

Pulmonary Hypertension and Cardiovascular Sequelae in 54 Dogs

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ABSTRACT

Records for 54 dogs with pulmonary hypertension were retrospectively reviewed. The severity of disease was classified as mild, moderate, or severe based on the estimated peak right ventricular/pulmonary artery pressures using spectral Doppler echocardiography. Pressure was estimated using tricuspid/pulmonary valve regurgitant jets. In dogs classified as mildly or moderately affected, the most common underlying problem was chronic valvular disease, but in dogs classified as severely affected, respiratory disease was most common. The cardiac sequelae (cor pulmonale) paralleled the severity of the pulmonary hypertension, with the severe classification particularly impacted. Typical echocardiographic findings in severely affected dogs included an enlarged right ventricle, a flattened interventricular septum, tricuspid regurgitation, and a small left ventricle. A poor therapeutic response and high mortality characterized the severe classification. Mild and moderate cases were easier to manage because half of these dogs had chronic valvular disease. Heartworms did not appear to be a major problem in the dogs, but pulmonary thromboembolism, pul-

monary arterial disease, or both were identified in animals that were necropsied.

INTRODUCTION

Pulmonary hypertension is defined as increased blood pressure in the pulmonary vascular system.¹ In dogs, pulmonary arterial hypertension is the most commonly recognized form and is often associated with heartworm infection. The mechanical and immunologic effects of the worms can lead to various degrees of increased pulmonary vascular resistance and pressure. This study summarizes 54 cases of pulmonary hypertension in which heartworm disease played a minor role.

Identifying the presence of pulmonary hypertension has become easier with new technologies. The rapidly improving technology that drives echocardiography has made interrogation of the heart more rapid, comprehensive, and accurate. Echocardiographic techniques can noninvasively estimate intravascular and intracavitary pressures in many dogs with various degrees of pulmonary hypertension. This ability to quickly and easily identify clinical cases of pulmonary hypertension has been a major diagnostic advancement.

Canine pulmonary hypertension ranges widely in severity. Pulmonary hypertension associated with left heart failure tends to be mild and can often be effectively managed, whereas dogs with severe pulmonary vascu-

lar disease can have pressure increases in the right ventricle and pulmonary artery that are four to five times normal. Because severe cases have a high mortality, rapid identification and aggressive therapy is required; however, there is a significant lack of knowledge about the etiopathophysiology of this syndrome, often making therapeutic efforts fruitless.

The purpose of this report is to present 54 cases of canine pulmonary hypertension classified as mild, moderate, or severe. Historical, clinical, and necropsy results are summarized. All cases are reviewed; however, particular emphasis is given to severe cases because of the advanced nature of the problem and the high and rapid mortality. Therapeutic considerations are discussed, and control of pulmonary vascular tone is highlighted.

MATERIALS AND METHODS

Subjects

Fifty-four dogs with various degrees of pulmonary hypertension were identified in the Cardiac Center of the Virginia-Maryland Regional College of Veterinary Medicine over a 34-month period (August 2000–May 2003). The study commenced with the establishment of a comprehensive cardiology service and the purchase of a fully equipped echocardiographic instrument. The standard echocardiographic protocol included interrogation of the right side of the heart, pulmonary artery, and related heart valves. This approach proved reliable for identifying dogs with either tricuspid or pulmonary valve regurgitant jets or both. Three operators performed the echocardiographic studies.

At the end of the study period, all cases with a diagnosis of pulmonary hypertension were retrospectively collated and summarized. Neither chemical restraint nor anesthesia was used during the echocardiographic studies; however, some dogs were receiving drugs, depending on the underlying problem.

Echocardiograms

A comprehensive echocardiogram was made

for all dogs using a Vingmed System FIVE (GE). The system has a two-phase array of multifrequency transducers (4.4–8.0 and 1.5–3.6 MHz); however, the spectral Doppler velocities were usually performed with the lower frequency transducer. In many cases, the harmonic frequencies (1.5, 1.6, 1.7 MHz) were used to record blood flow profiles. The velocity profiles were made with the Doppler beam alignment within 20 degrees of blood flow.

Continuous/pulsed-wave Doppler modalities were used and selected based on the magnitude of the jet being interrogated and the need to achieve high-quality velocity profiles. The tricuspid regurgitation jets were typically evaluated from the left-side caudal and cranial windows (left lateral recumbency); however, acceptable alignment could be achieved for some dogs from the right long-axis view (right lateral recumbency). A few dogs had jets of pulmonary artery regurgitation that were assessed from the right short-axis view and usually could be appreciated from the left cranial window. Peak jet velocities were converted to estimated right ventricular and pulmonary artery systolic pressures using the Bernoulli equation ($P = 4V^2$). Velocity profiles were visually evaluated for magnitude, and two or more complexes were measured for nearly all dogs to provide peak velocity estimates.

The dogs were assigned to one of three categories based on the estimated peak right ventricular/pulmonary artery systolic pressures as follows: mild = 30 to 55 mm Hg, moderate = 56 to 79 mm Hg, and severe = above 79 mm Hg (Table 1). None of the 54 dogs had any historical, clinical, or echocardiographic evidence of subvalvular or valvular pulmonic stenosis. A six-lead electrocardiogram was performed for 19 dogs. Sixteen dogs had a lead II electrocardiogram included as part of echocardiographic examination. Forty-eight dogs had thoracic radiographs available for review. Most of the radiographs were taken at the teaching hospital, but in some cases, quality referral films were included. Four dogs were necropsied. The mortality data was collected by telephone contact with the dog owners.

Table 1. Distribution of Dogs with Pulmonary Hypertension Within Category of Severity, Age, Weight, and Breeds

	Mild pulmonary hypertension (30–55 mm Hg)	Moderate pulmonary hypertension 56–79 mm Hg)	Severe pulmonary hypertension (>79 mm Hg)
Age (yr)			
Mean	9.8	10.1	11.4
Range	2–15	0.3–16	7–17
Weight (kg)			
Mean	13.7	7.1	20.6
Range	3.6–38.2	3.2–16.8	2.0–67.7
Breeds			
Australian shepherd	1	0	0
Boston terrier	3	2	0
Beagle	1	3	0
Cocker spaniel	1	0	1
Dachshund	1	1	0
Dalmatian	1	0	1
German shepherd	0	0	1
Jack Russell terrier	0	1	1
Labrador retriever	1	0	2
Lhasa apso	1	0	0
Miniature dachshund	0	1	0
Miniature poodle	1	0	1
Miniature schnauzer	2	0	0
Mixed-breed	5	5	3
Pomeranian	0	1	0
Rottweiler	1	0	0
Scottish terrier	0	0	1
Shetland sheep dog	2	0	1
Shih Tzu	1	0	0
Toy poodle	0	1	0
West Highland white terrier	1	1	1
Wheaton terrier	0	0	1
Yorkshire terrier	0	0	1
TOTAL	23	16	15

RESULTS

The 54 dogs ranged in weight from 2.0 to 67.7 kg (4.4–149 lb), and the mean weight was 13.7 kg (30.1 lb). Mixed-breed dogs (n = 13) made up 24% of the population; the remainder were purebreds (Table 1). Dogs were 4 months to 17 years of age (mean = 10.5 years). Thirty-nine dogs were at least 10 years old, and 11 of these were at least 13 years old.

Based on severity of pulmonary hypertension and clinical diagnosis, the distribution of cases is summarized in Table 2. The peak right ventricular pressures were derived from spectral Doppler profiles using tricuspid regurgitation jets.

The most common historical complaints were respiratory in nature. Thirty-seven dogs had respiratory signs, and coughing was the most common sign reported (n = 21). Other respiratory signs included dyspnea, tachypnea, orthopnea, and wheezing. Some animals had multiple respiratory signs. The distribution of respiratory signs among the categories was mild = 13, moderate = 12, and severe = 12. Other historical problems or diagnoses included diabetes mellitus, Cushing's disease, rear limb paralysis, mammary neoplasia, pitting limb edema, vomiting, weakness, and syncope.

On physical examination, 18 dogs had find-

Table 2. Severity of Pulmonary Hypertension in 54 Dogs by Diagnosis

	Mild pulmonary hypertension (30–55 mm Hg)	Moderate pulmonary hypertension 56–79 mm Hg)	Severe pulmonary hypertension (>79 mm Hg)
Chronic valvular disease	12	8	2
Respiratory disease	3	6	10
Collapsed trachea	2	1	0
Dilated cardiomyopathy	2	0	0
Heartworms	2	0	1
Patent ductus arteriosus	0	1	0
Pancreatitis	1	0	0
Pulmonary artery thrombosis	0	0	2
Neoplasia	1	0	0
Total	23	16	15

ings compatible with left heart failure (mild = 10, moderate = 5, severe = 3), and four dogs had right heart failure (mild = 3, moderate = 1). One animal in the mild category had generalized heart failure (dilated cardiomyopathy).

There were numerous other physical findings with multiple signs in some dogs; however, the most common finding on physical examination was a systolic murmur (n = 34). The systolic murmurs ranged in intensity from grade II to V/VI. Based on pulmonary hypertension severity, systolic murmurs were distributed as follows: mild = 12, moderate = 12, and severe = 10. Among the mildly affected dogs, 12 had systolic murmurs ranging in intensity from grade II to IV. All murmurs were heard best in the mitral area, but five dogs had a systolic murmur in the tricuspid region that was the same intensity or one grade less intense than the mitral murmur. In the moderate category, the intensity of the systolic murmurs ranged from grade II to V. Six dogs had murmurs that were loudest in the mitral area, five had murmurs that were loudest in the tricuspid area, and one had a murmur that was the same intensity bilaterally. In the severe group, 10 dogs had murmurs ranging from grade II to IV. Four dogs had low-intensity, grade II to III systolic murmurs heard best in the tricuspid area. One dog had a grade II murmur that was heard equally well in the mitral and tricuspid regions.

Four dogs had grade II to IV murmurs heard best in the mitral area. One dog had a grade III murmur heard best in the aortic area.

Physical examination revealed respiratory crackles, wheezes, or rubs in eight dogs. One dog in the mild group had pulmonary crackles and another had a pleural friction rub. Four dogs in the moderate group and two dogs in the severe group had pulmonary crackles.

Other physical findings in the mild category included weak femoral pulse, pitting ventral edema, hepatomegaly, neurologic deficits, and syncope, each of which were observed in one dog. In the moderate group, one dog had ascites and an exaggerated jugular pulse, one was cyanotic and exhibited rear leg weakness, and one dog had neurologic deficits. In the severe group, two dogs were depressed and dehydrated, two were weak (one of which was cyanotic), and one dog was recumbent and reluctant to rise.

Fourteen dogs had abnormal electrocardiograms. Two dogs in the severe category had right-axis deviation and one had ventricular premature complexes. In the moderate category, two dogs had atrial premature complexes, one had ventricular premature complexes, and one had right-axis deviation. Of the seven dogs in the mild category with abnormal electrocardiograms, two had atrial premature beats, one had ventricular premature complexes, one had atrial fibrillation, one had accelerated idioventricular rhythm,

one had P mitrale, and one had right-axis deviation.

Quality thoracic radiographs were available for 48 dogs. In the mild category, 11 dogs had an abnormal pulmonary parenchymal/vascular pattern, and nine dogs had normal lung patterns. The cardiac silhouette was normal in three dogs, whereas nine dogs were classified as having generalized cardiomegaly. Of these nine, six dogs had a prominent left atrium. Five dogs had right ventricular enlargement. A large main pulmonary artery was noted in one dog, and pleural effusion was observed in another.

Fifteen dogs in the moderate category had radiographs available for review. Ten had an abnormal pulmonary parenchymal/vascular pattern. Eleven dogs had generalized cardiomegaly, two had right ventricular enlargement, one had pleural effusion, one had enlarged pulmonary artery segment. Radiographs were normal for one dog. Thirteen of the 15 dogs in the severe category had thoracic radiographs. Eleven showed an abnormal pulmonary parenchymal/vascular pattern. Six dogs had right ventricular enlargement, and three of the six had a large main pulmonary artery segment. One dog had isolated pulmonary artery enlargement, and three had generalized cardiomegaly.

A complete blood count was performed one or more times for 47 dogs. Normal results were seen in 21 dogs. Twenty dogs had mildly elevated white blood cell counts. One dog with a patent ductus arteriosus and pyometra had a marked leukocytosis. A stress leukogram was a common finding. Four dogs had high platelet counts, two had low platelet counts, and one dog with heartworms had a high eosinophil level (10%; absolute count = 1,080/ μ L). One or more blood chemistry profiles were completed for 47 dogs. Abnormalities were noted in all three pulmonary hypertension categories. Thirteen dogs in the mild category had elevated serum alkaline phosphatase (ALP) and five had an elevated blood urea nitrogen (BUN). In the moderate category, seven dogs had elevated ALP, three dogs had ele-

vated alanine transferase, and four dogs had an elevated BUN. In the severe category, nine dogs had elevated ALP, four dogs had elevated alanine transferase, four had elevated BUN. Electrolyte abnormalities were noted in two dogs.

Urine evaluations were performed for 20 dogs. Two dogs had low specific gravity resulting from furosemide administration. There was increased protein and blood in the urine of five dogs, one of which had glomerulonephritis. Blood gases were evaluated for two dogs suspected of being hypoxic based on clinical evaluation. The blood gas values supported this clinical assessment.

The heartworm status was available on all 54 dogs. Forty-eight dogs had a recent negative antigen test, were on a monthly or semiannual preventative, or both. Five dogs were not on a preventative and had not had a recent antigen test. One dog was only 4 months old, and preventive treatments had not been initiated.

The magnitude of the echocardiographic findings paralleled the severity of the pulmonary hypertension (Figure 1). In the mild category, 22 dogs had tricuspid regurgitation, and this was the most common echocardiographic finding, followed by mitral regurgitation identified in 17 dogs. Fourteen dogs had mitral and tricuspid regurgitation. Right ventricular enlargement was noted in one dog. The Doppler-estimated right ventricular/pulmonary artery peak systolic pressures ranged from 34 to 52 mm Hg (mean = 43.2 mm Hg). One dog with heartworm disease did not have tricuspid regurgitation but had pulmonary regurgitation. The derived pulmonary artery diastolic pressure ranged from 36 mm Hg at the beginning of diastole to 16 mm Hg at the end of diastole.

In the moderate group, 16 dogs had tricuspid regurgitation and 10 had mitral regurgitation. Nine dogs had mitral and tricuspid regurgitation. Right atrial and right ventricular enlargement was noted in five dogs. The Doppler-derived peak right ventricular and pulmonary artery systolic pres-

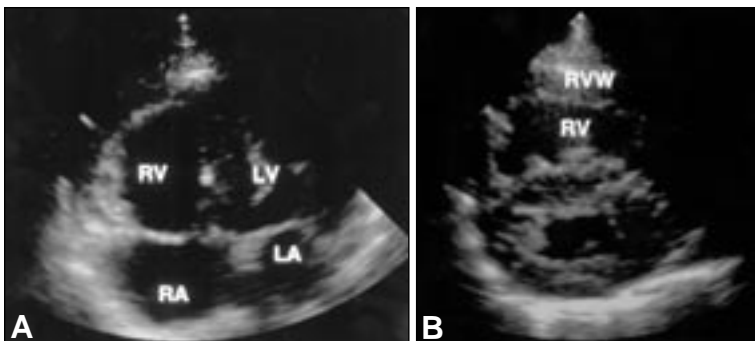


Figure 1. Panel **A** is from the left caudal window showing an enlarged right atrium and ventricle when compared with the left atrium and ventricle for an 8-year-old mixed-breed dog with sudden onset of respiratory insufficiency, including cyanosis. This dog had tricuspid regurgitation. Using this regurgitant jet, the peak right ventricular pressure was approximately 130 to 140 mm Hg (reference value 25–30 mm Hg) using continuous wave Doppler. Panel **B** shows the right short-axis view. This view is characterized by thickening of the right ventricular free wall, an enlarged right ventricle, flattening of the interventricular septum, and a small left ventricular chamber.

ures ranged from 60 to 79 mm Hg (mean = 69 mm Hg).

In the severe category, all dogs had tricuspid regurgitation, one had pulmonary regurgitation and four had mitral regurgitation. The Doppler-estimated peak right ventricular pressure ranged from 80 to 140 mm Hg (mean = 102 mm Hg).

The 15 dogs in the severe group all had various combinations of echocardiographic changes. All had tricuspid regurgitation, 10 had flattening of the interventricular septum, six had an enlarged right ventricle, two had an enlarged right atrium, two had an enlarged main pulmonary artery, and 10 had right ventricular free wall hypertrophy. The left ventricle was small in 11 dogs based on M-mode measurements of left ventricular systolic and diastolic diameters (Figure 1).

Treatment of the cases varied considerably depending on the degree of pulmonary hypertension and the underlying etiology (Table 2). In the 23 dogs with mild disease, the most common therapies were furosemide or enalapril or both (nine dogs) for complications associated with chronic valvular disease. Other therapies included cough suppressants, bronchodilators, and miscellaneous medications directed at prob-

lems such as neoplasia, pancreatitis, and collapsed trachea. In the moderate group, eight dogs had chronic valvular disease and were treated with enalapril, furosemide, or both. Six dogs had respiratory disease; treatment included antibiotics, bronchodilators, cough suppressants, prednisone, and butorphanol. In the severe category, treatment varied greatly and changed often; however, the

focus was on reducing the pulmonary vascular resistance. Oxygen was standard therapy, drugs included furosemide, enalapril, antibiotics, steroids, prazosin, bronchodilators, heparin, hydralazine, and sildenafil.²⁻⁴ None of the therapy was administered in a controlled fashion.

The overall mortality for the 54 dogs was high because most of the dogs were middle-aged or older when examined, and the data accumulation period was 34 months. Eleven of the dogs were lost to follow-up. Of the remaining 43, 34 were dead by the time of this reporting. In the severe category, all but one dog died, and most of these dogs died within days of presentation to the teaching hospital. The surviving dog has been alive for 8 months following pulmonary hypertension diagnosis with underlying chronic valvular disease (mitral and tricuspid regurgitation). One other dog in the severe group lived 11 weeks after diagnosis but had a poor quality of life. Five of the mild group are alive and 12 are dead. Four dogs in the moderate category are alive and eight have died.

A necropsy was performed for four dogs, all from the severe category. A 10-year-old Wheaton terrier had idiopathic vas-

cular disease in the main pulmonary artery, which became the location for a large thrombus. This dog had severe respiratory compromise and died within 1 hour of presentation to the teaching hospital.

A 14-year-old mixed-breed dog had pneumonia with many alveoli filled with neutrophils and macrophages. Many of the smaller pulmonary arteries were thickened due to smooth muscle proliferation.

A 13-year-old Labrador retriever also had evidence of pneumonia, with terminal bronchioles and alveoli containing lymphocytes, plasma cells, and neutrophils. Arteriosclerotic changes were seen in some pulmonary arteries.

The fourth dog necropsied was a 12-year-old Scottish terrier with multiple medical problems leading to pulmonary thrombosis.

DISCUSSION

Overview

Broad medical principles are apparent from the review of these cases. It is clear that pulmonary hypertension will be increasingly recognized in the clinical setting because of rapidly improving, noninvasive technology in the area of echocardiography. It is clear that the level of pulmonary hypertension can vary widely. In the severe category, systolic pressures in the right ventricle and pulmonary artery approached systemic levels. These pressures, coupled with cor pulmonale, usually lead to rapid cardiovascular and respiratory decompensation and death.

Although the number of dogs necropsied was limited, there was substantial evidence that heartworms did not play any major role in 51 of the cases. Of the three dogs identified as possible cases of heartworm infection, the diagnosis is doubtful in two. One 11-year-old dog in the mild category had radiographic evidence compatible with heartworms, but a recent antigen test was negative. The other was an 8-year-old dog of mixed breeding that had been treated for adult heartworms 3 years prior to the onset of severe pulmonary hypertension. There was

no evidence of chronic heartworm problems in the intervening time, and the sudden onset of respiratory insufficiency and death in 38 hours might not have been related to heartworms. The third dog did have heartworms. Irrespective of these three cases, this study dispels the notion that heartworm infection is the most common cause of pulmonary hypertension in the dogs referred to our hospital.

It is also clear from this study that tricuspid regurgitation is a common finding in dogs with pulmonary hypertension. In the severe cases, this is probably related to the increase in right ventricular systolic pressure, but some of the mild and moderate cases were probably caused by tricuspid regurgitation related to chronic valvular disease. Tricuspid regurgitation is an echocardiographic window into the right heart and pulmonary vasculature allowing, rapid, noninvasive identification of pulmonary hypertension. It is likely there are cases of pulmonary hypertension that do not have tricuspid/pulmonary valvular insufficiencies, and therefore, the Doppler technique used in these dogs would not apply.

Finally, it is clear from the literature and these clinical cases that more information is needed about etiology, pathophysiology, and therapy of severe pulmonary hypertension in dogs. Other investigators have addressed pulmonary hypertension in dogs with results similar to those found in this study.¹ Much is known about control of normal pulmonary vascular tone (see below), but data and tests needed to evaluate important vasoactive substances in the dog are limited. Assuming that the specific etiology and deranged vascular physiology could be determined, there is no assurance that drugs presently exist to correct the underlying problem(s).

Types of Pulmonary Hypertension

Pulmonary hypertension is separated into primary and secondary cases. Primary pulmonary hypertension cases are those without a known etiology and are considered rare in the dog.^{5,6} Secondary pulmonary hypertension in humans is a common

sequela of chronic obstructive pulmonary disease, and in dogs, it can be caused by bronchiectasis, emphysema, infiltrative pulmonary diseases, chronic pulmonary embolism, and left heart failure.⁶

Control of Pulmonary Vascular Tone

In recent years, great progress has been made in understanding the mechanisms involved in the control of pulmonary arterial function. Multispecies research has shown that pulmonary vascular resistance can vary widely, and increasingly, the endothelial cells lining the pulmonary vessels appear to play a major role because the cells are directly or indirectly involved with many of the substances that can cause vasodilatation or vasoconstriction of the pulmonary arteries.

Indeed, endothelial cells can appear histologically normal but can be functionally abnormal. Prostaglandins (PGs) are important in pulmonary vascular regulation. Prostacyclin (PGI₂) and PGE₂ are vasodilators, whereas PGF_{2α} and PGA₂ are vasoconstrictors. Prostacyclin can be released by the endothelial cells and, in addition to vasodilatation, can inhibit platelet aggregation through activation of adenylate cyclase. Nitric oxide has a biological action similar to prostacyclin in that it causes relaxation of vascular smooth muscle. Nitric oxide is released from endothelial cells in response to physiologic stimuli, including thrombin, bradykinin, and shear stress. Nitric oxide inhibits platelet activation and creates an antithrombotic property on the endothelial surface.⁵

Other vasoconstrictors include thromboxane from platelets and macrophages, endothelin from endothelial cells, and angiotensin II generated in the lung by conversion of angiotensin I to angiotensin II. Endothelin has a long half-life that can lead to prolonged vasoconstriction. Serotonin is vasoactive and can act as a growth factor and contribute to medial hypertrophy and promote vascular remodeling.⁵ No attempt was made to identify or quantitate the vasoactive substances in the 54 dogs studied here.

Low alveolar gas tension is a strong stimulus for rapid pulmonary vasoconstriction. This is a well-recognized adaptive mechanism for shunting blood flow away from poorly ventilated areas to those that are better ventilated. Hypoxia inhibits outward potassium currents resulting in depolarization of the pulmonary vascular smooth muscle. This depolarization allows calcium entry into voltage-dependent calcium channels, promoting vascular contraction. Hypoxia can mobilize calcium from the sarcoplasmic reticulum, mitochondrial membrane, and blunt production of nitric oxide.⁵ Acidosis frequently accompanies hypoxia and can act synergistically with hypoxia to promote pulmonary vasoconstriction.⁷

Based on history and clinical signs, many of the dogs in this study (particularly in the severe group) had signs of respiratory insufficiency. These dogs were placed in an enhanced oxygen environment while in the hospital, but oxygen appeared to have no significant impact on the outcome of these cases. Serial evaluation of peak right ventricular pressure was done for many of these dogs using continuous wave Doppler, but significant reduction in right ventricular systolic pressure was not achieved in any of these cases.

Cardiac Effects of Pulmonary Hypertension

Cor pulmonale is heart disease secondary to pulmonary parenchymal disease or the associated blood vessels or both. The right ventricle is primarily involved, and hypertrophy, dilation, or both can be present. In humans, chronic cor pulmonale implies obstructive or restrictive lung disease, whereas acute cor pulmonale suggests acute pulmonary hypertension from massive pulmonary embolism.⁷ The normal right ventricle has an output that is equivalent to the left ventricle; however, pulmonary artery pressure is much lower than the systemic blood pressure, making the design and function of the two ventricles quite different.⁸ The right ventricular free wall is thin, making it a highly compliant chamber that can easily accommodate

increases in filling pressures. Systolic pressures in the right ventricle and pulmonary artery are usually less than 30 mm Hg, and the right ventricular-end diastolic pressure is usually less than 6 mm Hg. Mean pulmonary artery pressures range from 10 to 18 mm Hg. The right ventricle is limited in its ability to increase wall tension and systolic ejection pressure in response to acute increased afterload that can occur in pulmonary hypertension. If the pulmonary hypertension develops gradually, the right ventricle is better able to adapt to the increase in workload. In chronic cases, the right ventricle hypertrophies and becomes less compliant.⁸ Although these adaptive mechanisms are designed to compensate for the high pulmonary vascular pressures and serve to maintain cardiac output, the trade-off is a right ventricle that cannot respond in a normal physiologic manner.

The echocardiographic manifestations of pulmonary hypertension can be dramatic (Figure 2). Dogs with advanced respiratory disease and hyperinflation of the lungs can be difficult to image due to echo window reduction. The advanced cases usually demonstrate moderate-to-severe right ventricular dilatation. Interventricular septal flattening is often dramatic, particularly during systole. Severe flattening is usually identified in cases where the right ventricular systolic pressures approach systemic levels. Elevated right ventricular diastolic pressures can cause paradoxical interventricular septal motion where the septum moves to the left during diastole as a result of increased right ventricular pressure and volume overload. The main pulmonary artery may appear enlarged. It is important to interrogate the right ventricular outflow tract and pulmonary valve to eliminate pulmonary stenosis as a cause of right ventricular hypertension; however, most of the dogs with pulmonary hypertension are middle-aged or older, which reduces the possibility of an unrecognized congenital lesion. The left ventricle may appear small when compared with the large right ventricle, or it can be absolutely small due to low cardiac output secondary to

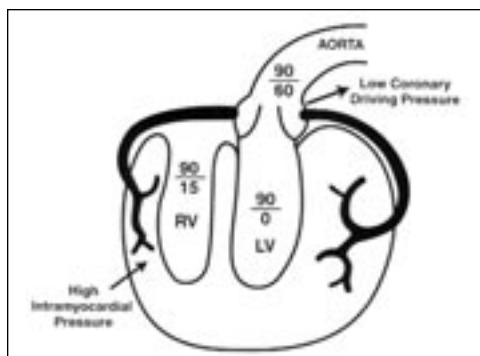


Figure 2. This drawing highlights some of the suspected cardiac effects of severe pulmonary hypertension. The increased pulmonary vascular resistance elevates right ventricular systolic pressure (90 mm Hg) creating a major increase in afterload in a normally compliant chamber. The increased systolic pressure elevates right ventricular intramyocardial pressure. The high intramyocardial pressure and low coronary driving pressure combine to create a “stressed” right ventricle leading to acute cardiovascular decompensation. The low coronary driving pressure is derived from the reduced left heart preload and low systemic pressures.

obstruction to pulmonary blood flow. With substantial tricuspid regurgitation, the right atrium may be enlarged.^{6,9,10}

Spectral Doppler echocardiography provides an effective, noninvasive technique for estimating right ventricular and/or pulmonary artery pressures.¹ The appropriate jets are usually easy to identify, particularly in severe cases. The peak jet velocity and the Bernoulli equation are used to calculate the pressure difference between the right ventricle/right atrium and/or the pulmonary artery/right ventricle. The absolute pressure in these structures can be determined by adding an estimated right atrial pressure to the derived values; however, this is often not necessary because the addition of an estimated pressure will not change category designation, particularly in the severe cases.

Pulmonary Hypertension

Treatment of primary pulmonary hypertension in humans can include administration of oxygen, digoxin, adenosine, prostacyclin infusion, nitric oxide, and high-dose calcium

channel blockers.⁵ Treatment of secondary pulmonary hypertension may involve oxygen, anticholinergics, β -adrenergic agonists, theophylline, corticosteroids, digitalis, nitric oxide, and angiotensin-converting enzyme (ACE) inhibitors. In humans with chronic obstructive pulmonary disease, only oxygen has been shown to consistently vasodilate the pulmonary circulation.⁷ Oxygen relieves pulmonary vasoconstriction, which allows right ventricular stroke volume to increase, and it enhances oxygen delivery to the vital organs. Sildenafil has been shown to reduce hypoxia-induced pulmonary hypertension in humans and mice, but its use in dogs has been limited.^{2,3} Recommended treatment of pulmonary hypertension and associated problems in dogs includes oxygen, antibiotics, bronchodilators, calcium channel blockers, α blockers, salt restriction, ACE inhibitors, and diuretics.^{6,10}

The therapeutic goal in these dogs was related to the underlying problem causing the pulmonary hypertension. In the mild and moderate categories, chronic valvular disease was the most common problem and was typically treated with enalapril or furosemide. Indeed, the magnitude of the pulmonary hypertension was used as a therapeutic guide in the dogs with chronic valvular disease. Primary respiratory disease appeared to be the underlying problem in 10 cases categorized as severe. These dogs received supplemental (40%) oxygen and specific drugs as described earlier.

Future Considerations

The major hurdle in dealing with canine pulmonary hypertension is understanding the etiology and pathophysiology of the syndrome. It is assumed that pulmonary parenchymal disease precedes pulmonary vascular disease; however, this is not always obvious. A few dogs had no physical or radiographic signs of primary pulmonary parenchymal disease but had severe pulmonary hypertension. The lack of necropsy studies makes final judgments about parenchymal disease difficult at best. Furthermore, the complex cascade of events

involved in controlling pulmonary vascular tone could easily be disturbed in a number of ways. In the clinical situation, there is no practical way to evaluate the pulmonary vascular tone quickly or to assay the substances that play a major role in control of pulmonary vascular tone; therefore, each case becomes an experiment with the goal of finding a plan that will substantially reverse the hypertension. In severe cases, this approach has been ineffective in the authors' hospital.

Better understanding of pulmonary hypertension will result from appropriate research. Further characterization of parenchymal diseases of the lung as well as comprehensive evaluation of the pulmonary vascular abnormalities will be critical. Assays of vasoactive substances and histochemical studies of the pulmonary vessels may be particularly rewarding. Newer drugs, such as the endothelin-receptor antagonist bosentan need to be evaluated in appropriate clinical trials.¹¹ In time, the treatment and management of severe canine pulmonary hypertension may be less empirical, more rational, and more successful.

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