothorax at the University of Wisconsin

The School of Veterinary Medicine at the University of Wisconsin is currently conducting a prospective randomized clinical trial looking at the relative efficacies of cisterna chyli ablation with thoracic duct ligation and of pericardectomy with thoracic duct ligation. This trial, to be conducted over a 4 year period, is funded by the Morris Animal Foundation. In order to minimize any potential for variation in treatment, all of these surgeries are being done by one surgeon. Dogs with chylothorax are randomized into one group or the other as they come in. The purpose of this sponsored clinical trial is to evaluate each of these procedures to determine if they offer an improvement over the current standard of therapy (thoracic duct ligation alone) and if either procedure may be superior and hence provide a new standard of treatment for chylothorax. As additional treatment goals of this trial, we are also looking at whether either of these procedures are effective as salvage procedures should the other treatment fail. Thus, any dogs that fail to resolve their chylothorax can be reentered into the trial for further treatment. I am not aware of any other objective trials currently being conducted on this disease process.

The results obtained in this trial so far have been encouraging. We have achieved an approximately 80-85% resolution rate for spontaneous chylothorax in dogs and have also had success with second procedures for salvage of failed treatments. The trial is ongoing and continuing to recruit new patients. For further information on this trial, look at:

http://www.vetmed.wisc.edu/dss/ChyloThoraxTrial/page1.php

or contact:

Dr. Jonathan McAnulty School of Veterinary Medicine University of Wisconsin

Email: mcanultj@svm.vetmed.wisc.edu

Phone: 608-263-7600

Diagnosis and Treatment of Lung Lobe Torsion in the Dog

Jonathan F. McAnulty DVM, Ph.D.
Associate Professor of Surgery
School of Veterinary Medicine
University of Wisconsin

What is lung lobe torsion?

Lung lobe torsion is a disease condition where a lobe of one of the lungs rotates around its long axis, pinching off the air flow through the bronchus and the blood flow through the pulmonary arteries and veins. The most commonly affected lung lobe is the right middle lobe. Nearly as often, however, the left cranial lung lobe can be torsed. Nearly all of the lung lobes have the potential for torsion but these two are the majority of those cases that are reported.

What causes lung lobe torsion?

The cause of lung lobe torsion is not known. In humans, division of supporting ligaments to the lungs during surgery combined with deflation of the lobes is thought to predispose to lung lobe torsion. In animals, the cause is less clear. Predisposing factors in the dog may include collapse of lung lobes, trauma, pneumonia or manipulation during surgery. In addition, accumulation of air or fluid in the chest may predispose to lung lobe twisting. There is no evidence to suggest that rotating a dog in any particular direction under anesthesia plays a role in lung lobe torsion

The Afghan hound is particularly prone to lung lobe torsion. Afghans are reported to be 133 times more likely to develop lung lobe torsion than other breeds. In the Afghan hound there is also an association between lung lobe torsion and chylothorax. The relationship between these two conditions is not clear. In any given individual, it is possible that a lung lobe torsion may result in chylothorax due to damage or distortion of the thoracic duct. However, it is equally likely that chylothorax may predispose to lung lobe torsion due to collapse and malpositioning of the lung lobes due to the accumulated fluid in the chest. It is possible that the progression from chylothorax to lung lobe torsion is predominant in the Afghan hound compared to other breeds because the chylothorax condition is more likely to persist in this breed after surgical treatment of the lung lobe torsion. In the literature, 92% of reported cases where chylothorax, detected at the time of surgery for lung lobe torsion, persisted after treatment of the torsion were in Afghan hounds. The Afghan hound may also be more susceptible to injury to the lymphatic vessels in the chest as it is also common in Afghans for chylothorax to develop after treatment for lung lobe torsion.

What are the signs of lung lobe torsion?

A progressive difficulty in breathing, cough, depression which in some cases may be combined with gastrointestinal signs (vomiting, inappetance or diarrhea) are seen with lung lobe torsion. On physical examination, respiratory signs are the predominant abnormality. Difficulty breathing, coughing and dull heart and lung sounds are usually noted. Fever and other nonspecific signs may also be encountered.

Diagnosis

Chest radiographs will be suggestive of a consolidated lung lobe and will show fluid accumulation in the chest cavity. In some cases, the amount of fluid is so large that chest films are obscured and the fluid will need to be drained in order to obtain good films. Needle aspiration of the chest is performed to help relieve the respiratory distress and for fluid analysis. The fluid is usually hemorrhagic but can upon occasion be clear, slightly bloody or chylous in appearance. Cytology will reveal a cell count and type indicating inflammation (neutrophils, lymphocytes, RBCs). If an underlying disease predisposed to the lung lobe torsion the fluid analysis may reflect that disease and be less diagnostic for the lung lobe torsion. Ultrasound has been used to aid in diagnosis of lung lobe torsion but can be difficult to interpret. Similarly, contrast bronchial studies and tracheal endoscopy may play a role in diagnosing difficult cases.

Treatment of lung lobe torsion

The treatment for lung lobe torsion is surgical removal of the affected lung lobe. In severely affected animals, it may be necessary to stabilize them prior to surgery. Drainage of the fluid from the chest and provision of supplemental oxygen may be necessary. Intravenous fluid administration and antibiotics are generally needed in the pre- and post-operative period. If a chylothorax is present at the time of lung lobe removal, it may be advisable to treat this condition as well. However, this should be based on the relative stability of the dog under anesthesia as appropriate treatment of the chylothorax may add substantially to the overall surgical and anesthetic time.

After removal of the lung lobe, a chest tube is placed to provide the ability to evacuate any additional fluid or air that may accumulate in the chest. Continued supportive therapy may be required up to several days after surgery.

A sample of the removed lung tissue should be submitted for culture and sensitivity. Antibiotics are continued after surgery and then changed, if necessary, based on the culture results. In general, antibiotics may be discontinued if the dog is recovered well and has no signs of infection.

Outcomes and Prognosis of Dogs with Lung Lobe Torsion

The prognosis for dogs treated for lung lobe torsion may range from fair to poor. If there is an underlying disease such as cancer, the long term prognosis is guarded at best. Most animals with an uncomplicated spontaneous lung lobe torsion that have no predisposing diseases will be successfully treated. However, the prognosis for recovery from surgery is substantially affected by how long the torsion has been present prior to surgery and how sick the dog is at the time of surgery. Death can occur due to the systemic effects of inflammatory mediators generated by the presence of the dead and decaying lung lobe in the chest.

In most breeds, if chylothorax is present at the time of lung lobe torsion it will often resolve within 7 days of surgery for the torsed lung. However, if chylothorax is present in the Afghan hound, the prognosis may be guarded to poor. In 1986, it was reported that only 17% of Afghans with chylothorax survived to 6 months after surgery.

As newer treatments for chylothorax have been introduced, it is hoped that this result will have been improved somewhat. However, the analysis of a more contemporary case series has not been done.

Hemangiosarcoma in the Dog

Jonathan F. McAnulty DVM, Ph.D.
Associate Professor of Surgery
School of Veterinary Medicine
University of Wisconsin

Hemangiosarcoma is a malignant cancer that arises from the cells lining the blood vessels, the endothelial cells. This tumor can arise anywhere in the body but has a strong predilection for the pericardium, heart and the spleen. Hemangiosarcoma occurs most commonly in middle age to older dogs, particularly in the larger breeds, but can occur in any breed. German Shepherds are the most commonly affected breed with Golden Retrievers and Labrador Retrievers the next most common breeds seen with this disease. However, many breeds of dogs have been reported with hemangiosarcoma and it can occur in any breed type.

Hemangiosarcoma is an aggressive cancer that tends to metastasize early in the course of the disease. The spleen is the most common site of origin and accounts for up to 65% of all canine hemangiosarcomas. Hemangiosarcoma is the most common primary cardiac tumor but may also be seen in the heart as a result of spread from other sites. There are 3 forms of hemangiosarcoma that are described. These are the skin form, splenic hemangiosarcoma and the heart base form of the tumor.

Skin Form of Hemangiosarcoma

Skin forms of hemangiosarcoma have the potential to be the least aggressive and malignant and thus have the greatest chance of a cure by surgery. The skin forms are classed as either dermal or subcutaneous (also referred to as hypodermal). The dermal form of hemangiosarcoma looks like a red or black growth on the skin. It is associated with sun exposure and may be more common in on exposed lightly haired skin or on areas with short white fur. Approximately 1/3 of these tumors will spread internally in a malignant fashion and so must be removed as soon as it is detected.

The hypodermal (subcutaneous) hemangiosarcoma lies under the skin (which usually looks normal). Up to 60% of these tumors will spread internally. The outlook is worse if spread is already detected by either radiographs or ultrasound at the time of the initial diagnosis. The treatment of choice for these tumors is usually surgery and chemotherapy. Survival times after surgery alone is approximately 6 months.

Splenic Form of Hemangiosarcoma

Hemangiosarcomas of the spleen frequently go unnoticed until they get quite large. Often, a dog may present for collapse and an intraabdominal bleed is identified as the source of the collapse. This sudden bleeding can occur when the tumor grows

spontaneously large enough to rupture and then bleeding occurs. Immediate treatment for intraabdominal bleeding is required if the dog is presented with collapse. This will entail stabilization with fluids and possibly blood and emergency splenectomy if bleeding is ongoing. These tumors are aggressive malignancies. 25% of dogs with a splenic hemangiosarcoma also have a heart base tumor. Many will have visible spread to the liver at the time of surgery. Survival times after splenectomy for hemangiosarcoma are approximately 2 months.

Heart base Form of Hemangiosarcoma

The heart base form of hemangiosarcoma has life-threatening effects due to bleeding, similar to that seen with the splenic form. When these tumors begin to bleed outside the heart, the pericardial sac fills with blood and creates a condition called tamponade which prevents filling of the heart chambers and reduces the pumping action of the heart. A presumptive diagnosis is made by ultrasound, radiography and a needle aspirate of the pericardium. If the mass can be aspirated a more definitive diagnosis can be made. The main differential for a bloody effusion of the pericardial sac is an inflammatory pericarditis. Thus, it is necessary to see malignant cells on either a biopsy or fluid analysis before presuming that hemangiosarcoma is present. In some cases, the tumor may be lodged on the atrial appendage and be amenable to surgical removal. In other instances, the tumors and not resectable and the best treatment is to perform a pericardectomy or create a pericardial window to allow the blood to drain out and relieve the cardiac tamponade. 2/3 of cardiac hemangiosarcomas have spread at the time of diagnosis. Survival after surgery is approximately 4 months with surgery alone.

Diagnosis of Hemangiosarcoma

Definitive diagnosis of hemangiosarcoma is made by performing histopathologic examination of tissue removed during surgery. A presumptive diagnosis can confidently be made in the case of a large splenic mass where obvious multiple gross metastases can be seen in other organs, usually the liver.

It is important to recognize that, in the absence of obvious aggressive metastasis, a large splenic mass does not always indicate a dangerous malignancy. In a case where the only abnormality seen at surgery is a splenic mass, it is possible that the lesion could be a splenic hematoma or a splenic hemangioma. These abnormalities can be cured by surgery and carry a good long-term prognosis. For this reason, we always recommend that a definitive diagnosis by histopathology be made of any isolated masses before considering anything drastic like euthanasia.

Treatment of Hemangiosarcoma

The treatment of hemangiosarcoma can be either palliative or therapeutic. In palliative treatment, surgery is usually the sole choice of therapy. The goal of palliative therapy is to alleviate the acute problems, such as intraabdominal bleeding, to provide a short period of good quality life before recurrence or death. The short survival times after surgery alone make this approach less desirable for many owners. The therapeutic approach to treatment will necessitate adding chemotherapy to the surgical treatment. Chemotherapy protocols usually employ powerful agents that can have significant side

effects. Survival times with surgery combined with chemotherapy will generally vary between 200 and 400 days depending on the stage of the disease at the start of treatment.

In summary, hemangiosarcoma is a serious malignancy with a poor prognosis for long-term survival. It is key not to mistake a benign splenic lesion for hemangiosarcoma. The longest survivals will be obtained by surgery and chemotherapy together. However, survival to a year after surgery would not occur with the majority of cases.