STANDARD ARTICLE

Stenting of the caudal aorta and aortic trifurcation for the treatment of thrombosis in 7 dogs

Kelly A. Gavin[1] | Chick Weisse[2] | Allyson C. Berent[2]

[1]Department of Internal Medicine, Veterinary
Emergency and Referral Group, Brooklyn, New
York, USA

[2]Department of Interventional Radiology and
Endoscopy, Animal Medical Center, New York,
New York, USA

Correspondence
Kelly A. Gavin, Department of Internal
Medicine, Veterinary Emergency and Referral
Group, 196 4th Avenue, Brooklyn, NY 11217,
USA.
Email: kgavin@vergbrooklyn.com

Abstract

Background: Aortic and aortoiliac thrombosis in dogs causes disease and death.

Objective: To describe the procedure and outcomes for stenting the caudal aorta and aortoiliac trifurcation.

Animals: Seven client-owned dogs that underwent aortic/aortoiliac stenting for treatment of thrombosis.

Methods: Retrospective multi-center investigation. Medical records were reviewed for dogs that underwent stenting of the aorta or aortoiliac trifurcation between 2008 and 2020. Information collected included history, signalment, clinicopathologic data, diagnostic imaging, procedure reports, and outcomes.

Results: Seven dogs with an occlusive thrombus located at or near the aortic trifurcation were included. Four of 7 dogs were non-ambulatory. Hind limbs were paretic in 5 dogs, paralyzed in 1 dog, and claudication alone was noted in 1 dog. Five of the 7 dogs had protein-losing nephropathy (PLN). Of 5 dogs with PLN, 1 had protein-losing enteropathy (PLE) and controlled hypothyroidism and 1 had caudal aortic chondrosarcoma. Two dogs had no identified underlying disease. Angiography was performed before catheter directed thrombolysis and stent placement. No deaths occurred during the procedure. Postoperative complications included pain (4/7), bruising and edema (3/7), bruising only (1/7), and edema only (1/7). Median survival time (MST) of the 7 dogs was 264 days (range, 1-1053 days). Five of 7 dogs were ambulatory within 2 days of stenting and survived to discharge with a MST of 425 days (range, 208-1053 days).

Conclusions and Clinical Importance: Stenting of the aorta and aortoiliac trifurcation can provide an apparently safe and effective treatment with rapid return to ambulation for some dogs with aortic thrombosis.

KEYWORDS
anticoagulation, aortoiliac, hypercoagulability, leriche syndrome, rivaroxaban, stents, thrombolysis

---

1 | INTRODUCTION

Infrarenal aortic and iliac artery thrombosis in dogs can be associated with severe disease. Clinical signs depend on the extent and chronicity of the occlusion and can include exercise intolerance, lameness, pain, and collapse.[1-6] Hind limb paresis or paralysis, absent femoral pulses, absent distal limb pulses, and cold hind extremities are common physical examination findings.[2-5,7]

Aortoiliac thrombosis in dogs is believed to be an in-situ occurrence secondary to a prothrombotic state.[1,4,6,8] Risk factors for hypercoagulability include protein-losing nephropathy (PLN), protein-losing enteropathy (PLE), hyperadrenocorticism, hypothyroidism, neoplasia, and recent corticosteroid administration.[1-11] Many cases have no identifiable cause.[3,5]

The duration and severity of clinical signs influence therapeutic recommendations and prognosis. Medical therapy is often recommended in ambulatory dogs with chronic thrombi, whereas procedural intervention is more commonly considered in acute non-ambulatory dogs with life-threatening loss of limb perfusion.[1,3,12]

Goals of therapy include re-establishing hind limb blood flow before ischemia progresses to necrosis and life-threatening sequelae, preventing reperfusion injury, and preventing thrombus recurrence. A variety of pharmaceutical therapies are used in aortic thrombosis management in dogs. These include platelet inhibition by administration of aspirin or clopidogrel, anticoagulation by administration of unfractionated heparin, low molecular weight heparin, factor Xa inhibitors, or warfarin and systemic thrombolysis using tissue plasminogen activator (TPA) or streptokinase.[1,3,8,13,14]

Combined interventional techniques such as rheolytic thrombectomy, catheter directed thrombolysis/thrombectomy, balloon angioplasty, and vascular stenting can allow for return to function without the prolonged time and protracted recovery associated with medical therapy and surgery, respectively.[1,12,15]

There is currently no standardized medical or surgical protocol for treating aortic thrombosis in dogs.[7,16] The authors hypothesized that catheter directed thrombolysis and vascular stenting accompanied by antiplatelet and anticoagulation therapy would provide a rapid, safe, and effective treatment option for re-establishing blood flow to the hind limbs, facilitating rapid return to ambulation of dogs with aortic and aortoiliac thrombosis.

2 | MATERIALS AND METHODS

2.1 | Case selection

A review of medical records from the Mathew J. Ryan Veterinary Hospital of the University of Pennsylvania and the Animal Medical Center was conducted for dogs diagnosed with aortic thrombosis that received treatment by the authors with catheter-directed thrombolysis and vascular stenting, with or without balloon angioplasty between June 2008 and March 2020. Eight dogs received stents during this time period; however, records were only available for 7 dogs.

2.2 | Medical record review

The following data were recorded for each dog: signalment, history, clinical signs, physical examination findings, laboratory hematologic, biochemical, and coagulation findings, radiology reports, procedural reports, treatments, intraoperative and postoperative complications, short-term outcomes (≤14 days), long-term outcomes (>14 days), and necropsy reports. Acute presentation was defined as a duration of clinical signs for ≤5 days and chronic presentation was defined as >5 days. Hypertension was defined as a systolic blood pressure ≥ 160 mm Hg.[17] Imaging reports were generated by radiologists. Complications were defined as any clinically important change from the preoperative to postoperative period because of anesthesia, procedural intervention, or drugs administered. Clinicopathologic findings designated as perioperative occurred within 24 hours of the stenting procedure. Follow-up information was obtained from the medical record where the treatment was performed or from the referring veterinarian.

2.3 | Procedures

The specific procedures performed were not standardized; however, the following basic protocol was generally used. Stenting was performed under general anesthesia. Crystalloid fluid therapy was administered throughout the peri-anesthetic period. Dogs were placed in dorsal recumbency. The skin of the neck was clipped and prepared aseptically. Arterial access was achieved via the carotid arteries. The artery was isolated by blunt dissection, ligated distally (cranially), and catheterized allowing for placement of an introducer sheath. A combination of angled hydrophilic guide wire and angled diagnostic catheter was advanced under fluoroscopic guidance to the infrarenal aorta. Arteriography, using 50% iohexol contrast medium, was performed to identify the extent of the thrombosis and affected vessels. The catheter-wire combination was then advanced distal to the filling defect into an external iliac artery and sometimes down the limb. Tissue plasminogen activator was infused into the thrombus through the catheter as it was pulled retrograde back to the level of the aortic bifurcation. The angled diagnostic catheter was exchanged for a marker catheter and arteriography performed to determine affected vessel diameters and length of the thrombosis. For trifurcation lesions, a guide wire was placed into each external iliac artery and 2 separate laser-cut nitinol self-expanding metallic stents, typically delivered through the same vascular sheath, were passed over each wire and deployed simultaneously engaging one another in the terminal aorta, termed "kissing stents." Repeat arteriography was performed to confirm vessel patency (Figure 1). Additional overlapping stents were added as necessary if occlusion persisted beyond the
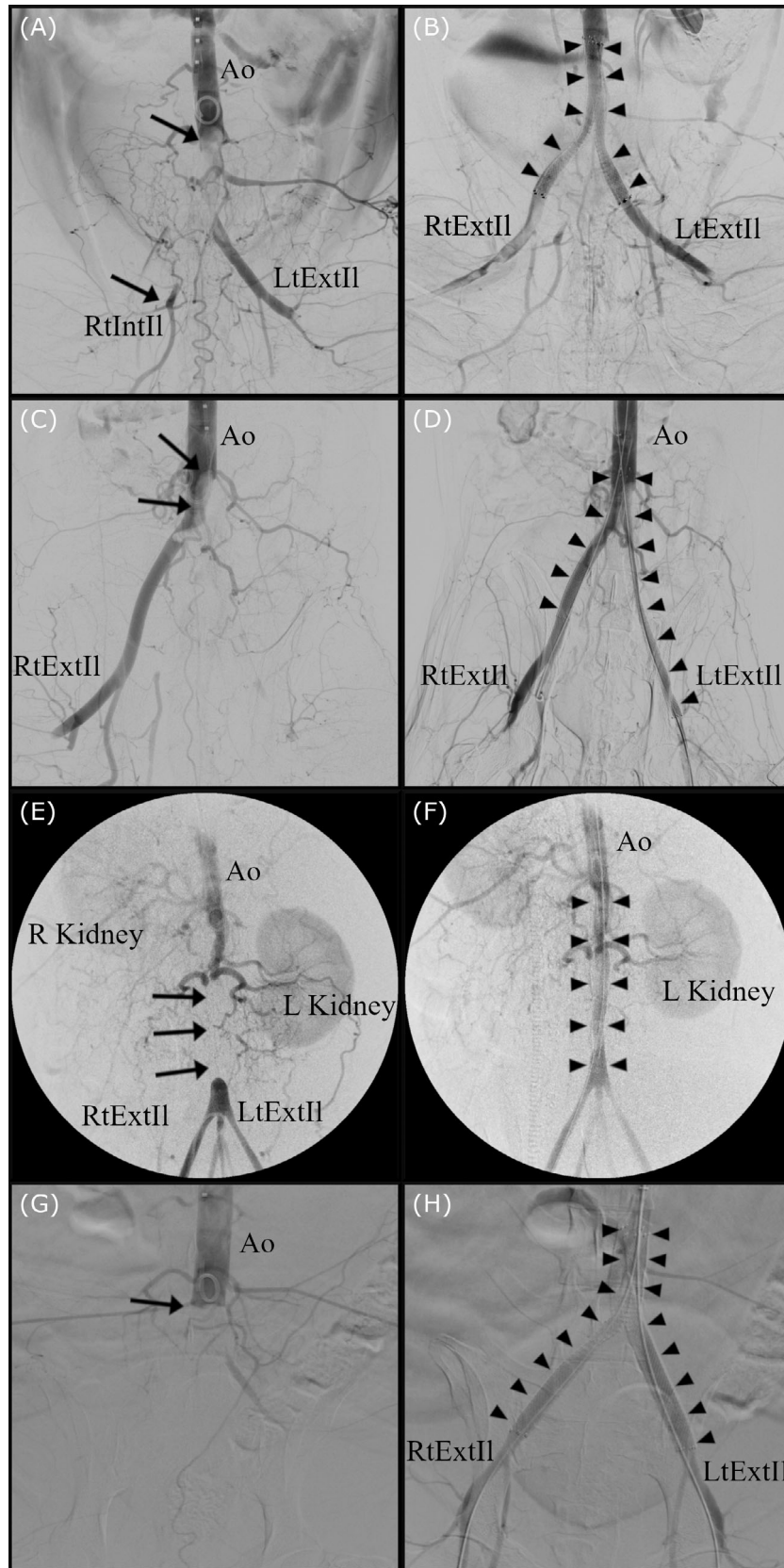
GAVIN ET AL.

Journal of Veterinary Internal Medicine ACVIM

Open Access

American College of
Veterinary Internal Medicine

443
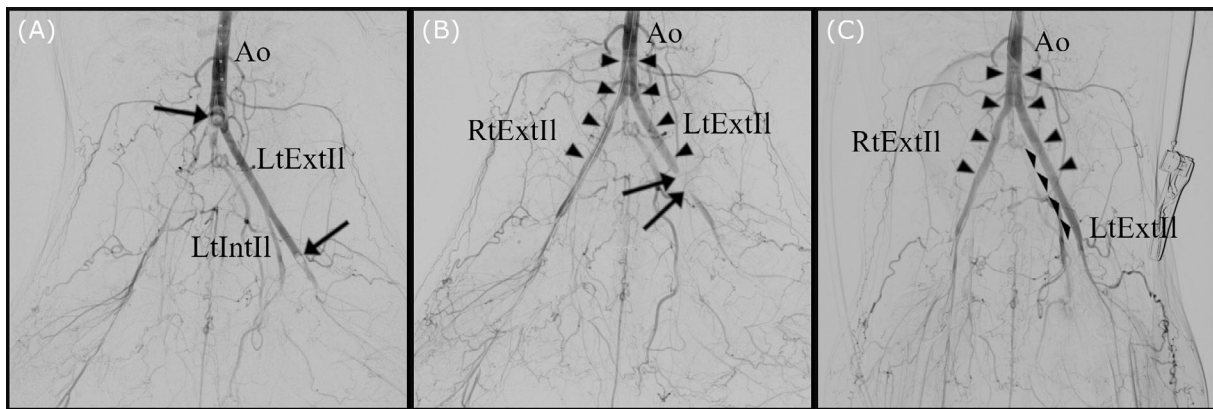

FIGURE 1 Legend on next page.

FIGURE 2 Serial DSA images of a 6-year-old male neutered mix-breed dog before stent placement (A), after placement of 2 initial "kissing" stents (B) and after placement of a third stent extending down the left external iliac (LtExtIl) artery (C). (A) Terminal aortic (Ao) DSA through marker pigtail catheter demonstrating filling defect (arrow) cranial to the aortic bifurcation with diminished internal and right external iliac artery perfusion. Thrombus in the caudal aorta (Ao) and right external iliac artery (RtExtIl; upper arrow) with collateralization is noted. There is moderate flow through the left internal iliac artery (LtIntIl). Distal thrombi were appreciated in the LtExtIl (lower arrow). The aortoiliac thrombus compromises blood flow through the right external iliac artery with no visible flow through the right internal iliac artery. (B) Repeat DSA image after placement of 2 "kissing" stents (arrowheads) revealing improved flow through the stents with persistent filling defects at the distal external iliac arteries but overall improved but still diminished flow through both external iliac arteries. A filling defect (arrows) is appreciated distal to the stent (arrowheads) placed in the LtExtIl. (C) Repeat DSA image after placement of a third stent (broad arrowheads) distal to the first in the LtExtIl resulting in improved blood flow and opacification of the left hind limb

stented area (Figure 2). The limbs were palpated to confirm restoration of femoral pulses. The introducer was removed, and the common carotid artery was ligated using encircling ligatures proximal (caudal) to the arteriotomy site. Subcutaneous tissues and skin were closed routinely.

3 | RESULTS

3.1 | Dogs

Seven dogs satisfied criteria for inclusion. Two dogs were treated at the Mathew J. Ryan Veterinary Hospital of the University of Pennsylvania between 2008 and 2009. Five dogs were treated at the Animal Medical Center from 2010 to 2020.

3.2 | Preoperative and perioperative findings

3.2.1 | Signalment

Four castrated male dogs and 3 spayed female dogs were included. The median age and weight of the dogs were 8.3 years (range, 6.0-13.8 years) and 36.5 kg (range, 18.8-43.6 kg), respectively. Breeds included 2 Greyhounds, 2 Labrador Retrievers, 1 Golden Retriever, 1 Soft Coated Wheaten Terrier, and 1 mixed breed dog.

FIGURE 1 Digital subtraction angiogram (DSA) images of 4 dogs, a 13-year-old female spayed Soft-Coated Wheaten Terrier (A,B), a 12-year-old male neutered Greyhound (C,D), a 7-year-old female spayed Labrador Retriever (E,F), and an 8-year-old male neutered Golden Retriever (G,H) before (A,C,E,G) and after (B,D,F,H) stent placement. (A) Terminal aortic (Ao) DSA through marker pigtail catheter demonstrating filling defect (upper arrow) cranial to the aortic bifurcation extending distally into the external iliac arteries (ExtIl) in a 13-year-old female spayed Soft-Coated Wheaten Terrier. Both internal iliac artery origins are occluded with distal reconstitution of the right internal iliac artery (RtIntIl) visible (lower arrow). (B) Repeat DSA image after placement of 2 "kissing" stents (arrowheads) revealing improved flow through the stents with persistent filling defects at the distal external iliac arteries but overall improved flow. (C) Terminal aortic (Ao) DSA through marker catheter demonstrating left external iliac artery (LtExtIl) and bilateral internal iliac artery origin occlusions secondary to a large distal aortic/LtExtIl thrombus (arrows) with a moderate amount of collateral circulation in a 12-year-old male neutered Greyhound. A lesser degree of right external iliac artery (RtExtIl) occlusion is also appreciated. (D) Repeat DSA image after placement of 2 "kissing" stents (arrowheads) revealing improved flow through the stents with restoration of LtExtIl blood flow and improvement of RtExtIl patency after stent placement (arrowheads). The comparative improved overall opacification demonstrates the improved perfusion to the hind limbs. (E) Dual aortic (Ao) and terminal aortic DSAs through catheters demonstrating a thrombus limited to the aorta (Ao) resulting in complete aortic occlusion (arrows) caudal to the renal arteries obstructing blood flow to the terminal aorta in a 7-year-old female spayed Labrador Retriever. The renal artery circulation appears normal. Prominent collateral circulation is observed helping to reconstitute the terminal aorta as well. (F) Repeat DSA image after placement of 2 side-by-side aortic stents (arrowheads) revealing restoration of blood flow to the caudal Ao. (G) Terminal aortic (Ao) DSA through marker pigtail catheter demonstrating filling defect (arrow) cranial to the aortic trifurcation extending distally into the external iliac (ExtIl) arteries in an 8-year-old male neutered Golden Retriever. Both internal iliac artery origins are occluded. (H) Repeat DSA image after placement of 2 "kissing" stents (arrowheads) revealing improved flow through the stents with restoration of left external iliac artery (LtExtIl) and right external iliac artery (RtExtIl) blood flow

3.2.2 | History

Four dogs were previously diagnosed with PLN, 1 of which had a history of concurrent PLE and controlled hypothyroidism. One dog was diagnosed with PLN after presentation and chondrosarcoma in the caudal aorta and unrelated pulmonary sarcoma at necropsy. Four dogs had a history of hypertension. Two dogs had no pertinent medical history before presentation. Medications being administered at the time of presentation included benazepril (2/7), doxycycline (2/7), enalapril (1/7), amlodipine (1/7), melatonin (1/7), lignans (1/7), Soloxine (1/7), carprofen (1/7), omeprazole (1/7), metronidazole (1/7), tylosin (1/7), codeine (1/7), amantadine (1/7), fluoxetine (1/7), alprazolam (1/7), aspirin (1/7), and pyridostigmine (1/7). No dog was receiving corticosteroids long term or at the time of presentation.

3.2.3 | Presenting complaints and clinical signs

Medical records for all 7 dogs included information regarding clinical signs and physical examination findings at presentation. Five dogs had an acute onset of clinical signs with a median duration of 1 day and a range from 1 hour to 5 days. Two dogs had a chronic progressive onset of clinical signs of 3- and 6-weeks duration. Six dogs were evaluated for hind limb abnormalities ranging from lameness to paralysis. One dog was initially evaluated for exercise intolerance at the end of walks as the sole complaint. Details are summarized in Table S1.

3.2.4 | Preoperative physical examination

Preoperative physical examination findings included weak or absent distal hind limb pulses (7/7), weak or absent femoral pulses (6/7), hind limb paresis (5/7), lameness (4/7), hind limb paralysis (1/7), and hypertension (1/5). Four of 7 dogs were non-ambulatory. Severity of bilateral physical examination findings (ie, paresis, lameness, pulse deficits) often varied between limbs and was asymmetrical in 5 dogs. The dog that presented for exercise intolerance had unremarkable hind limb orthopedic and neurologic examinations. Details are summarized in Table S1.

3.2.5 | Preoperative diagnostic imaging

The presence of a thrombus was diagnosed via ultrasonography in all 7 dogs. Six dogs had a thrombus at the aortic trifurcation and 1 dog had a 9.5 cm thrombus located caudal to the origin of the left renal artery, terminating cranial to the aortic trifurcation. Additional findings noted on abdominal ultrasonography included pancreatic edema in 1 limb (2/7), adrenal mass/nodule (2/7), hepatic nodules (2/7), small intestinal segmental corrugation (1/7), small intestinal multifocal mucosal speckling (1/7), splenic nodules (1/7), adrenal asymmetry (1/7), renal calculi (1/7), and abdominal effusion (1/7).

3.3 | Intraoperative findings

3.3.1 | Angiogram

Angiography confirmed the presence of a thrombus involving the aorta or the aorta and aortic trifurcation and a decrease or cessation in distal blood flow in all 7 dogs. Images were available for evaluation for all 7 dogs. Additional findings included unilateral (2/7) or bilateral (4/7) internal iliac artery origin occlusion (6/7), thrombi in 1 or both femoral or distal arteries (5/7), and thrombus material dislodging in real time from a large thrombus at the trifurcation to the branching of the internal and external iliac arteries (1/7).

3.3.2 | Procedure

The procedure was performed under general anesthesia in all 7 dogs. Median anesthesia time (5/7) was 1 hour 45 minutes (range, 1 hour, 40 minutes-3 hours, 5 minutes). Median procedure time (6/7) was 1 hour, 45 minutes (range, 1 hour, 13 minutes-2 hours 37 minutes). Arterial points of access included the right carotid artery (3/6), unspecified carotid artery (1/6), bilateral carotid arteries (1/6), and simultaneous carotid and right femoral artery (1/6). Catheter-directed thrombolysis with TPA (1.25-8 mg total dose) was distributed into multiple locations within the thrombi in all 7 dogs. Two stents were placed in 6 of 7 dogs and 3 stents were placed in 1 dog. In the dog that received 3 stents, repeat angiography revealed continued occlusion in the left distal external iliac artery after stent placement; therefore, a third stent was deployed extending further distally (Figure 2). Adjunctive procedures included IV TPA CRI at 0.5 mg/kg over an hour (1/7) and angioplasty with a 5 mm × 4 cm percutaneous transluminal angioplasty balloon inflated 3 times across the expanse of a nearly completely occluded right external iliac artery (1/7). Procedural variations between individual dogs are summarized in Table S2.

3.3.3 | Intraoperative complications

Three (3/7; 43%) intraoperative complications were recorded. Regurgitation during anesthetic induction and subsequent development of pneumonia during the course of hospitalization was noted in 1 dog. One dog with an arrhythmia, which was identified at initial examination, exhibited periods of sinus arrest with ventricular escape complexes and a paroxysmal accelerated idioventricular rhythm. In 1 dog, a stent delivery system nose cone became detached upon stent deployment and was successfully captured with a snare.

3.4 | Short-term results

3.4.1 | Postoperative diagnostic imaging

Four ultrasounds were performed postoperatively. Stent placement and blood flow were documented in the caudal aorta in 1 dog and in

both the caudal aorta and iliac arteries in 3 dogs. Persistent thrombi were noted in the right pelvic limb arteries in 2 of 4 dogs.

3.4.2 | Postoperative medications

All dogs received antithrombotic therapy in the postoperative period. Medications used in the postoperative period while hospitalized included clopidogrel (5/7), aspirin (4/7), enoxaparin (5/7), and unfractionated heparin (2/7). Drug dosages and combinations varied widely between dogs. Monitoring tests were chosen according to the mechanism of action of the anticoagulant used. Medication protocols and corresponding monitoring tests are summarized in Table S3.

3.4.3 | Postoperative complications

Hind limb pain between days 1 and 7 (4/7), pigmenturia on day 2 (2/7), hind limb edema with ecchymoses (2/7), hind limb and ventral abdominal edema with ecchymoses (1/7), hind limb ecchymoses only (1/7), and hind limb edema only (1/7) were noted postoperatively. Two of the 4 dogs that exhibited ecchymoses were greyhounds. Local effects of reperfusion injury marked by bruising and edema of the hind limbs and ventral abdomen were treated with N-acetylcysteine (70-75.8 mg/kg IV q6-8h; 2/7), pentoxifylline (16.7 mg/kg PO q8h; 1/7), and dexamethasone SP (0.1 mg/kg IV once; 1/7). Severe hypoalbuminemia developed in 2 dogs with PLN, necessitating treatment. One dog (albumin 1.4 g/dL, reference interval 2.7-3.9 g/dL) was treated with human albumin (2.5 g/kg IV) once on day 2 after stent placement and the other dog (albumin 1.4 g/d/L, reference interval 2.5-3.7 g/dL) received fresh frozen plasma (10 mL/kg IV) once on day 3. Anemia characterized by a PCV of 22% developed in 1 dog on day 3, necessitating a blood transfusion. The PCV of this dog upon presentation, before fluid therapy, was 63%. Discharged dogs with the postoperative complications of ecchymosis and edema (2/5) and hypoalbuminemia with or without anemia (2/5) that necessitated treatment had a mean hospitalization time of 9 days, compared to 4 days in dogs without these complications. Postoperative complications did not affect median survival time (MST). The 1 dog with bilateral carotid ligation had no related adverse clinical signs.

3.4.4 | Short-term outcome

Bilateral femoral pulses (6/7) and bilateral (6/7) and unilateral (1/7) distal hind limb pulses were palpable within 1 and 2 days, respectively. One dog presenting with only claudication signs (ie, pain or cramping attributable to decreased blood flow) that was discharged 3 days after stent placement did not have palpable femoral pulses noted until rechecks at days 11 (left only) and 48 (bilateral). This dog was never non-ambulatory.

Hypertension was documented in 7 of 7 dogs perioperatively. Five dogs required anti-hypertension medication while hospitalized and after discharge.

Of the 4 dogs that were non-ambulatory at presentation, the 1 that presented with peracute clinical onset of hind limb paralysis and lack of deep pain sensation was euthanized 24 hours after stent placement. Necropsy revealed a locally extensive subacute thrombus in the left renal artery, a poorly differentiated focal pulmonary sarcoma, and a luminal chondrosarcoma at the aortic trifurcation resulting in focal attenuation of the stents. The stents remained patent, however. One of these 4 dogs became independently ambulatory within 1 day of stenting. Two of the 4 dogs became ambulatory with assistance 1 and 2 days after stent placement, and independently ambulatory between 8 to 12 days and 4 days after stent placement, respectively.

Of the 3 dogs that presented ambulatory, 2 remained independently ambulatory on day 1 after stent placement, and 1 was ambulatory with assistance on day 1 and independently ambulatory by day 2 after stent placement. One of these 3 dogs suddenly collapsed with extreme pain on a walk while hospitalized 7 days after stent placement; This dog was receiving an unfractionated heparin CRI, while being monitored with daily measurement of activated partial thromboplastin time, and low dose aspirin postoperatively. The dog was subsequently euthanized. Necropsy and histopathology revealed an acute thrombus completely obstructing the stents. Postoperative orthopedic and neurologic examination findings are summarized in Table S4.

Five dogs survived to hospital discharge with a median duration of hospitalization of 7 days (range, 3-11 days). All discharged dogs were continued on antithrombotic therapy. Antithrombotic medications prescribed at discharge from the hospital included clopidogrel (3/5), aspirin (2/5), enoxaparin (2/5), dalteparin (1/5), and rivaroxiban (1/5).

3.5 | Long-term outcome and rethrombosis

Long-term follow-up information was available for all 5 dogs that were discharged from the hospital. Two dogs had bleeding while receiving antithrombotic medications. Spontaneous bleeding from the skin on the neck was noted in 1 dog on day 302 after stent placement. The dog was receiving clopidogrel (4 mg/kg PO q24h) and enoxaparin (1 U/kg SC q8h). Anti-Xa activity (1.2 U/mL) was at the upper limit of the reference interval (0.5-1.2 U/mL) 2 hours after administration and thromboelastography confirmed a hypocoagulable state. Clopidogrel was continued at the same dose and enoxaparin was decreased to 0.8 U/kg SC q8h. In the second dog, bleeding occurred at a surgical site after a mast cell tumor removal performed at another clinic on day 48 after stent placement. This dog was receiving dalteparin (143.5 U/kg SQ q24h), aspirin (0.48 mg/kg PO q24h), and clopidogrel (1 mg/kg PO q24h), which was not discontinued before the elective surgery. Administration of clopidogrel was continued, while that of aspirin was stopped for 1 week and dalteparin was stopped permanently. Subperiosteal, articular, and perioral hemorrhage were noted

in this dog on days 133 151, and 165 while receiving aspirin (0.48 mg/kg PO q24h) and clopidogrel (1 mg/kg PO q24h). Prothrombin time and activated partial thromboplastin time were severely prolonged on day 165 when all antiplatelet and anticoagulant medication were discontinued. This dog was ultimately diagnosed with chronic disseminated intravascular coagulation likely secondary to advanced splenic neoplasia on day 256 and euthanized on day 264.

Four of 7 dogs had documented repeat thrombus formation, 2 of which had clinical signs consistent with partial or complete arterial obstruction at the time of diagnosis of the recurrence. Medications being administered at the time of rethrombosis included clopidogrel (1 mg/kg PO q24h; 1/4), rivaroxaban (1 mg/kg PO q24h; 1/4), low-dose aspirin, and unfractionated heparin (doses unavailable; 1/4), and aspirin (0.55 mg/kg PO q24h) and sporadically administered dalteparin (82.2 U/kg SC q24h; 1/4). Ultrasonographic examination revealed that 3 obstructions were partial and 1 was complete at diagnosis. The dog with the complete obstruction became acutely non-ambulatory while hospitalized on day 7 and was euthanized. Two of the partial obstructions were incidental findings during evaluations for unrelated illness on days 112 and 455 after stent placement. The third dog with a partial obstruction was presented for exercise intolerance and hind limb paresis on day 239. The median time to diagnosis of rethrombosis for all 4 dogs was 175 days (range, 7-455 days). Of discharged dogs that experienced rethrombosis (3/5), the median time to diagnosis of rethrombosis was 239 days (range, 112-455 days). MST after initial detection of rethrombosis for the 3 surviving dogs was 313 days with a range of 230-814 days. Details regarding rethrombosis in the individual dogs are summarized in Table S5. One discharged dog with initial detection of nonclinical rethrombosis at day 455 was ultimately euthanized for thrombus progression 257 days later.

Development of chronic hind limb muscle atrophy was noted in 4 of 5 discharged dogs. One dog diagnosed with extensive femoral artery thrombus before stent placement developed severe ipsilateral quadriceps contracture resulting in chronically impaired stifle flexion.

The MST of all 7 dogs was 264 days (range, 1-1053 days). MST of the 5 discharged dogs was 425 days (range, 208-1053 days). Of the dogs that survived to discharge, those with an acute presentation (4/5) had a MST of 568 days (range: 208-1053 days) and the 1 discharged dog with chronic signs survived 264 days. All 5 dogs that were discharged after stent placement have been ultimately euthanized. Reasons for euthanasia in these discharged dogs include splenic neoplasia (2/5), acute progression of chronic aortoiliac thrombosis (1/5), acute femur fracture secondary to osteosarcoma (1/5), and oral neoplasia (1/5).

4 | DISCUSSION

This retrospective study describes catheter-directed thrombolysis and the placement of stents in the aorta and aortoiliac trifurcation under fluoroscopic guidance to relieve the signs of acute and chronic arterial obstruction. The procedure has been shown to be brief, safe, and effective in restoring limb perfusion without the development of life-threatening reperfusion injury in this small study sample of dogs.

The clinical difference between the acute and chronic presentation for aortic thrombosis has been well recognized in veterinary medicine.[2,5,6] Five of the 7 dogs in this study had acute limb ischemia at presentation, 4 of which were non-ambulatory. Dogs with acute disease present with more severe clinical signs with higher percentages having pain, neurological deficits, increased frequency of bilateral involvement and non-ambulatory status, and are less likely to survive to hospital discharge.[5,6] While the low numbers of dogs in the current study within acute and chronic disease cohorts make adequate comparison challenging, no discrepancy in survival rates to discharge or overall survival time is noted, possibly highlighting the efficacy of stenting in acutely affected dogs.

The dog that presented with only chronic exercise intolerance in this study most closely mirrors the clinical presentation of Leriche Syndrome in humans.[18] To the authors' knowledge, this presentation has not been reported in dogs. Leriche Syndrome is an aortoiliac occlusive disease marked by chronic onset of diminished femoral pulses, impotence, and claudication induced by exercise. The underlying pathogenesis is an insidious accumulation of atherosclerotic plaque and lipid in the aortoiliac arteries leading to stenosis.[19] Future pursuit of postmortem gross and histopathologic examination on dogs with a similar chronic presentation could further characterize the pathogenesis.

Chronic cases in dogs might be underrepresented owing to subtle signs such as mild hind limb paresis and exercise intolerance or claudication, which could go unnoticed by owners or be misinterpreted by veterinarians. It is likely that dogs with a chronic presentation develop collateral circulation to ameliorate their limb dysfunction, similar to humans.[20,21] Before the eventual diagnosis of aortic or aortoiliac thrombosis in the 2 chronically affected dogs, clinical signs were ascribed to myasthenia gravis and tick-borne disease, respectively, and disease specific therapies had been instituted. The increased potential for misdiagnosis in chronic presentations highlights the importance of assessing blood flow during evaluation of mild hind limb abnormalities or exercise intolerance.

Reports have described the use of vascular stents in the vena cava, left hepatic vein, pulmonary artery, pulmonic valve, and the right atrium in dogs.[22-27] Aortic trifurcation stenting has been performed in humans to treat patients with aortoiliac occlusive disease for over 30 years and is often accompanied by ancillary therapies such as systemic heparinization, local thrombolysis, and balloon angioplasty.[28-34] Prompt heparin anticoagulation at presentation improves outcomes in limb ischemia in humans by preserving microcirculation and preventing thrombus propagation.[21,35,36] In humans, local TPA infusion improves perfusion and decrease intraoperative risk of embolization during stenting.[30] Balloon dilation before stent placement is commonly performed in people and results in improved outcomes over stenting alone; however, underlying vascular stenoses might be present in humans, which is not typically seen in dogs.[31-34] It is challenging to determine the degree of clinical benefit of these ancillary

448 | **Journal of Veterinary Internal Medicine** ACVIM
Open Access
American College of
Veterinary Internal Medicine

GAVIN ET AL.

therapies in the current study. However, given the known benefits to humans, investigation is warranted.

In the current study, angiography often demonstrated complete occlusion of internal and partial occlusion of the external iliac arteries. The authors believe the initial vascular obstruction often occurs distally, at the level of the internal iliac artery bifurcation; however, clinical signs are not evident because of the collateral circulation provided by the external iliac arteries. Once the thrombus propagates proximally and begins to occlude the external iliac arteries (or thromboemboli travel down the external iliac arteries into the femoral arteries), clinical signs develop. The femoral arteries can be safely ligated in dogs because of the prominent collateral circulation provided by (patent) internal iliac arteries.[37] However, in dogs with aortoiliac thrombosis, the internal iliac arteries are typically occluded and cannot provide the required collateral circulation necessary when the femoral arteries have diminished blood flow, and therefore clinical signs develop. In the current study, only the external iliac arteries were stented for aortoiliac thrombosis, leaving the often occluded internal iliac arteries intact. This was designed to minimize the reperfusion injury by only re-establishing patency to the limbs, and therefore limiting the volume of tissues undergoing this potential inflammatory process.

Anesthetic complications including regurgitation and an arrhythmia were not considered specific to the procedure. Thrombus fragment migration noted during 1 procedure and detachment of a nose cone were ultimately considered to be of no clinical consequence (as the nose cone was removed). In humans, the most common complications of endovascular stenting of the aortoiliac trifurcation are groin hematomas (from vascular access), followed by pseudoaneurysms and distal limb emboli.[38,39] The most common postoperative complication in this study was local reperfusion injury characterized by edema and ecchymosis. It is possible that the incidence of postoperative ecchymoses is increased because of the breed distribution, as 2 of the 4 dogs that experienced this complication were greyhounds, which have a greater predilection for postoperative hemorrhage.[40]

Reperfusion injury is a destructive, multi-factorial, inflammatory process that occurs when re-established blood flow develops after prolonged ischemia causing continued tissue damage.[41] Reperfusion injury is not a pertinent concern in humans with aortoiliac occlusive disease because of the chronic nature of the condition and resultant collateral vascularization.[42] In contrast, aortic thrombotic disease in cats is associated with a profound, acute onset. Unexpectedly, reperfusion injury did not contribute to morbidity in cats after rheolytic thrombectomy for distal aortic thrombosis.[15] In the present study, an association was suggested between more severe local reperfusion injury and longer hospitalization times.

N-acetylcysteine, pentoxifylline, and dexamethasone SP were used as anti-inflammatories and free radical scavengers to treat reperfusion injury in some dogs in the current study; however, the clinical benefit is unclear. Volatile anesthetics and alpha-2 agonists have been used for their cytoprotective properties to treat reperfusion injury after vascular interventions in humans with minimal success, but no standard therapeutic protocol has been established.[43]

Clinicopathologic changes that affected therapy after stenting included anemia and hypoalbuminemia. Anemia was suspected to be due to severe ventral and hind limb ecchymoses and hypoalbuminemia was largely attributed to underlying PLN compounded by IV fluid therapy and local inflammation. Hypoalbuminemia should be anticipated in dogs with PLN undergoing stenting with fluid therapy. Gross pigmenturia, noted in 2 dogs, was most likely myoglobinuria secondary to local reperfusion injury.

All 7 dogs had hypertension during hospitalization in the present study. Hypertension is considered a risk factor for thrombosis in humans and contributes to the prothrombotic state.[44] In a recent study of 100 dogs with aortic thrombosis, 62% had a Doppler blood pressure > 160 mm Hg.[5] Given this suspected association, careful monitoring and treatment of hypertension should be considered in these dogs.

In 3 of the 4 non-ambulatory dogs, time to ambulation after stenting was favorable in the current study. The authors are not aware of available statistics in other studies of dogs. Given the re-established femoral and distal pulses by days 1 and 2 postoperatively, any brief delay to ambulation might have resulted from discomfort associated with local reperfusion injury rather than vascular compromise.

In the present study, complete or nearly complete rethrombosis within the stents was associated with acute and severe clinical signs resulting in euthanasia, whereas partial rethrombosis, often noted incidentally, was managed medically. This suggests that severity of clinical signs at the time of rethrombosis might be related to both the degree and acute nature of obstruction which could directly affect outcome. Accordingly, increased frequency of ultrasonographic monitoring to modify therapy before thrombosis progression is prudent. The high rate (60%) of long-term rethrombosis found in the present study and the high prevalence of hypercoagulability-promoting chronic comorbidities found in this (71%) and other studies (42%-77%) suggest that life-long antithrombotic therapy, including platelet inhibition in conjunction with anticoagulation, might be justified for dogs after stent placement.[2,3,5] Although warfarin and rivaroxiban are safe and effective for treating thrombosis in dogs, no consensus currently exists for the prevention of rethrombosis in dogs.[3,16,45-49]

Historically, prognosis for aortoiliac thrombosis has been grave with limited survival in acute and non-ambulatory cases, regardless of treatment.[2,3,5] In contrast, dogs that survived to discharge (5/7) in the current study, sustained a reasonable quality of life between 208 and 1053 days. A study of 13 dogs receiving unspecified therapy reported a 270-day MST of the 53% of dogs that survived to discharge compared to the current study with a MST of 568 days for acute presentations and a MST of 425 days overall of the 71% of dogs that survived to discharge.[6] Survival data in a recent study of dogs with aortic thromboses treated with a variety of therapies excluding stent placement reported that 63% of hospitalized dogs survived to discharge; however, only 33% of dogs discharged from the hospital were alive at 180 days.[5] Causes of death and MST were not disclosed.[5] In contrast, the present study reported 71% (5/7) survival to discharge and 100% (5/5) of discharged dogs were alive longer than 180 days after intervention. The disparity in 180-day survival rates suggests a possible improvement in long-term survival with stenting therapy in this small study sample of dogs.

Limitations of the present study include retrospective design and low case number. Variability of therapy, because of lack of consensus, amongst a small cohort resulted in low numbers of cases within unique sets of independent variables. Consequently, comparison of cases within such small groupings is limited. Presentation at different stages of disease progression and degrees of severity further complicated comparison of cases.

In conclusion, the present study supports that aortic and aortoiliac stenting can be a safe and effective procedure in dogs to quickly re-establish vessel patency with minimal severe complications.

ACKNOWLEDGMENT

CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Doxycycline was reported as a treatment for tick-borne disease as part of the history in 1 dog.

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

Kelly A. Gavin https://orcid.org/0000-0002-6202-4310
Chick Weisse https://orcid.org/0000-0001-5202-9962

REFERENCES

1. Dunn M, Scansen BA. Interventional radiology Management of Vascular Obstruction. *Vet Clin North Am Small Anim Pract*. 2018;48(5):819-841.
2. Lake-Bakaar GA, Johnson EG, Griffiths LG. Aortic thrombosis in dogs: 31 cases (2000-2010). *J Am Vet Med Assoc*. 2012;241(7):910-915.
3. Winter RL, Sedacca CD, Adams A, et al. Aortic thrombosis in dogs: presentation, therapy, and outcome in 26 cases. *J Vet Cardiol*. 2012; 14(2):333-386.
4. Van Winkle TJ, Liu SM, Hackner SG. Clinical and pathological features of aortic thromboembolism in 36 dogs. *J Vet Emerg Crit Care*. 1993;3: 13-21.
5. Ruehl M, Lynch AM, O'Toole TE, et al. Outcome and treatments of dogs with aortic thrombosis: 100 cases (1997–2014). *J Vet Intern Med*. 2020;34(5):1759-1767.
6. Gonçalves R, Penderis J, Chang YP, et al. Clinical and neurological characteristics of aortic thromboembolism in dogs. *J Small Anim Pract*. 2008;49(4):178-184.
7. Williams TP, Shaw S, Porter A, et al. Aortic thrombosis in dogs. *J Vet Emerg Crit Care (San Antonio)*. 2017;27(1):9-22.
8. Boswood A, Lamb CR, White RN. Aortic and iliac thrombosis in six dogs. *J Small Anim Pract*. 2000;41(3):109-114.
9. Teshima T, Hara Y, Taoda T, et al. Cushing's disease complicated with thrombosis in a dog. *J Vet Med Sci*. 2008;70(5):487-491.
10. MacGregor JM, Rozanski EA, McCarthy RJ, et al. Cholesterol-based pericardial effusion and aortic thromboembolism in a 9-year-old mixed-breed dog with hypothyroidism. *J Vet Intern Med*. 2004;18(3): 354-358.
11. Kohnken R, Durham JA, Premanandan C, et al. Aortic chondroid neoplasia in two Labrador retriever dogs. *J Vet Cardiol*. 2015;17(4): 314-320.
12. Dunn M, Weisse C. Thrombectomy and thrombolysis: the interventional radiology approach. In: Weisse C, Berent A, eds. *Veterinary Image-Guided Interventions*. 1st ed. Ames, IA: John Wiley & Sons Inc.; 2015:464-478.
13. Clare AC, Kraje BJ. Use of recombinant tissue-plasminogen activator for aortic thrombolysis in a hypoproteinemic dog. *J Am Vet Med Assoc*. 1998;212(4):539-543.
14. Ramsey CC, Burney DP, Macintire DK, et al. Use of streptokinase in four dogs with thrombosis. *J Am Vet Med Assoc*. 1996;209(4):780-785.
15. Reimer SB, Kittleson MD, Kyles AE. Use of rheolytic thrombectomy in the treatment of feline distal aortic thromboembolism. *J Vet Intern Med*. 2006;20(2):290-296.
16. DeLaforcade A, Bacek L, Blais MC, et al. Consensus on the rational use of antithrombotics in veterinary critical care (CURATIVE): domain 1-defining populations at risk. *J Vet Emerg Crit Care (San Antonio)*. 2019;29(1):37-48.
17. Acierno MJ, Brown S, Coleman AE, et al. ACVIM consensus statement: guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *J Vet Intern Med*. 2018; 32(6):1803-1822.
18. Leriche R, Morel A. The syndrome of thrombotic obliteration of the aortic bifurcation. *Ann Surg*. 1948;127(2):193-206.
19. Brown KN, Muco E, Gonzalez L. Leriche syndrome. *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2021.
20. Norgren L, Hiatt WR, Dormandy JA, et al. Inter-society consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg*. 2007;45 (Suppl S):S5-S67.
21. Olinic DM, Stanek A, Tătaru DA, et al. Acute limb ischemia: an update on diagnosis and management. *J Clin Med*. 2019;8(8):1215.
22. Schlicksup MD, Weisse CW, Berent AC, et al. Use of endovascular stents in three dogs with Budd-Chiari syndrome. *J Am Vet Med Assoc*. 2009;235(5):544-550.
23. Taylor S, Rozanski E, Sato AF, et al. Vascular stent placement for palliation of mass-associated chylothorax in two dogs. *J Am Vet Med Assoc*. 2017;251(6):696-701.
24. Hoehne SN, Milovancev M, Hyde AJ, et al. Placement of a caudal vena cava stent for treatment of Budd-Chiari-like syndrome in a 4-month-old ragdoll cat. *J Am Vet Med Assoc*. 2014;245(4):414-418.
25. Sosa I, Swift ST, Jones AE, et al. Stent angioplasty for treatment of canine valvular pulmonic stenosis. *J Vet Cardiol*. 2019;21:41-48.
26. Barncord K, Stauthammer C, Moen SL, et al. Stent placement for palliation of cor triatriatum Dexter in a dog with suspected patent foramen ovale. *J Vet Cardiol*. 2016;18(1):79-87.
27. Weisse C, Scansen BA, Berent AC, et al. Transatrial stenting for long-term management of cardiac tumor obstruction of the right atrium in 3 dogs. *J Vet Intern Med*. 2020;35(1):120-129.
28. Palmaz JC, Richter GM, Noeldge G, et al. Intraluminal stents in atherosclerotic iliac artery stenosis: preliminary report of a multicenter study. *Radiology*. 1988;168(3):727-731.
29. Clair DG, Beach JM. Strategies for managing aortoiliac occlusions: access, treatment and outcomes. *Expert Rev Cardiovasc Ther*. 2015; 13(5):551-563.
30. Liu M, Zhang F. Endovascular management of aorta-Iliac stenosis and occlusive disease by kissing-stent technique. *Stem Cells Int*. 2016; 2016:4035307.
31. Kudo T, Chandra FA, Ahn SS. Long-term outcomes and predictors of iliac angioplasty with selective stenting. *J Vasc Surg*. 2005;42(3):466-475.
32. Timaran CH, Stevens SL, Freeman MB, et al. External iliac and common iliac artery angioplasty and stenting in men and women. *J Vasc Surg*. 2001;34(3):440-446.

33. Klein WM, van der Graaf Y, Seegers J, et al. Dutch iliac stent trial: long-term results in patients randomized for primary or selective stent placement. *Radiology*. 2006;238(2):734-744.

34. Bekken JA, Jongsma H, de Vries JP, et al. Self-expanding stents and aortoiliac occlusive disease: a review of the literature. *Med Dev*. 2014; 7:99-105.

35. Eliason JL, Wainess RM, Proctor MC, et al. A national and single institutional experience in the contemporary treatment of acute lower extremity ischemia. *Ann Surg*. 2003;238(3):382-390.

36. Blaisdell FW, Steele M, Allen RE. Management of acute lower extremity arterial ischemia due to embolism and thrombosis. *Surgery*. 1978; 84(6):822-834.

37. Conrad MC, Anderson JL 3rd, Garrett JB Jr. Chronic collateral growth after femoral artery occlusion in the dog. *J Appl Physiol*. 1971;31(4): 550-555.

38. Groot Jebbink E, Holewijn S, Slump CH, et al. Systematic review of results of kissing stents in the treatment of Aortoiliac occlusive disease. *Ann Vasc Surg*. 2017;42:328-336.

39. Piffaretti G, Fargion AT, Dorigo W, et al. Outcomes from the multicenter Italian registry on primary endovascular treatment of aortoiliac occlusive disease. *J Endovasc Ther*. 2019;26(5):623-632.

40. Lara-García A, Couto CG, Iazbik MC, et al. Postoperative bleeding in retired racing greyhounds. *J Vet Intern Med*. 2008;22(3):525-533.

41. Cowled P, Fitridge R. Pathophysiology of reperfusion injury. In: Fitridge R, Thompson M, eds. *Mechanisms of Vascular Disease: A Reference Book for Vascular Specialists*. 1st ed. Adelaide, AU: University of Adelaide Press; 2011:331-350.

42. Ahmed S, Raman SP, Fishman EK. CT angiography and 3D imaging in aortoiliac occlusive disease: collateral pathways in Leriche syndrome. *Abdom Radiol*. 2017;42(9):2346-2357.

43. Yang B, Fung A, Pac-Soo C, et al. Vascular surgery-related organ injury and protective strategies: update and future prospects. *Br J Anaesth*. 2016;117 (Suppl 2):ii32-ii43.

44. Felmeden DC, Spencer CG, Chung NA, et al. Relation of thrombogenesis in systemic hypertension to angiogenesis and endothelial damage/ dysfunction (a substudy of the Anglo-Scandinavian cardiac outcomes trial [ASCOT]). *Am J Cardiol*. 2003;92(4):400-405.

45. Evans LA, Tansey C, Wiebe M, et al. A prospective evaluation of rivaroxaban on haemostatic parameters in apparently healthy dogs. *Vet Med Sci*. 2019;5(3):317-324.

46. Conversy B, Blais MC, Dunn M, et al. Anticoagulant activity of oral rivaroxaban in healthy dogs. *Vet J*. 2017;223:5-11.

47. Uchida M, Ohmi A, Fujiwara R, et al. Treatment with rivaroxaban and monitoring of coagulation profiles in two dogs with venous thromboembolism. *J Vet Med Sci*. 2020;82(9):1271-1276.

48. Yang VK, Cunningham SM, Rush JE, et al. The use of rivaroxaban for the treatment of thrombotic complications in four dogs. *J Vet Emerg Crit Care (San Antonio)*. 2016;26(5):729-736.

49. Blais MC, Bianco D, Goggs R, et al. Consensus on the rational use of antithrombotics in veterinary critical care (CURATIVE): domain 3-defining antithrombotic protocols. *J Vet Emerg Crit Care (San Antonio)*. 2019;29(1):60-74.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.