

Intracardiac heartworms in dogs: Clinical and echocardiographic characteristics in 72 cases (2010-2019)

Abigail E. Romano | Ashley B. Saunders  | Sonya G. Gordon | Sonya Wesselowski 

Department of Small Animal Clinical Sciences,
 College of Veterinary Medicine and Biomedical
 Sciences, Texas A&M University, College
 Station, Texas

Correspondence

Ashley B. Saunders, Department of Small
 Animal Clinical Sciences, College of Veterinary
 Medicine and Biomedical Sciences, Texas
 A&M University, College Station, TX.
 Email: asaunders@cvm.tamu.edu

Abstract

Background: Heartworms, a cause of pulmonary hypertension (PH) in dogs, can migrate from the pulmonary arteries into the heart resulting in life-threatening caval syndrome (CS).

Objectives: To describe clinical and echocardiographic characteristics in dogs with intracardiac heartworms including estimated heartworm burden and frequency of PH and pigmenturia.

Animals: Seventy-two client-owned dogs with heartworms.

Methods: Retrospective study. Data collected from an electronic medical records search for dogs with intracardiac heartworms included clinicopathologic, echocardiographic, and procedural findings. Dogs with heartworms isolated to the pulmonary arteries were excluded.

Results: Estimated intracardiac heartworm burden was low in 14 of 72 (19%) and high in 58 of 72 (81%) dogs. The majority were small breed (54/72; 75%; 29/72; 40% Chihuahuas) and had a high likelihood of PH (67/72; 93%). Pigmenturia was the second most common clinical finding (31/72; 43%) after lethargy (32/72; 44%). Anemia (37/55; 36%), pigmenturia (30/58; 52%), and bilirubinuria (28/36; 78%) were significantly more common in dogs with a high worm burden ($P < .05$). Based on the presence of anemia, pigmenturia, and clinical signs, 18 of 72 dogs (25%) were considered to have CS.

Conclusions and Clinical Importance: Although the majority of dogs with intracardiac heartworms had a high worm burden and high likelihood of PH, only 25% had clinical evidence of CS. Echocardiography is a useful tool to identify intracardiac heartworms, detect likelihood of PH, and could be useful for staging heartworm positive small breed dogs for intracardiac heartworm migration.

KEYWORDS

canine, caval syndrome, *Dirofilaria immitis*, hemolysis, pigmenturia, pulmonary hypertension

Abbreviations: Ao, aorta; AT:ET, acceleration time to ejection time ratio; CS, caval syndrome; LA:Ao, left atrium to aorta ratio; LVIDd, left ventricular internal dimension at end-diastole; LVIDdN, left ventricular internal dimension at end-diastole normalized to body weight; LVIDs, left ventricular internal dimension at end-systole; LVIDsN, left ventricular internal dimension at end-systole normalized to body weight; PH, pulmonary hypertension; PR, pulmonary regurgitation; PT, pulmonary trunk; PT:Ao, pulmonary trunk diameter to aorta diameter ratio; RA, right atrium; RPAD, right pulmonary artery distensibility; RV, right ventricle; TR, tricuspid regurgitation; RA:LA, right atrium diameter to left atrium diameter ratio.

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1 | INTRODUCTION

Heartworm disease is an important mosquito-borne disease in dogs caused by the filarial nematode, *Dirofilaria immitis*. Adult heartworms typically reside in the pulmonary arteries, causing inflammation and endothelial damage. Some infected dogs remain asymptomatic, while others develop cough, dyspnea, syncope, exercise intolerance, weight loss, and lethargy.¹⁻⁶ Clinical signs relate to the host's immune response, worm burden, and duration of infection.^{1,3-5,7,8}

Retrograde migration of heartworms into the right ventricle (RV) and right atrium (RA) is likely multifactorial. Proposed causes include high pulmonary artery pressures, reduced cardiac output, large heartworm burden, simultaneous or delayed maturation of worms, and administration of preventative or adulticide therapy.^{2,7,9-13} The presence of intracardiac heartworms can result in caval syndrome (CS), a life-threatening complication also known as dirofilarial hemoglobinuria.^{9,14,15} In CS, heartworms within the RA obstruct blood flow and result in lysis of red blood cells.^{2,11,15,16} The presence of hemoglobinuria in a dog with intracardiac heartworms is considered indicative of CS.¹⁷⁻¹⁹ Assessment of worm burden is based on estimated number of worms in the pulmonary arteries on echocardiographic evaluation or from worm recovery at necropsy.^{6,7,17,20} Caval syndrome occurs in dogs with high and low worm burdens.^{7,14,15,20,21} Additionally, not all dogs with intracardiac heartworms have clinical signs of infection or CS.^{7,8,20} Manual extraction of worms via the jugular vein in dogs with CS results in resolution of hemoglobinuria and anemia.^{9,14,15,22} Dogs that undergo successful heartworm extraction and survive to discharge typically have a good long-term prognosis.¹

Pulmonary hypertension (PH) is a sequela of heartworm infection that contributes to clinical signs and right heart failure.⁷ The presence of heartworms in the pulmonary arteries causes proliferative endarteritis, narrowing of the arterial lumen, decreased arterial distensibility, and arterial embolism resulting in increased pulmonary arterial pressure.^{23,24} Echocardiography is important in identifying and quantifying PH.²⁵ Increased pulmonary pressure is 1 potential contributing factor for retrograde worm migration into the RA.^{2,8,15}

The objectives of this study were to describe the clinical and echocardiographic characteristics of dogs with intracardiac heartworms and to describe the frequency of pigmenturia and PH in this group. We hypothesized that many but not all dogs with intracardiac heartworms would have evidence of pigmenturia and PH and that presence of heartworms in the RA could inhibit the ability to echocardiographically quantify PH.

2 | MATERIALS AND METHODS

2.1 | Animals (case selection)

Electronic medical records from Texas A&M University Veterinary Medical Teaching Hospital were searched to identify dogs that were referred for CS, had heartworm extraction performed, or had intracardiac heartworms identified on echocardiogram between May 2010 and September 2019. Echocardiographic reports and images underwent

cardiologist review to confirm the presence of heartworms, characterized as hyperechoic parallel lines representing the cuticle of the worm, within the RA and RV. Dogs were excluded if heartworms were documented only in the pulmonary arteries. In addition, the total number of Chihuahuas and Labrador Retrievers admitted to either the emergency or cardiology service during the same time frame was recorded.

2.2 | Medical records review

Information recorded from medical records of dogs that met the inclusion criteria included signalment, body weight, body condition score, geographic location of residence, month of presentation, medical therapy, clinical presentation, physical examination findings, clinicopathologic and echocardiographic findings, and heartworm extraction information. Pigmenturia was defined as the presence of dark urine reported by the owner, referring veterinarian or veterinary medical teaching hospital based on visual observation or urinalysis report. Anemia was defined as a packed cell volume (PCV) < 37%.²⁶

2.3 | Echocardiography

All transthoracic echocardiographic studies were performed by a board-certified cardiologist or cardiology resident under direct supervision of a boarded cardiologist. The echocardiographic studies were reviewed on a digital workstation (GE EchoPAC v203; GE Medical Systems, Horten, Norway), and measurements were made for this study by a board-certified cardiologist (ABS). An average of 3 measurements was obtained when possible except for tricuspid and pulmonic valve regurgitation velocities, which were recorded as the maximum value. Measurements included left ventricular internal dimension at end-diastole and end-systole (LVIDd and LVIDs) from M-mode measurements of the left ventricle in a right parasternal short-axis view that were normalized to body weight (LVIDdN, LVIDsN).²⁷ Left ventricular fractional shortening was calculated from M-mode measurements. Dogs were considered to have left ventricular dimensions outside of the 95% confidence interval if the LVIDdN was < 1.27 or > 1.85 or if LVIDsN was < 0.71 or > 1.26.²⁷ Left atrium to aorta ratio (LA:Ao) was calculated from measurements of the LA and Ao obtained in a right parasternal short-axis view.²⁸ The diameters of the RA and LA were measured in a right parasternal, long-axis 4 chamber view across the mid-section of each chamber parallel to the mitral or tricuspid annulus 1 click before mitral or tricuspid valve opening.^{29,30} For the purposes of this study, an RA:LA ratio was calculated as the long-axis diameter of the RA to the long-axis diameter of the LA as an estimate of RA enlargement. Right atrial pressure was estimated as 5 mmHg when the RA was normal size, 10 mmHg if RA enlargement was present, and 15 mmHg if ascites was present.^{31,32} Right ventricular diameter measurement was planned but could not be consistently performed when high worm burdens were present. Therefore, RV enlargement was subjectively characterized from a right parasternal long axis view as none, mild, moderate, or severe as previously described, with severe

enlargement indicating the right ventricular chamber was larger than the left.^{33,34} The pattern of enlargement was subjectively characterized as concentric hypertrophy, eccentric hypertrophy, or both. Interventricular septal flattening was evaluated throughout the cardiac cycle and recorded when present.

In right parasternal short-axis heart base views, diameter of the aortic valve (Ao) and diameter of the pulmonary trunk (PT) midway between the pulmonary valve and branch pulmonary arteries were measured. A PT:Ao ratio was calculated, and PT:Ao ratio > 1.0 was considered an indicator of pulmonary artery enlargement.³⁴ Measurements of the right branch pulmonary artery were obtained to calculate right pulmonary artery distensibility (RPAD) as previously described.³⁴ Values < 30% indicated reduced RPAD and values < 22% were consistent with severe PH.^{24,34,35}

Tricuspid valve regurgitation (TR) and pulmonary valve regurgitation (PR) were recorded as present, absent, or in the case of TR, present but unable to be measured owing to the presence of intracardiac heartworms. Peak velocity of tricuspid (systolic timing) and pulmonary (early diastolic timing) valve regurgitation was measured when Doppler recordings were available. Transpulmonic velocity profiles obtained with pulse-wave Doppler were reviewed, and the presence of mid-systolic notching during deceleration was recorded when present.³³ Transpulmonic acceleration time and ejection time were measured and acceleration time to ejection time (AT:ET) ratio was calculated. An AT:ET ratio < 0.30 was considered evidence of PH.^{34,36} Likelihood of PH was categorized based on recent consensus statement recommendations that used a probability-based approach for assessing PH.²⁵ Briefly, this included a combination of peak systolic TR velocity and changes observed at anatomic sites (ventricles, pulmonary artery, RA, and vena cava). A high likelihood of PH was characterized as a peak systolic TR velocity > 3.4 m/s plus an echocardiographic sign of PH at 1 anatomic site, or TR velocity 3.0-3.4 m/s plus echocardiographic signs of PH at 2 anatomic sites, or TR velocity ≤ 3.0 m/s or unable to measure TR plus echocardiographic signs of PH at 3 anatomic sites. Likelihood of PH was considered intermediate with similar TR

description but when fewer anatomic sites were present and considered low when TR was ≤ 3.0 m/s or not measurable and ≤ 1 anatomic site was abnormal.

The location of heartworms within the RA, RV, and pulmonary arteries was recorded. The intracardiac worm burden within the RA was assessed in multiple views of the heart and estimated as low (a few worms; estimated < 5) or high (more than a few in the RA and fills the RA) (Figure 1, Video S1, and Video S2). Estimated worm burden was classified without knowledge of the dog's clinical status, presence or absence of pigmenturia, or whether or not heartworm extraction was performed. The presence of concurrent congenital or acquired heart disease was recorded. Arrhythmias and effusion (pericardial, pleural, ascites) were recorded if present during the initial evaluation or observed during the echocardiogram.

2.4 | Statistical analysis

Descriptive statistics (mean, median, SD, and range) were calculated. Continuous variables were assessed for normality using the Shapiro-Wilk test and reported as mean ± SD or median and range (minimum-maximum). Data were compared using Student's *t* test if normally distributed and Mann-Whitney *U* test if not normally distributed. Categorical data were compared with Fisher's exact test or chi-squared analysis and was reported as frequency. Values of *P* < .05 were considered significant.

3 | RESULTS

Twenty-five dogs were excluded because preoperative echocardiogram images were unavailable (*n* = 1) or because heartworms were identified only in the pulmonary arteries (*n* = 24). Seventy-two dogs met the inclusion criteria. Clinical characteristics are reported in Table 1. Breeds included Chihuahua (*n* = 29), mixed breed (*n* = 10),

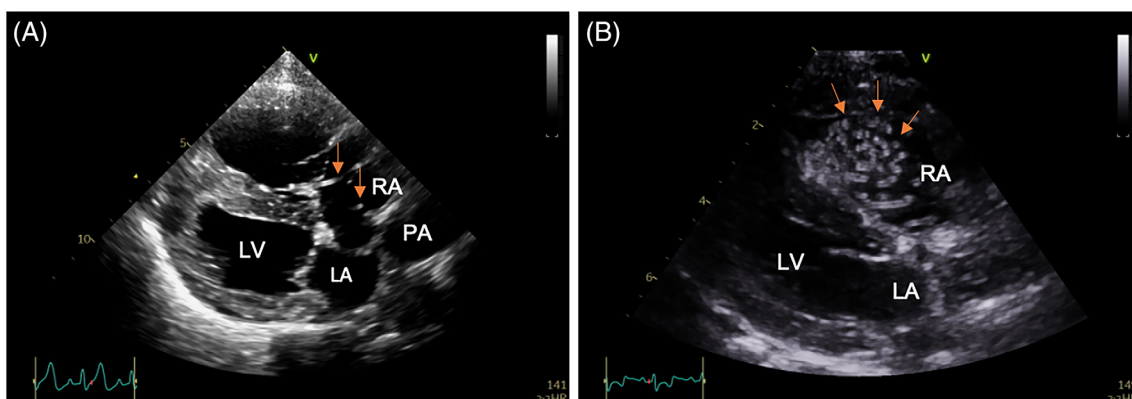


FIGURE 1 Echocardiographic images of the heart from a right parasternal long-axis 4 chamber view in 2 dogs with intracardiac heartworms that appear as parallel hyperechoic lines (arrows). Panel A is an example of an estimated low worm burden (a few worms present in the right atrium; estimated < 5). Panel B is an example of an estimated high worm burden (more than a few worms and fills the right atrium). LA, left atrium; LV, left ventricle; PA, pulmonary artery; RA, right atrium

Dachshund (n = 8), Labrador retriever (n = 4), American Pit Bull terrier (n = 2), Pekingese (n = 2), Boxer (n = 2), poodle (n = 2), and 1 each of Havanese, Golden retriever, German shepherd dog, Yorkshire terrier, French bulldog, Great Pyrenees, Italian greyhound, Staffordshire terrier, Cavalier King Charles spaniel, Papillon, Shetland sheepdog, Boston terrier, and miniature pinscher. Small breed dogs (adult, < 10 kg) represented the majority (75%) of the study population. During the same time frame, 1943 Chihuahuas and 2973 Labrador retrievers were admitted to either the emergency or cardiology service resulting in a prevalence of 1.5% in Chihuahuas versus 0.1% in Labrador

retrievers. Median body condition score was 5 on a scale of 9 (range, 2-8). At the time of presentation, all dogs resided in Texas. Month of presentation is presented in Figure 2. The total number of heartworm extractions performed was evenly distributed across all 4 seasons (Figure 2).

At presentation, 38 of 72 dogs (53%) were reportedly receiving heartworm prevention, 24 of 72 (33%) were receiving doxycycline or minocycline, and 24 of 72 (33%) were receiving prednisone or prednisolone. Six dogs had recent administration of a single dose of melarsomine. A total of 23 of 72 (32%) were receiving 1 or more

TABLE 1 Clinical characteristics of 72 dogs with intracardiac heartworms classified by estimated heartworm burden

| Characteristic | All dogs | High worm burden | Low worm burden | P |
|-----------------------------------|--------------------------|---------------------------|------------------------|---------|
| Number | 72 | 58/72 (81%) | 14/72 (19%) | NA |
| Age | 4.9 ± 2.6 | 4.7 ± 2.5 | 6.0 ± 3.2 | NS |
| Sex | 40 M (56%) 32 F (44%) | 32 M (5-5%) 26 F (45%) | 8 M (57%) 6 F (43%) | NS |
| Weight (kg) | 5.1 (1.2-38.2) | 4.9 (1.2-38.2) | 7.9 (1.6-30.0) | NS |
| Small breed | 54 (75%) | 46/58 (79%) | 8/14 (57%) | NS |
| Chihuahua | 29 (40%) | 25/58 (43%) | 4/14 (29%) | NS |
| Lethargy | 32 (44%) | 27/58 (47%) | 5/14 (36%) | NS |
| Pigmenturia | 31 (43%) | 30/58 (52%) | 1/14 (7%) | <.002 |
| Inappetence | 27 (38%) | 23/58 (40%) | 4/14 (29%) | NS |
| Cough | 24 (33%) | 20/58 (35%) | 4/14 (29%) | NS |
| Dyspnea | 24 (33%) | 21/58 (36%) | 3/14 (21%) | NS |
| Ascites | 22 (31%) | 15/58 (26%) | 7/14 (50%) | NS |
| Syncope | 6 (8%) | 3/58 (5%) | 3/14 (21%) | NS |
| Complete blood cell count | | | | |
| Anemia (packed cell volume < 37%) | 40/68 (59%) | 37/55 (67%) | 3/13 (23%) | <.005 |
| Leukocytosis (WBC > 17 000) | 33/53 (62%) | 30/46 (65%) | 3/7 (43%) | NS |
| Eosinophilia (> 1250) | 10/49 (20%) | 9/42 (21%) | 1/7 (14%) | NS |
| Thrombocytopenia (< 175 000) | 25/48 (52%) | 21/41 (51%) | 4/7 (57%) | NS |
| Microfilaria | 19/54 (35%) | 18/46 (39%) | 1/8 (13%) | NS |
| Chemistry | | | | |
| Increased ALT (> 130 U/L) | 24/56 (43%) | 19/46 (41%) | 5/10 (50%) | NS |
| Increased ALP (> 147 U/L) | 15/56 (27%) | 12/46 (26%) | 3/10 (30%) | NS |
| Increased BUN (> 29 mg/dL) | 24/67 (36%) | 20/53 (38%) | 4/14 (29%) | NS |
| Increased creatinine (> 2 mg/dL) | 3/67 (4%) | 2/53 (4%) | 1/14 (7%) | NS |
| Hyperalbuminemia (> 3.6 g/dL) | 12/55 (22%) | 10/46 (22%) | 2/9 (22%) | NS |
| Hyperglobulinemia (> 3.8 g/dL) | 28/53 (53%) | 25/45 (56%) | 3/8 (38%) | NS |
| Hyperbilirubinemia (> 1.0 mg/dL) | 20/55 (36%) | 20/55 (36%) | 0/9 (0%) | NS |
| Urine | | | | |
| Proteinuria | 41/44 (93%) | 35/38 (92%) | 6/6 (100%) | NS |
| Bilirubinuria | 30/42 (71%) | 28/36 (78%) | 2/6 (33%) | <0.05 |
| Procedure | | | | |
| Extraction performed | 47 (65%) | 46/58 (79%) | 1/14 (7%) | <.00001 |
| Heartworms extracted | 23 (3-77) | 18 (3-77) | 3 | NA |

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; F, female; M, male; NA, not applicable; NS, not significant; WBC, white blood cell.

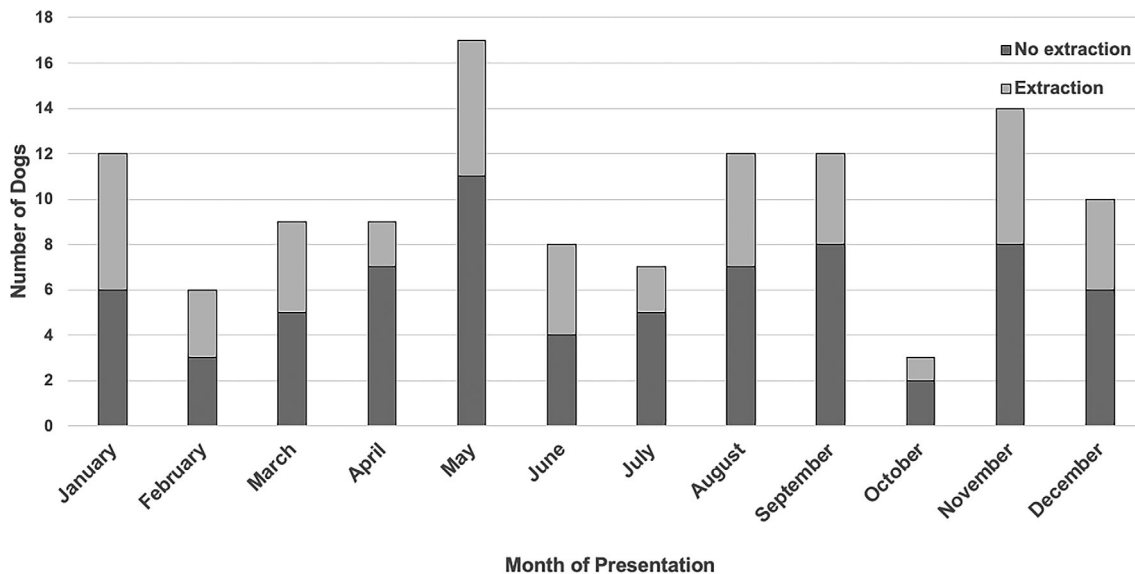


FIGURE 2 Frequency distribution of 72 dogs with (47) and without (25) heartworm extraction performed grouped by month of year at the time of presentation. Number of extractions performed was equally distributed between seasons (Winter = December, January, February; Spring = March, April, May; Summer = June, July, August; Fall = September, October, November)

medications including furosemide in 15 of 72 (21%), benazepril or enalapril in 13 of 72 (18%), pimobendan in 9 of 72 (13%), sildenafil in 4 of 72 (6%), spironolactone in 2 of 72 (3%), and digoxin in 1 of 72 (1%).

Clinical characteristics are reported in Table 1. The most common clinical signs were lethargy in 32 of 72 (44%), pigmenturia in 31 of 72 (43%), inappetence in 27 of 72 (38%), dyspnea in 24 of 72 (33%), and cough in 24 of 72 (33%). Four of the 31 dogs with pigmenturia (13%) were prescribed antibiotics for presumptive urinary tract infection prior to referral. Syncope was reported in 6 of 72 (8%) dogs, including dogs in both worm burden groups.

At presentation, 10 of 69 (15%) dogs were reportedly depressed. Mucous membranes were pale in 37 of 66 (56%), pink in 28 of 66 (42%), and grayish pink in 1 of 66 (2%). Patient variables included mean body temperature of 100.8 F (SD 1.3), mean heart rate of 140 beats per minute (SD 30), and median respiratory rate of 40 breaths per minute (range, 20-124 breaths per minute). Pulse quality was reported as good in 77% (43/56), fair in 9% (5/56), poor in 9% (5/56), bounding in 4% (2/56), and thready in 2% (1/56) of dogs. Jugular pulses were reported in 14 of 72 (19%) dogs. Crackles were reported on lung auscultation in 8 of 72 (11%) dogs. A cardiac auscultation abnormality was reported in 68 of 72 dogs that included murmur in 64 of 68 (94%), gallop in 3 of 68 (4%), and split S2 in 1 of 68 (2%). The murmur was systolic in the majority in which it was recorded (52/54; 96%) with a median murmur grade of 5 out of 6 (range, 2-6). Murmur location was reported in 58 dogs and was categorized as right sided in 45 of 58 (78%), left sided in 10 of 58 (17%), and both right and left sided in 3 of 58 (5%). In 2 dogs with concurrent mild pulmonic stenosis, murmur timing was characterized as systolic and diastolic.

Selected clinicopathologic results are reported in Table 1. Compared to dogs with a low worm burden, dogs with high worm burden

were more likely to be anemic ($P < .005$), have pigmenturia ($P < .002$), and bilirubinuria ($P < .05$). Anemia was present in 22 of 31 dogs (71%) with pigmenturia and in 18 of 38 dogs (47%) without pigmenturia. With regard to the entire study population, mean packed cell volume was 34% (SD 12; range, 13%-60%) in 67 dogs, and median total solids was 7.3 g/dL (range, 4.0-8.8 g/dL) in 65 dogs. Median total white blood cell count was 19 200/ μ L (range, 4900-40 700/ μ L; reference: 6,000-17 000/ μ L) in 53 dogs. Median eosinophil count was 250/ μ L (range, 0-9106/ μ L; reference: 100-1250/ μ L) in 49 dogs. Eosinophilia was uncommonly reported (10 of 49 dogs), and all but 1 had a high estimated worm burden. Median platelet count was 163 500/ μ L (range, 5000-514 000/ μ L clumped not reported; reference: 200 000-500 000/ μ L) in 48 dogs; thrombocytopenia (platelet count $<$ 175 000/ μ L) was similar between worm burden groups. Median alanine aminotransferase was 92 U/L (range, 10-2480 U/L; reference: 10-130 U/L) and median alkaline phosphatase was 78 U/L (range, 10-1488 U/L; reference: 24-147 U/L) in 56 dogs. Median blood urea nitrogen was 25 mg/dL (range, 6-86 mg/dL; reference: 5-29 mg/dL) and creatinine was 0.62 mg/dL (range, 0.3-2.45 mg/dL; reference: 0.5-1.5 mg/dL) in 67 dogs. Median albumin was 3.2 g/dL (range, 1.7-4.6 g/dL; reference: 2.4-3.6 g/dL) in 55 dogs and globulin was 3.9 g/dL (range, 2.3-5.6 g/dL; reference: 1.7-3.8 g/dL) in 53 dogs. Of the dogs that had a urinalysis performed, 93% (41/44) had proteinuria, 68% (30/44) had bilirubinuria, and 45% (20/44) had hematuria ($>$ 5 red blood cells per high power field). Seven of these had proteinuria only while the remaining had combinations including 16 dogs with proteinuria, bilirubinuria, and hematuria reported. A urine protein to creatinine ratio was available to quantify proteinuria in 12 of 41 dogs (29%), all of which had an estimated high heartworm burden and significant proteinuria based on a ratio $>$ 0.5. A total of 97% (70/72) dogs had a positive heartworm antigen test or microfilaria identified.

Echocardiographic estimated intracardiac heartworm burden was low in 14 of 72 (19%) and high in 58 of 72 (81%). Heartworm location based on echocardiography included the RA in 71 of 72 (99%) and RV in 58 of 72 (81%). Worms were also identified in the PT in 38 of 72 (53%) and right branch of the pulmonary artery in 57 of 72 (79%). In the 38 dogs with heartworms identified both intracardiac and in the PT, estimated intracardiac worm burden was high in 35 (92%) and low in 3 (8%).

Echocardiographic measurements are reported in Table 2. With the exception of LA:Ao, none of the echocardiographic variables were significantly different between high or low heartworm burden groups. Left ventricular internal dimensions were not enlarged in any dog and measured small in 37 out of 72 dogs (51%). Right ventricular enlargement was severe in 40 out of 72 (56%). In the 70 dogs with RV enlargement, hypertrophy was classified as concentric (n = 17), eccentric

(n = 2; 1 dog with concurrent third-degree AV block), or both (n = 51). Diameter of the RA was larger than the left in most dogs (65/71, 92%) based on RA:LA > 1. Enlargement of the PT was also common (61/71, 86%) based on a PT:Ao > 1. A high likelihood of PH was supported by a RPAD index < 30% in 49 of 69 dogs (71%) and transpulmonic velocity profile AT:ET ratio < 0.30 in 34 of 68 dogs (50%). Values < 22% for RPAD index suggested severe PH in 36 of 69 (52%) including 28 of 55 (51%) with a high worm burden and 8 of 14 (57%) with a low worm burden. Mid systolic notching of transpulmonic velocity profiles was rarely identified (n = 3).

Tricuspid valve regurgitation was documented in the majority of dogs (69/72, 96%) but could not be measured in 18 dogs because of the presence of heartworms (n = 15) or because the regurgitant jet was too small to acquire a Doppler signal (n = 3). Peak TR regurgitation velocity was suggestive of severe PH (> 4.5 m/s) in 9 of 52 dogs

TABLE 2 Echocardiographic variables in 72 dogs with intracardiac heartworms classified by estimated high (N = 58) and low (N = 14) heartworm burden

| Variable | All dogs | N | High | N | Low | N | P |
|--|---------------------|----|---------------------|----|---------------------|----|------|
| LVIDd (cm) | 1.75 (0.51-4.00) | 72 | 1.76 (0.91-4.00) | 58 | 1.92 (0.51-3.26) | 14 | NS |
| LVIDdN | 1.06 ± 0.30 | 72 | 1.07 ± 0.29 | 58 | 1.00 ± 0.36 | 14 | NS |
| LVIDdN < 1.27 | 53 (73.6%) | 72 | 43 (74%) | 58 | 10 (71%) | 14 | NS |
| LVIDs (cm) | 1.01 (0.16-3.20) | 72 | 1.06 (0.16-3.2) | 58 | 0.92 (0.16-1.93) | 14 | NS |
| LVIDsN | 0.58 ± 0.25 | 72 | 0.60 ± 0.25 | 58 | 0.50 ± 0.27 | 14 | NS |
| LVIDsN < 0.71 | 47 (65.2%) | 72 | 36 (62.1%) | 58 | 11 (78.6%) | 14 | NS |
| FS (%) | 42.47 (19.23-86.55) | 72 | 42.36 (19.23-82.64) | 58 | 49.43 (27.54-86.55) | 14 | .06 |
| LA:Ao short axis | 1.26 ± 0.19 | 71 | 1.24 ± 0.17 | 57 | 1.38 ± 0.24 | 14 | <.01 |
| LA diameter (cm) | 1.76 (0.52-3.51) | 71 | 1.71 (0.52-3.54) | 58 | 2.28 (1.19-3.10) | 14 | NS |
| RA diameter (cm) | 2.28 (1.12-6.31) | 71 | 2.32 (1.12-6.31) | 58 | 2.13 (1.29-4.62) | 13 | NS |
| RA:LA | 1.39 (0.62-4.29) | 71 | 1.36 (0.68-4.29) | 58 | 1.49 (0.62-1.74) | 13 | NS |
| RA:LA > 1 | 65 (91.5%) | 71 | 55 (94.8%) | 58 | 10 (76.9%) | 13 | .07 |
| RV enlargement none/mild/moderate/severe | 2/6/24/40 | 72 | 0/4/24/30 | 58 | 2/2/0/10 | 14 | NA |
| Septal flattening | 39 (54.1%) | 72 | 33 (56.9%) | 58 | 6 (42.9%) | 14 | NS |
| TR present | 69 (95.8%) | 72 | 56 (96.6%) | 58 | 13 (92.9%) | 14 | NS |
| TR (m/s) | 3.83 (1.50-5.41) | 52 | 3.83 (2.70-5.41) | 40 | 3.79 (1.50-4.96) | 12 | NS |
| PR present | 53 (73.6%) | 72 | 42 (72.4%) | 58 | 11 (78.6%) | 14 | NS |
| PR (m/s) | 2.89 (1.22-3.82) | 49 | 2.81 (1.22-3.82) | 39 | 3.22 (1.30-3.80) | 10 | .07 |
| PT:Ao | 1.31 ± 0.31 | 71 | 1.32 ± 0.32 | 57 | 1.28 ± 0.27 | 14 | NS |
| PT:Ao > 1 | 61 (85.9%) | 71 | 49 (85.9%) | 57 | 12 (85.7%) | 14 | NS |
| AT:ET | 0.29 (0.14-0.55) | 68 | 0.30 (0.14-0.55) | 55 | 0.28 (0.19-0.41) | 13 | NS |
| AT:ET < 0.3 | 34 (50%) | 68 | 26 (47.2%) | 55 | 8/13 (61.5%) | 13 | NS |
| RPAD index | 22.97 ± 13.31 | 69 | 24.01 ± 13.85 | 55 | 18.89 ± 10.43 | 14 | NS |
| RPAD index < 30% | 49 (71%) | 69 | 37 (67.2%) | 55 | 12 (85.7%) | 14 | NS |
| RA pressure estimate 5/10/15 mmHg | 5/51/16 | 72 | 2/45/11 | 58 | 3/6/5 | 14 | NA |

Abbreviations: AT:ET, acceleration time to ejection time ratio; FS, fractional shortening; LA, left atrium; LA:Ao, left atrium to aorta ratio; LVIDd, left ventricular internal dimension at end-diastole; LVIDdN, left ventricular internal dimension at end-diastole normalized to body weight; LVIDs, left ventricular internal dimension at end-systole; LVIDsN, left ventricular internal dimension at end-systole normalized to body weight; NA, not applicable; NS, not significant; PR, pulmonary regurgitation; PT:Ao, pulmonary trunk diameter to aorta diameter ratio; RA, right atrium; RA:LA, right atrium diameter to left atrium diameter ratio; RPAD, right pulmonary artery distensibility; RV, right ventricle; TR, tricuspid regurgitation.

in which it could be measured (3 low worm burden, 6 high worm burden).

The likelihood of PH was high in 67 of 72 dogs (93%), intermediate in 3 of 72 dogs (4%), and low in 2 of 72 dogs (3%). A high likelihood of PH was estimated based on TR > 3.4 m/s plus an echocardiographic sign of PH at 1 anatomic site in 38 dogs, TR 3.0-3.4 m/s plus echocardiographic signs of PH at 2 anatomic sites in 8 dogs, TR ≤ 3.0 m/s plus echocardiographic signs of PH at 3 anatomic sites in 3 dogs, no TR plus echocardiographic signs of PH at 3 anatomic sites in 3 dogs, and TR present but unable to measure due to the presence of worms plus echocardiographic signs of PH at 3 anatomic sites in 15 dogs.

Dogs were categorized into 4 groups based on the presence or absence of pigmenturia and a high likelihood of PH. In the 67 dogs with a high likelihood of PH, pigmenturia was identified in 29 (43%). In the 5 dogs without a high likelihood of PH, pigmenturia was identified in 2 (40%), both of which had a high worm burden. Three dogs did not have evidence of either pigmenturia or PH.

Congenital heart disease or pericardial communication was documented in 6 of 72 (8%) and included mild pulmonic stenosis (4), tricuspid valve dysplasia (1), and peritoneal pericardial diaphragmatic hernia (1). Degenerative valve disease was documented in 15 of 72 dogs (21%), with 14 classified as stage B1 (no left atrial or left ventricular enlargement).³⁷ One dog with left atrial enlargement but without left ventricular enlargement had a high likelihood of PH (TR 3.9 m/s plus 2 anatomic sites) and was not classified because of the potential confounding effects of PH on the left ventricle.²⁵ Left base murmurs were reported in 3 of 4 dogs with pulmonic stenosis, and left apical murmurs were reported in 3 of 15 dogs with degenerative valve disease (none of the 3 dogs had left atrial enlargement).

Pericardial effusion was documented in 7 of 72 (10%) and estimated as scant in all cases. Pleural effusion was documented in 4 of 72 (6%) and estimated as mild in all cases. Ascites was identified in 22 of 72 (31%), including 15 dogs with a high worm burden and 7 dogs with low worm burden. All dogs with ascites had a high likelihood of PH.

Electrocardiographic abnormalities, acquired from 6-lead ECG or contemporaneous ECG during echocardiography, were documented in 15 of 72 dogs (21%) and included supraventricular premature complexes in 9, ventricular premature complexes in 7, second-degree atrioventricular block in 1, and third-degree atrioventricular block in 1, with combinations of arrhythmias (typically supraventricular and ventricular premature complexes) documented in 3 dogs.

The number of heartworm extraction procedures and worms extracted is reported in Table 2. Extraction was performed without complication in 1 dog with an estimated low worm burden. One dog with an estimated high worm burden had 2 extractions performed within 24 hours when worms out of reach deep in the pulmonary arteries migrated into the RA after initial successful intracardiac worm extraction. Heartworm extraction was performed in 19 of the 29 Chihuahuas with a median of 10 worms removed (range, 3-51). The total number of dogs that had extraction performed was evenly distributed over all meteorological seasons as follows (Figure 2): Winter (December, January, February) totaled 15 dogs with 13 extractions

performed; Spring (March, April, May) totaled 23 dogs with 12 extractions performed; Summer (June, July, August) totaled 16 dogs with 11 extractions performed; Fall (September, October, November) totaled 18 dogs with 11 extractions performed. A low number of intraoperative complications occurred and included 1 dog that required a blood transfusion and 4 dogs with cardiopulmonary arrest (3 were euthanized, 1 died). Postoperative complications were also rare and included 1 dog euthanized due to progressive shock and suspected disseminated intravascular coagulopathy and 1 with skin incision dehiscence.

Heartworm extraction was not performed in 25 of 72 dogs (35%). In 12 dogs, the procedure was not recommended due to low estimated worm burden and no evidence of hemolysis, and in 11 dogs, it was recommended but declined by owners. For the remaining 2 dogs, 1 dog had intracardiac worms migrate to the PT after stabilization with intravenous administration of fluids, dexamethasone sodium phosphate IV, and oxygen supplementation and 1 dog with a high worm burden remained oxygen dependent and too unstable for a procedure, with owners electing euthanasia.

4 | DISCUSSION

This study describes clinical and echocardiographic characteristics of dogs with intracardiac heartworms. The majority of dogs (75%) in this study were adult, small breeds (< 10 kg), most notably Chihuahuas. Chihuahuas accounted for 40% of the total study group representing 1.5% of those admitted to the emergency or cardiology service, had variable estimated worm burdens, and had a highly variable number of worms removed (3-55). The overrepresentation of small breed dogs could relate to breed popularity; however based on the large difference in prevalence in the Chihuahua (1.5%) versus the Labrador Retriever (0.1%), it might represent a real and clinically relevant difference indicating a predisposition for worm migration in small dogs independent of worm burden coupled with the relatively small size of the dogs compared with the length of the worms.

Caval syndrome occurs in 13% to 20% of heartworm-positive dogs,^{7,15,19,38} and it is defined in a variety of ways. Clinical evidence of CS has most recently been summarized as a "sudden onset of severe lethargy and weakness accompanied by hemoglobinemia and hemoglobinuria."⁹ In early descriptions, prior to the availability of echocardiography, CS was also referred to as dirofilarial hemoglobinuria or liver failure syndrome and was described as acute onset illness (eg, dyspnea, anorexia, lethargy, weakness, jugular distension) with evidence of hemolysis (eg, anemia, hemoglobinuria, pale mucous membranes) in a dog with microfilaria, known heartworm infection or abnormally distributed worms within the right heart.^{7,10,14,15} Auscultation abnormalities in dogs with heartworm disease complicated by PH or CS include a systolic right heart murmur from TR or presence of worms, diastolic left base murmur from PR, gallop, and split S2.^{9,11} A heart murmur or other auscultatory abnormality was present in nearly every dog in this study often irrespective of concurrent underlying heart disease (eg, pulmonic stenosis, degenerative valve disease). This might serve as an indicator that intracardiac worms or PH are present

in a heartworm positive dog, but is not specific for CS.^{8,15} Although intracardiac heartworms can result in CS in dogs,^{3,7,10,11,22} only 25% of dogs in our study had evidence of anemia, pigmenturia, and clinical signs consistent with CS. In part, the lower percentage of CS was attributed to maintaining the stricter definition of CS for dogs in this study. The development of CS is likely a multifactorial process related to dog size, worm burden, and overall hemodynamics including high pulmonary artery pressure and changes in cardiac output.^{7,12,20,39}

Echocardiography is the diagnostic test of choice to confirm intracardiac worms in dogs with suspected CS. It could also be a useful screening tool for staging heartworm-positive small breed dogs to confirm worm location prior to developing a treatment protocol. In this study, we also described the use of echocardiography for estimating intracardiac worm burden and used those estimates to further characterize the population, though no antemortem test can definitively determine actual heartworm number.^{9,17} Within our study population, over 80% of dogs with intracardiac worms had an estimated high worm burden.

Pigmenturia, an abnormal urine color that can represent bilirubin, myoglobin, hemoglobin, or blood, was used as an indicator of potential hemolysis in this study. It was the second most commonly reported clinical sign and was described in nearly half of the population. Pigmenturia due to hemoglobinuria, an indicator of red blood cell lysis secondary to worms near the tricuspid valve, can be intermittently observed in dogs when worms migrate into the right heart.^{10,14} A urinalysis was not always performed to confirm the source of pigmenturia prior to heartworm extraction in our study, particularly when a heartworm positive dog with pigmenturia had clinical signs and echocardiographic confirmation of intracardiac worms. Anemia was present in dogs with and without pigmenturia. The absence of anemia in dogs with pigmenturia suggests a short-term presence of intracardiac worms or low worm burden. In those dogs with reported pigmenturia, 13% were prescribed antibiotics for suspected urinary tract infection prior to referral, some of which were male dogs without reported clinical signs of a urinary tract infection. This highlights the importance of recognizing pigmenturia as a potential sign of heartworm disease and CS, especially in dogs with unknown heartworm status.

Similar to previous reports, leukocytosis was present in 62% of dogs, primarily those from the high worm burden group.^{1,3,4,5,11,19} Eosinophilia was a relatively uncommon finding with a frequency of only 20% in those dogs in which it was evaluated, and all 10 dogs with a peripheral eosinophilia were small breed with predominately high estimated worm burden. Proteinuria, which occurs in 19% of dogs with heartworm infection and 50% of dogs with CS,^{5,15,40} was identified in the majority of dogs with intracardiac heartworms in this study.

Caval syndrome occurs most often in late winter and throughout the spring and into summer.^{2,9-11,14-16,22} The number of heartworm extractions performed in this study was even across seasons. This is likely due to the temperate conditions of Texas year-round and does not take into account dogs that had extraction recommended but not performed.

Removal of worms is recommended when migration of worms into the right heart chambers produces the sudden onset of severe

clinical signs.⁹ Heartworm removal is associated with poor outcomes in severely affected dogs,¹⁴ but survival to discharge is associated with a good long-term prognosis.¹ Treatment recommendations for heartworm disease are primarily based on the presence or absence of clinical signs and CS rather than heartworm burden.⁹ The results of our study suggest that differentiating high from low worm burden might be important to consider when developing a treatment plan that includes heartworm extraction in an individual dog. Dogs with a high worm burden were more likely to have anemia, pigmenturia, and bilirubinuria. Dogs with low worm burdens were unlikely to have pigmenturia in our study and in two dogs, intracardiac heartworms were incidentally found during work up of right heart failure and suspected PH. Dogs with severe heartworm disease that do not have evidence of hemolysis (including pigmenturia) can have clinical signs attributed to PH and right heart failure.^{8,20,41} All dogs with a murmur and ascites in this study had evidence of PH, a finding that has been previously reported.⁴² Dogs with intracardiac heartworms with low worm burdens that do not have active hemolysis might benefit from medical therapy as opposed to manual extraction. At our institution, dogs with a high worm burden (with or without evidence of CS) are more likely to have worm extraction recommended than dogs with low worm burden and right heart failure attributed to PH.

In heartworm disease, changes to the pulmonary arteries are characterized by intimal thickening and proliferation and occur within the first 18 months of the disease process in experimentally infected dogs.^{7,43,44} The majority of dogs in our study group had a high likelihood of PH based on echocardiographic assessment and recently described consensus statement guidelines.²⁵ Only 5 dogs in this study population did not have a high likelihood of PH, although 1 of these was receiving sildenafil at the time of presentation. A low likelihood of PH might be more likely to occur early in the heartworm disease process or in dogs that are receiving medications to lower pulmonary artery pressures. The presence of intracardiac heartworms, in particular high worm burdens, can impede echocardiographic assessment of PH. Traditionally, the severity of PH has been assigned based on peak systolic TR pressure gradient obtained via echocardiography; however, this was not advocated as a sole measure of PH severity in recent consensus statement guidelines.²⁵ In our study, only 17% of dogs had a high TR pressure gradient (peak velocity > 4.5 m/s) suggesting severe PH. In part, this was attributed to an inability to measure TR in approximately one third of dogs with a high worm burden due to worms in the RA that prevented adequate spectral Doppler characterization. Other echocardiographic parameters evaluating PH in dogs include RPAD index and PT:Ao.^{24,35,45} In our study, RPAD index was abnormal more often than PT:Ao and 52% of dogs had evidence of severe PH based on RPAD index < 22%. Pulmonary artery pathology and RPAD remain unchanged for at least 10 months after adulticide therapy, suggesting some changes persist long term.^{6,24,46} Interpretation of echocardiographic variables estimating the likelihood of PH across the spectrum of heartworm disease stages requires further study.

Parasitic embolism contributes to increased pulmonary artery pressures in heartworm disease.^{42,47,48} Migration of worms from the right heart back into the pulmonary arteries occurs after induction of

anesthesia for heartworm extraction and with stabilization prior to heartworm extraction, and is associated with the administration of pimobendan and sildenafil.^{1,41,49} Nine dogs in our study had intracardiac heartworms at presentation despite receiving phosphodiesterase inhibitors (eg, pimobendan, sildenafil), similar to a previous report.¹ Pimobendan and sildenafil have vasodilatory effects through phosphodiesterase inhibition, while pimobendan also is a positive inotrope able to increase cardiac output. Supplemental oxygen therapy was described in the stabilization of many of the dogs in the literature managed for CS, and might have been a contributing factor to worm migration given the vasodilatory effects of oxygen.

This study has several limitations including the retrospective design. Worm burden and presence of PH were based on estimates and likelihood, not direct observation or measurement.

In conclusion, small breed dogs with heartworm disease might be at increased risk for intracardiac heartworm migration. Although the majority of dogs with intracardiac heartworms had a high worm burden and high likelihood of PH, only 25% had clinical evidence of CS. Echocardiography is a useful tool to identify intracardiac heartworms and estimate likelihood of PH. It could also be useful for screening heartworm positive small breed dogs prior to developing a treatment protocol.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

ORCID

Ashley B. Saunders  <https://orcid.org/0000-0001-9908-3894>

Sonya Wesselowski  <https://orcid.org/0000-0002-0637-8288>

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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