2022 Update of the Consensus on the Rational Use of Antithrombotics and Thrombolytics in Veterinary Critical Care (CURATIVE) Domain 1- Defining populations at risk

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Abbreviations: ADP, adenosine diphosphate; AF, atrial fibrillation; ATE, arterial thromboembolism; CURATIVE, Consensus on the Rational Use of Antithrombotics and Thrombolytics in Veterinary Critical Care; DIC, disseminated intravascular coagulation; HE, hepatic encephalopathy; IMHA, immune-mediated hemolytic anemia; LOE, level of evidence; NRIMHA, nonregenerative immune-mediated hemolytic anemia; PECO, Population Exposure Comparison Outcome; PLE, Protein-losing enteropathy; PLN, protein-losing nephropathy; PRCA, pure red blood cell aplasia; PSS, portosystemic shunt; PTE, pulmonary thromboembolism; PVT, portal vein thrombosis; TEG, thromboelastography; VAP, vascular access port.

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**Abstract**

**Objectives:** To expand the number of conditions and interventions explored for their associations with thrombosis in the veterinary literature and to provide the basis for prescribing recommendations.

**Design:** A population exposure comparison outcome format was used to represent patient, exposure, comparison, and outcome. Population Exposure Comparison Outcome questions were distributed to worksheet authors who performed comprehensive searches, summarized the evidence, and created guideline recommendations that were reviewed by domain chairs. The revised guidelines then underwent the Delphi survey process to reach consensus on the final guidelines. Diseases evaluated in this iteration included heartworm disease (dogs and cats), immune-mediated hemolytic anemia (cats), protein-losing nephropathy (cats), protein-losing enteropathy (dogs and cats), sepsis (cats), hyperadrenocorticism (cats), liver disease (dogs), congenital portosystemic shunts (dogs and cats) and the following interventions: IV catheters (dogs and cats), arterial catheters (dogs and cats), vascular access ports (dogs and cats), extra-corporeal circuits (dogs and cats) and transvenous pacemakers (dogs and cats).

**Results:** Of the diseases evaluated in this iteration, a high risk for thrombosis was defined as heartworm disease or protein-losing enteropathy. Low risk for thrombosis was defined as dogs with liver disease, cats with immune-mediated hemolytic anemia, protein-losing nephropathy, sepsis, or hyperadrenocorticism.

**Conclusions:** Associations with thrombosis are outlined for various conditions and interventions and provide the basis for management recommendations. Numerous knowledge gaps were identified that represent opportunities for future studies.

**KEYWORDS**

arrhythmias, heartworm disease, protein-losing enteropathy, vascular devices

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**1 INTRODUCTION**

Thrombosis continues to be recognized as a contributor to morbidity and mortality among companion animals experiencing a variety of disease processes, and there are a growing number of publications relating to the use of antithrombotics in veterinary medicine. The lack of veterinary studies quantifying risk factors for thrombosis in specific disease states complicates decision-making regarding the use of antithrombotics. The 2019 Consensus on the Rational Use of Antithrombotics in Veterinary Critical Care (CURATIVE) guidelines examined populations at risk for thrombosis and defined a series of recommendations related to therapeutic use, monitoring, and discontinuation of antithrombotic therapy.\(^1\)\(^{-5}\) A number of additional conditions potentially associated with thrombosis were considered in this second evaluation of the veterinary literature in an effort to promote best practices for the use of antithrombotics.

As in the previous iteration of the CURATIVE guidelines, the association between diseases and thrombosis was evaluated using a standard Population Exposure Comparison Outcome (PECO) question format. For conditions considered to be potentially associated with thrombosis, the veterinary literature was examined to determine whether in dogs or cats (Population, P), the development of a disease (Exposure, E), as opposed to remaining disease free (Comparison, C), was associated with the development of thrombosis (Outcome, O). Recommendations for or against antithrombotic therapy based on risk for thrombosis were further refined using a Delphi survey process where CURATIVE group members were asked to agree or disagree with guideline recommendations and to suggest alternative wording as necessary. The results of the Delphi surveys and the resulting draft guidelines are available at supplementary data (S1). It should be noted that the CURATIVE Steering Committee made some minor wording changes to the draft guidelines for clarity and consistency after the Delphi surveys were completed, resulting in the final recommendations discussed below. Where appropriate, knowledge gaps were included to highlight specific areas of limitation and to encourage further investigation.
2 | PECO QUESTION: HEARTWORM DISEASE (DOGS)

In dogs (P), is the development of heartworm disease (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

2.1 | Guidelines

1.1 Heartworm (dogs)

a. Heartworm disease is associated with pulmonary artery thrombosis in dogs, with risk increasing with disease severity.
b. We recommend that antithrombotic therapy be considered in dogs with heartworm disease, particularly in those with more severe disease and those undergoing adulticide therapy.

2.2 | Evidence summary

Most available evidence supported the PECO question (17 studies), with 2 studies considered neutral and none opposed. Proving thrombosis in clinical settings, particularly in the pulmonary arteries, is challenging, and studies were only included if a thrombus was confirmed by angiography, ultrasound, or histopathology. Studies reporting thrombin generation (ie, D-dimers) and platelet reactivity were included to support or refute the association between dirofilariasis and a hypercoagulable state but with lower quality evidence scores. Overall, there is a strong association between clinical dirofilariasis and thrombosis and thromboembolism in dogs, with indications that this risk increases with disease severity, adulticide therapy and potentially with the presence of microfilaria.

Numerous studies document the presence of thrombi in dogs with dirofilariasis, universally in the same vascular bed as the worms. In a case series of 3 dogs with caval syndrome, 2 had extensive large and small vessel thrombosis throughout the pulmonary vasculature (LOE 5). In an experimental infection study of 20 healthy dogs (LOE 3), lung histopathology showed varying degrees of thrombi in all dogs, frequently associated with worm fragments. While most reports focus on the pulmonary vasculature, a small case series also documented worm-associated thrombi in 3/5 dogs suffering from aberrant worm migration involving the aorta, medial iliac, and femoral arteries.

Concentrations of D-dimer are increased in up to 40% of heartworm-infected dogs, with higher concentrations seen in dogs with microfilaria. Similarly, plasma D-dimer concentrations correlated with disease severity (LOE 3–5), increasing immediately after adulticide treatment (LOE 2), and decreasing with disease resolution (LOE 3). Platelet reactivity is also increased in infected dogs (LOE 3), with enhanced serotonin release and platelet aggregation in response to collagen and adenosine diphosphate (ADP) in infected dogs. Infected dogs are also more likely to experience thrombocytopenia (< 150,000 platelets/μL) than noninfected dogs. Consistent with increased platelet reactivity, greater doses of aspirin, aspirin/dipyridamole or ticlopidine are needed to inhibit ADP-induced aggregation in infected dogs, particularly following embolization of dead worms. Necropsy lesions were less severe in dogs receiving ticlopidine than in those receiving no antiplatelet agent in one report (LOE 3). Antiplatelet therapy may diminish platelet adhesion, myointimal proliferation and vascular occlusion in infected dogs.

Adulticide treatment may increase thrombotic risk depending upon the protocol used, although older studies involving thiacetarsamide may be confounded by the thrombogenicity of the drug itself. Preceding adulticide treatment with doxycycline with or without ivermectin may lessen the number of arterial lesions compared to the administration of melarsamine without pretreatment (LOE 5). Treatment of dogs with patent infection following surgical worm implantation with a combination of imidacloprid, moxidectin, and doxycycline resulted in more thrombotic occlusion (on histopathology) than in untreated infected dogs (LOE 3). Thrombi were frequently associated with worm fragments, suggesting that this therapy resulted in worm death and subsequent embolism. In some dogs with preexisting dirofilariasis, pulmonary artery insertion of a large number (20–50) of dead worms resulted in intimal proliferation of pulmonary arteries, dilation of main and lobar pulmonary arteries and obstruction of blood flow (LOE 3). The infusion of homogenized Dirofilaria antigen into the pulmonary arteries of dogs led to thrombosis within 1 hour of administration, but these thrombi were not detectable 5 days later, suggesting that Dirofilaria are thrombogenic but that actual worms are required for persistent thrombosis. The transient nature of these thrombi confirms the antigenicity of the heartworm but suggests that solid worm fragments are necessary to support prolonged thrombus residence.

2.3 | Knowledge gap

Further investigation of the contribution of microfilaria, especially to the thrombogenic risk of heart work disease, is warranted, particularly as the AHS does not currently recommend the use of antithrombotics in the management of dogs with heartworm disease.

3 | PECO QUESTION: HEARTWORM DISEASE (CATS)

In cats (P), is the development of heartworm disease (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

3.1 | Guidelines

1.2 Heartworm disease (cats)

a. Heartworm disease may be associated with pulmonary artery thrombosis in cats.
b. We suggest that antithrombotic therapy be considered in cats with heartworm disease, particularly in those with more severe disease or where other risk factors for thrombosis exist.
3.2 | Evidence summary

Few studies of dirofilariasis in cats have evaluated thrombi or markers of ongoing thrombin generation. Two single case reports describe pulmonary arterial thrombi in cats with dirofilariasis, confirmed in one by histopathology.

A necropsy study of cats with naturally occurring dirofilariasis identified thrombi in 5/11 cats, although cats with thrombi often had comorbidities that might have contributed to thrombus formation (eg, lymphoma, hypertrophic cardiomyopathy, chronic nephritis). A single study of experimental heartworm infection described in 2 reports identified vascular occlusion and confirmed thrombi both with and without worm involvement. One study, considered neutral to the PECO question, identified proliferation of the pulmonary artery tunica media in cats with dirofilariasis, resulting in vascular occlusion in the absence of identified thrombi. It is not clear if this represents a true absence of thrombi, or simply that they were not described. This report also suggests the possibility of increased vascular reactivity and remodeling in cats with heartworm disease that may clinically mimic thrombosis but without actual thrombi. Overall, the literature suggests that thrombosis is a potential complication of dirofilariasis in cats, but the prevalence of thrombosis is unclear, and the degree of risk is difficult to quantify. As such, we suggest that antithrombotic therapy be considered for cats with dirofilariasis, particularly in animals with severe disease or where other risk factors for thrombosis exist.

3.3 | Knowledge gap

Studies with a primary aim of evaluating hemostatic changes and thrombotic complications in cats with dirofilariasis are needed to further characterize thrombogenic risk in this population, particularly as the American Heartworm Society does not currently recommend the use of antithrombotics in the management of cats with heartworm disease. In addition to characterizing the role of comorbidities, additional studies should differentiate the role of thrombosis versus vascular remodeling in causing vascular obstruction.

4 | PECO QUESTION: IMMUNE-MEDIATED HEMOLYTIC ANEMIA (IMHA) (CATS)

In cats (P), is the development of immune-mediated hemolytic anemia (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

4.1 | Guidelines

1.3 Immune-mediated hemolytic anemia (IMHA) (cats)

a. Immune-mediated hemolytic anemia in cats is weakly associated with pulmonary thromboembolism (venous thromboembolism).
b. There is no evidence that immune-mediated hemolytic anemia is a risk factor for arterial thromboembolism in cats.
c. We suggest that antithrombotic therapy be considered in cats with immune-mediated hemolytic anemia, where other risk factors for thrombosis exist.

4.2 | Evidence summary

Only 1 study suggested an association between IMHA and pulmonary thromboembolism (PTE; venous thromboembolism) in cats. The point prevalence of IMHA in this study of feline PTE was 7% (2/29 cats). An association between IMHA and PTE was not substantiated by the other major retrospective study describing feline PTE. The 52 reports deemed neutral to the PECO question included 396 cats in total with suspected IMHA in all of its forms (primary and secondary IMHA, pure red blood cell aplasia [PRCA] and nonregenerative immune-mediated hemolytic anemia [NRIMHA]). There was no report of thrombosis in any of these studies. In addition, these 52 reports included multiple other studies describing arterial and venous thrombosis in cats. None of the cats in these studies had IMHA. Although 1 report suggested an association between IMHA and PTE in cats, the collective weight of the 52 neutral studies including nearly 400 cases suggests that there is either no association or a weak association between IMHA and thromboembolic complications in cats and that the overall risk of thrombosis (venous or arterial) in cats with IMHA appears low. No studies were identified that suggested evidence contrary to the PECO question. On the basis that IMHA might be weakly associated with venous thromboembolism, we suggest that antithrombotic therapy be considered in cats with IMHA, where other risk factors for thrombosis exist.

4.3 | Knowledge gap

The mechanism explaining the differences between the thrombogenicity of IMHA in dogs versus cats is unknown.

5 | PECO QUESTION: PROTEIN-LOSING NEPHROPATHY (PLN) (CATS)

In cats (P), is the development of protein-losing nephropathy (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

5.1 | Guidelines

1.4 Protein-losing nephropathy (PLN) (cats)

a. Protein-losing nephropathy in cats is weakly associated with pulmonary thromboembolism (venous thromboembolism).
b. There is no evidence that protein-losing nephropathy is a risk factor for arterial thromboembolism in cats.

c. We suggest that antithrombotic therapy be considered in cats with protein-losing nephropathy, where other risk factors for thrombosis exist.

5.2 Evidence summary

Two studies suggest an association between PLN and PTE (venous thromboembolism) in cats. The prevalence of PLN in these 2 reports of feline PTE was 6–14% (4/29 cats and 1/17 cats). By comparison, neoplasia (34-35%) and cardiac disease (6-41%) were more commonly associated with PTE in cats in the same reports. Several of the reports describing histopathologic changes in cats with PLN or glomerulonephritis had evidence of fibrin deposition; however, none of the studies that reported histopathology described any micro- or macrovascular thrombosis. Numerous studies were considered neutral to the PECO question because they did not include a control group, they described arterial thrombosis and did not mention PLN, or they were reports focused on PLN that did not discuss or describe thrombosis. Although these reports were considered neutral, their collective weight suggests that there is either no association or a very weak association between PLN and arterial thromboembolic complications in cats and that the overall risk of thrombosis in cats with PLN is seemingly low. No studies were identified that suggested evidence contrary to the PECO question. On the basis that PLN might be weakly associated with venous thromboembolism, we suggest that antithrombotic therapy be considered in cats with PLN, where other risk factors for thrombosis exist.

6 PECO QUESTION: LIVER DISEASE (DOGS)

In dogs (P), is the development of hepatic disease (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

6.1 Guidelines

1.5 Liver disease (dogs)

a. Liver disease is associated with thrombosis in a small subset of dogs only, independent of the specific underlying disease.

b. We suggest that antithrombotic therapy be considered in dogs with liver disease following an assessment of the risk and benefit in individual patients or where other risk factors for thrombosis exist.

6.2 Evidence summary

Of the 32 reports included for review, 13 suggest that liver disease may be associated with the development of thrombosis (1 LOE 5, good; 1 LOE 2, fair; 8 LOE 5, fair; 3 LOE 5, poor).

Hepatic disease might be preferentially associated with thrombosis of certain vessels, particularly the portal and splenic veins. Hepatic disease was documented in 29/140 (21%) dogs with portal or splenic vein thrombosis but not in dogs with pulmonary or aortic thrombosis. While this suggests an association between hepatic disease and thrombosis, comorbidities, including glucocorticoid administration, neoplasia, kidney disease or recent surgery, were common, and their contribution to overall thrombotic risk in these dogs could not be determined.

Three studies employed thromboelastography (TEG) and documented a hypercoagulable state (but not thrombosis) in dogs with liver diseases, including extrahepatic biliary tract obstruction (10/10 dogs, 100%); chronic hepatopathies (7/21 dogs, 33.33%); and acute liver disease (2/21 dogs, 9.5%). These studies, while potentially relevant, do not directly address the PECO question.

Most studies were retrospective cohort studies or case series, typically without a control group. In one retrospective study, 8/96 (8%) dogs with liver disease that underwent CT angiography were diagnosed with portal vein thrombosis (PVT) while by comparison, 8/19 (42%) dogs with pancreatitis had PVT in the same study. This study also suggested that abdominal ultrasound may be insensitive for thrombosis detection compared to CT angiography, which suggests that studies using only abdominal ultrasound may underestimate the incidence of PVT. In a retrospective cohort study of 49 dogs with acute liver failure with or without signs of hepatic encephalopathy (HE), evidence of thrombosis was noted at necropsy in 4/23 (17.4%) dogs.

In conclusion, because of the retrospective or in vitro nature of most of the studies, the impact of potential comorbidities on the association between liver disease and thrombosis is difficult to ascertain. Overall, the veterinary literature supports an association between liver disease and thrombosis, particularly PVT and splenic vein thrombosis, in a subset of dogs with liver diseases. We suggest that antithrombotic therapy should be considered in dogs with liver disease following an assessment of the risk and benefit in individual patients recognizing that bleeding disorders may be present due to severe liver dysfunction. The presence of other risk factors for thrombosis should also prompt clinicians to consider antithrombotics for dogs with liver disease.

6.3 Knowledge gap

Prospective controlled studies are needed to better ascertain the risk of thrombosis in dogs with liver disease of various etiologies and the contribution of comorbidities to the overall prothrombotic risk.

7 PECO QUESTION: LIVER DISEASE (CATS)

In cats (P), is the development of hepatic disease (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?
7.1 | Guidelines

1.6 Liver disease (cats)

No guidelines for this PECO question were generated during the current CURATIVE iteration. This important question will be addressed in a future iteration of the CURATIVE guidelines.

8 | PECO QUESTION: CONGENITAL PORTOSYSTEMIC SHUNTS (CPSS) (DOGS)

In dogs (P), is the presence of a congenital portosystemic shunt (E), as opposed to remaining disease-free (C), associated with the development of thrombosis?

8.1 | Guidelines

1.7 Portosystemic shunts (dogs)

a. Surgical correction of congenital portosystemic shunts (cPSS) in dogs may be associated with thrombosis in the postoperative period.

b. We suggest that antithrombotic therapy be considered in dogs undergoing surgical correction of cPSS, following an assessment of the risk and benefit in individual patients or where other risk factors for thrombosis exist.

c. We recommend against routine use of antithrombotic therapy in dogs with cPSS.

8.2 | Evidence summary

Twelve reports met the criteria for review. Four reports supported the PECO question, with 7 considered neutral and 1 in opposition. In a retrospective study of 33 dogs with PVT (LOE 5, fair), 3 dogs had hepatic vascular anomalies, including 2 with cPSS, although the affected dogs had other risk factors, including recent splenectomy, the presence of an intravascular coil, portal hypertension or infectious disease. A retrospective case series of PVT (LOE 5, fair) reported thrombosis as a complication of cPSS ligation in 2 dogs. A case report of a dog with gallbladder infarction 48 hours after cPSS attenuation highlights the difficulty in determining the respective contribution to the risk of thrombosis of the cPSS and the surgical procedure.

Various studies evaluated the hemostatic profiles of dogs with cPSS. Most were deemed neutral to the PECO question because thrombosis was not investigated or reported. One study of dogs with cPSS (considered supportive of the PECO question) included TEG as a global coagulation assessment tool (LOE 5, good). This study showed that dogs with cPSS may be hypercoagulable despite clotting time prolongations, which supports hypocoagulability. Affected dogs also had decreased activities of the endogenous anticoagulants antithrombin and protein C. A prospective, observational study evaluating the diagnostic value of plasma protein C for detecting hepatobiliary disorders found that dogs with cPSS had significantly lower protein C activity than clinically ill dogs without cPSS (LOE 2, fair), potentially contributing to a hypercoagulable state. Thromboembolic disease was not reported in this study, although it was not the primary focus of the study and hence is considered neutral to the PECO question.

A study investigating the influence of cPSS on primary hemostasis found no clinically relevant alterations; hence, this study was judged to oppose the PECO question. Overall, there is some suggestion in the literature that cPSS increases the risk of thrombosis, particularly following surgical attenuation. These patients may be at risk of bleeding due to liver dysfunction; hence, antithrombotic therapy should be considered only after an assessment of the risk and benefit in individual patients, and routine administration of antithrombotic drugs for dogs with cPSS is not recommended.

9 | PECO QUESTION: CONGENITAL PORTOSYSTEMIC SHUNTS (CPSS) (CATS)

In cats (P), is the presence of a congenital portosystemic shunt (E), as opposed to remaining disease free (C), associated with the development of thrombosis (O)?

9.1 | Guidelines

1.8 Portosystemic shunts (cats)

a. Congenital portosystemic shunts (cPSS) may be associated with thrombosis in cats.

b. We recommend against routine use of antithrombotic therapy in cats with cPSS.

c. We suggest that antithrombotic therapy be considered in cats with cPSS, following an assessment of the risk and benefit in individual patients, when additional risk factors for thrombosis exist.

9.2 | Evidence summary

Four reports met the criteria for review. Evidence from 1 (LOE 5, fair) documented a possible association of cPSS with PVT in cats. In this case series, 3/6 cats had congenital PSS at the time of PVT identification. One of these cats had recently undergone shunt ligation that may have increased thrombotic risk. In a multicenter retrospective study of 34 cats with cPSS, 11 cats developed complications, and 6 of these died. However, thrombosis was not described in any cat, and hence, this study was judged to oppose the PECO question. Two other studies (LOE 5, fair) identified hemostatic abnormalities in cats with cPSS, but neither described thrombosis. These studies were considered neutral to the PECO question.
Overall, given the paucity of data to review, the risk of thrombosis associated with cPSS in cats cannot be clearly determined. As such, we recommend against routine use of antithrombotic therapy in cats with cPSS. Where more detailed assessments of risk versus benefit conducted in individual cats with cPSS are suggestive of thrombotic risk, where other risk factors for thrombosis are present, then we suggest antithrombotic therapy may be considered.

9.3 | Knowledge gap

Studies are needed to investigate the potential association of thrombosis and PVT in cats prior to shunt ligation to remove the confounding effect of shunt ligation on the overall hemostatic state.

10 | PECO QUESTION: CARDIAC ARRHYTHMIAS (DOGS)

In dogs (P), is the development of cardiac arrhythmias (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

10.1 | Guidelines

1.9 Cardiac arrhythmias (dogs)

a. Atrial fibrillation may be associated with arterial thrombosis in dogs, particularly where reduced left atrial appendage flow velocity exists.

b. We suggest that antithrombotic therapy for atrial fibrillation in dogs should be considered, where other risk factors for thrombosis exist.

c. We recommend against the use of antithrombotic therapy in dogs with arrhythmias other than atrial fibrillation, unless other risk factors for thrombosis exist.

10.2 | Evidence summary

Several reports of experimental models of rapid pacing-induced atrial fibrillation (AF) in dogs were considered relevant to the PECO question. Two reports comparing the coagulability of blood sampled from the right atrium to that of peripheral blood showed evidence of hypercoagulability in atrial, but not peripheral, blood after induction of AF. Other report demonstrated decreased trans-mitral and left atrial appendage flow velocities during AF and following conversion to sinus rhythm compared to baseline measurements; this blood stasis may predispose to thrombosis. Induced AF in dogs also upregulates gene expression for some procoagulant mediators. One experimental study was classified as neutral to the PECO question, as it did not detect significant changes in von Willebrand factor or P-selectin over time after the onset of induced AF, but the sample size was very small, and other coagulation parameters were not assessed. The only study deemed to oppose the PECO question showed no increase in the rate of thrombosis in 3 different canine models of AF following radiofrequency ablation compared to control dogs. While this opposes the PECO question, the relevance is likely impacted by the method of inducing AF.

Several potentially relevant case reports or case series were identified, but direct links between thrombosis and atrial fibrillation or other arrhythmias could not be made. One case report documented thrombosis in 3 dogs with AF, although 2/3 dogs had underlying mitral valve disease. In a case series of 39 Irish wolfhounds with congestive heart failure secondary to dilated cardiomyopathy and AF, 1 dog developed clinical signs consistent with arterial thromboembolism (ATE). A case series of 36 dogs with ATE documented AF in 1 dog, but ECG findings were not reported for all dogs. In a study of 7 dogs with thrombosis, 1 dog with bradial fibrillation had ventricular tachycardia and acute myocardial failure of unknown origin listed as the diagnosis.

Other case reports or case series were considered neutral to the PECO question because although thrombosis and arrhythmias were present concurrently, it was considered more likely that the arrhythmias developed subsequent to the thrombosis. In a case series of 16 dogs with splenic infarction, ventricular premature complexes were documented in 3 dogs, while in a report of 6 dogs with aortic or iliac arterial thrombosis, 1 dog was noted to have ventricular premature complexes. A single case report documented ATE and AF in a dog with hypothyroidism, but the case history implied that the ATE may have been present prior to atrial fibrillation.

Overall, the available evidence suggests that AF may be associated with arterial thrombosis in dogs, particularly where reduced left atrial appendage flow velocity exists, or when electrical cardioversion is attempted and as such antithrombotic therapy should be considered for these dogs. For dogs with other arrhythmias, we do not recommend the use of antithrombotic therapy unless other risk factors for thrombosis exist.

10.3 | Knowledge gap

The contribution of underlying structural cardiac changes to a prothrombotic state in dogs with cardiac arrhythmias remains unclear. Studies investigating hemostatic changes in dogs with cardiac arrhythmias in the absence of significant underlying cardiac disease and prior to the development of thrombosis are needed.

11 | PECO QUESTION: CARDIAC ARRHYTHMIAS (CATS)

In cats (P), is the development of cardiac arrhythmias (E), as opposed to remaining disease free (C), associated with the development of thrombosis (O)?
11.1 | Guidelines

1.10 Cardiac arrhythmias (cats)

a. Arrhythmias in cats with structural cardiac disease are associated with arterial thromboembolism.

b. We recommend the use of antithrombotic therapy for cats with arrhythmias and structural cardiac disease.

11.2 | Evidence summary

Ten studies related to this PECO question were reviewed. Most reports identified in cats supported the PECO question, with only 1 neutral and none opposing. A small number of reports in cats directly investigated the link between thrombosis risk and AF or other arrhythmias. However, most cats in these reports had underlying cardiomyopathy, limiting the ability to draw conclusions about the thrombogenicity of arrhythmias in isolation. One case series reported data on 50 cats with AF. Aortic thromboembolism was documented at presentation in 7/50 cats, and a total of 8 cats died or were euthanized due to ATE; it is unclear whether the deaths include all 7 cats that had ATE on presentation. All cats in this study had underlying structural heart disease, predominantly cardiomyopathy with left atrial enlargement. An observational clinical study performed by Schober et al identified reduced left atrial appendage flow velocity, a known risk factor for thrombosis, in 9 cats with cardiomyopathy and AF. A single case of ATE and left atrial ball thrombus was reported in a cat with hypertrophic cardiomyopathy and AF. A case–control study was reviewed that identified arrhythmias as significant risk factors in univariate analysis for the outcome of composite cardiac death in cats with hypertrophic cardiomyopathy, where 34/107 cardiac deaths were due to ATE. However, arrhythmia did not remain in the authors’ multivariate model. A follow-up to that study investigated the individual components of the composite outcome, and arrhythmia was not a significant predictor of death from ATE. However, the point estimate for the hazard ratio was above 1, and the confidence interval was wide, suggesting that further prospective studies are warranted to assess this relationship. Thus, this study was deemed neutral to the PECO question.

Most other relevant data in cats are contained in case series of cats with ATE or cardiomyopathy. These generally do not specifically investigate the association between arrhythmias and thrombosis. However, they demonstrate that the 3 conditions (ATE, cardiomyopathy, and arrhythmia) frequently coexist, so they were deemed to support the PECO question. In a case series of 127 cats with acute ATE, most of which had underlying cardiomyopathy, an arrhythmia was reported in 20 cats. In that series, 52 cats had ECG data reported, with 19 having arrhythmias, including ventricular premature complexes (13), AF (4), and atrial premature complexes (2). An older case series of 100 cats with ATE also detected abnormalities in 57 of the 67 cats that had an ECG performed, although this number included left atrial and ventricular enlargement patterns as well as true arrhythmias. In this study, common arrhythmias included isolated ventricular premature complexes (13), isolated supraventricular premature complexes (13), AF (3), ventricular tachycardia (2), and supraventricular tachycardia (2). A case series of 41 cats with restrictive cardiomyopathy documented ATE in 17 cats. In that report, arrhythmias were recorded in 19 of the 34 cats that had an ECG performed, although it is not possible to determine whether arrhythmias were specifically related to ATE based on the data presented. Common arrhythmias in that study included atrial premature complexes (9), AF (5), ventricular premature complexes (5), and right bundle branch block (4). A case series of clinical and necropsy data from 12 cats with arrhythmogenic right ventricular cardiomyopathy documented postmortem mural thrombosis in 2 cats. Arrhythmias were identified in the 8 cats that had ECG performed, including ventricular premature complexes (6), right bundle branch block (5), AF (4), ventricular tachycardia (3), first-degree AV block (2), and supraventricular tachycardia (1). It is not possible to determine from the report whether the cats with thrombosis had arrhythmias detected. An early case report of ATE in 5 cats identified an arrhythmia consistent with AF in one cat.

In summary, arrhythmias in cats with structural cardiac disease are associated with arterial thromboembolism, although it is difficult to determine the isolated contribution of the arrhythmia to thrombotic risk in these cats. Given the strong association between structural cardiac disease, arrhythmias and thromboembolism in cats, we recommend antithrombotic therapy for all affected cats.

11.3 | Knowledge gap

Further studies are needed to differentiate the contribution of arrhythmias to changes in coagulation status from those of underlying cardiomyopathy, cardiac dysfunction and blood flow alterations.

12 | PECO QUESTION: SEPSIS (CATS)

In cats (P), is the development of sepsis (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

12.1 | Guidelines

1.11 Sepsis (cats)

a. Sepsis is associated with the development of thrombosis in a small subset of cats.

b. We recommend against routine use of antithrombotic therapy in cats with sepsis.

c. We suggest that antithrombotic therapy be considered for cats with sepsis, following an assessment of the risk and benefit in individual patients or where other risk factors for thrombosis exist.
12.2 | Evidence summary

Hemostatic abnormalities are commonly identified in cats with sepsis, but thrombosis is infrequently reported. Three retrospective studies including 160 cats with sepsis described just 2 cats (1.3%) with pulmonary thrombosis noted at necropsy. In aggregate from 2 studies of cats with PTE, 6.5% cats (3/46) had sepsis. Sepsis was a common cause of disseminated intravascular coagulation (DIC) in cats, affecting 9/46 cats in 1 study. In 19/24 nonsurvivors necropsied in this study, intravascular fibrin deposition was identified, but the underlying conditions of cats that were examined postmortem were not listed, thereby limiting the quality of the evidence provided. A retrospective study of pulmonary histopathology in 148 cats with Cytauxzoon felis infection included 1 cat (0.7%) with pulmonary thrombi.

Four studies were considered neutral to the PECO question. A study investigating hemostatic changes in cats with sepsis showed changes consistent with coagulation activation, such as reduced protein C activity and increased D-dimer, but thrombosis was not described; hence, the study was deemed neutral to the PECO question. Another report described 10 cats undergoing adrenalectomy for hyperadrenocorticism. Two cats developed septic complications, and 1 experienced a fatal thromboembolic event. However, it is unclear whether thrombotic events occurred in cats with sepsis. Several case reports describe thrombotic complications of sepsis in cats, but multiple potential causes of thrombosis were present.

Overall, cats with sepsis commonly develop hemostatic abnormalities consistent with the activation of coagulation, but the incidence of thrombosis in cats with sepsis is low. In cats with sepsis that do develop thrombi, PTE is most described. The low overall incidence of thrombosis in cats with sepsis argues against routine use of antithrombotic therapy in these animals. We suggest that antithrombotic therapy be considered for cats with sepsis, particularly where other risk factors for thrombosis exist. Because cats with sepsis can develop DIC and experience clinical bleeding, antithrombotic medication should only be initiated after an assessment of the risk and benefit in individual patients.

12.3 | Knowledge gap

Studies specifically investigating the development of clinically relevant thrombosis in cats (microvascular and macrovascular) are needed to better understand the risk factors for thrombotic complications in this patient population.

13 | PECO QUESTION: PROTEIN-LOSING ENTEROPATHY (PLE) (DOGS)

In dogs (P), is the development of protein-losing enteropathy (E), as opposed to remaining disease free (C), associated with the development of thrombosis (O)?

13.1 | Guidelines

1.12 Protein-losing enteropathy (PLE) (dogs)

a. Protein-losing enteropathy in dogs is moderately associated with thrombosis that can affect the venous or arterial system.

b. We recommend antithrombotic therapy for all dogs with protein-losing enteropathy unless the risks (particularly gastrointestinal bleeding) are deemed to outweigh the potential benefit in individual patients.

13.2 | Evidence summary

A total of 96 reports were reviewed for this PECO question. Of these, 27 provided evidence suggesting a moderate to strong link between a diagnosis of PLE in dogs and the development of thrombotic complications, many of them life-threatening or fatal. The overall frequency of thrombosis reported in articles describing dogs with PLE was 46/1798 (2.6%), while the overall frequency of PLE in reports describing thrombosis was 9/699 (1.3%). This suggests that thrombosis is an important complication of PLE, even though PLE is not the most common cause of thrombosis seen in clinical practice. The retrospective nature (LOE 5) and the lack of a control group in these studies prohibits true risk assessment.

There were numerous reports that were considered neutral to the PECO question since they described canine PLE populations without mention of thrombotic complications or dogs with thrombosis without mention of PLE. Most reports of dogs with thrombosis identified an underlying disease other than PLE. Most of the articles describing dogs with PLE made no attempt to identify thrombosis formally, to explore the role of therapy with corticosteroids, or to study coagulation parameters. As therapy such as corticosteroids can represent an additional risk factor for thrombosis, the additive effects of multiple risk factors may impact overall coagulation status. Even some of the studies on PLE that identified thrombotic complications failed to provide details regarding the nature, extent, severity of the thrombus or any data regarding coagulation assessments performed. As such, the estimate of the incidence of thrombosis in PLE studies is most likely to be an underestimate of the risk. No studies were judged to be in opposition to the PECO question.

The overall weight of the studies available suggests a moderate to strong association between PLE and thrombosis. Both arterial and venous thrombotic complications were identified in dogs with PLE, although venous thrombosis was more common. As such, we recommend antithrombotic therapy for all dogs with protein-losing enteropathy unless the risks (particularly gastrointestinal bleeding) are deemed to outweigh the potential benefit in individual patients.
13.3 | Knowledge gap

The differences in coagulation status between dogs with PLE experiencing thrombosis and those that do not develop thrombosis are not clear, as most studies that describe thrombosis in dogs with PLE do not include hemostatic testing. The contribution of corticosteroid therapy to the overall prothrombotic risk is also not known.

14 | PECO QUESTION: PROTEIN-LOSING ENTEROPATHY (PLE) (CATS)

In cats (P), is the development of protein-losing enteropathy (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

14.1 | Guidelines

1.13 Protein-losing enteropathy (PLE) (cats)

a. Protein-losing enteropathy in cats is weakly associated with venous thromboembolism (pulmonary thromboembolism).

b. There is no evidence that protein-losing enteropathy is a risk factor for arterial thromboembolism in cats.

c. We suggest that antithrombotic therapy be considered for cats with protein-losing enteropathy, where other risk factors exist.

14.2 | Evidence summary

A review of the literature identified 17 studies relevant to the PECO question. Only 1 retrospective study suggested an association between PLE and PTE (venous thromboembolism) in cats. The incidence of PLE in this study of PTE in cats was 14% (4/29). There were no control groups, however, and hence, the risk of thrombosis in cats with PLE cannot be properly assessed. An association between PLE and PTE was not substantiated by the other major retrospective study describing PTE in cats. The 15 reports deemed neutral to the PECO question included 4 retrospective studies (LOE 5) describing a total of 82 cats with PLE (encompassing inflammatory bowel disease, lymphangectasia, and other causes) in which there was no report of thrombosis as a complication. In addition, within these 15 articles were 9 reports describing a total of 838 cats experiencing arterial or venous thrombosis in cats, but none of the cats in these studies had PLE as an underlying disease. The final 2 reports that were neutral to the PECO question were retrospective studies of 57 cats receiving dalteparin and 231 cats with reduced blood antithrombin concentrations. These studies were of poor quality given that they were not designed to address the PECO question; however, none of these cats had PLE. One study suggested that PLE may be associated with a risk of bleeding in cats based solely on coagulation testing and could be considered in opposition to the PECO question.

Although 1 study did suggest an association between PLE and PTE in cats, the collective weight of the 15 neutral studies including 82 PLE cases suggests that there is a weak association between PLE and thromboembolic complications in cats and that the overall risk of thrombosis (venous or arterial) in cats with PLE is seemingly low. As such, we suggest that antithrombotic therapy be considered for cats with protein-losing enteropathy, where other risk factors exist.

14.3 | Knowledge gap

Prospective studies with control groups are needed to better ascertain any association between PLE and thrombosis in cats.

15 | PECO QUESTION: HYPERADRENOCORTICISM (CATS)

In cats (P), is the development of hyperadrenocorticism (E), as opposed to remaining disease-free (C), associated with the development of thrombosis (O)?

15.1 | Guidelines

1.14 Hyperadrenocorticism (cats)

a. No evidence-based recommendations can be made regarding the use of antithrombotic therapy in cats with hyperadrenocorticism.

b. We suggest that antithrombotic therapy should not be routinely used in cats with hyperadrenocorticism.

15.2 | Evidence summary

The literature describing hyperadrenocorticism in cats is scarce, with most studies describing case series or case reports (LOE 5). Some reports included necropsy results or the findings of CT or abdominal ultrasound imaging, but none were focused on identifying thrombosis. Across all studies reviewed, a total of 75 cats were reported to have hyperadrenocorticism, and only 1 cat was diagnosed with PTE, as described in a retrospective study of 7 cats with hyperadrenocorticism. The scant literature suggests that the incidence of hyperadrenocorticism in cats is seemingly low but precludes evidence-based recommendations. As such, we suggest that antithrombotic therapy should not be routinely used in cats with hyperadrenocorticism.
16  |  16 PECO QUESTION: GLUCOCORTICOID ADMINISTRATION (CATS)

In cats (P), is glucocorticoid administration (E), as opposed to no glucocorticoid administration, (C), associated with the development of thrombosis (O)?

16.1  |  Guidelines

1.15 Glucocorticoid administration (cats)

a. No evidence-based recommendations can be made regarding the use of antithrombotic therapy in cats receiving exogenous glucocorticoids.

b. We suggest that antithrombotic therapy should not be routinely used in cats receiving exogenous glucocorticoids.

16.2  |  Evidence summary

Few studies were relevant to the PECO question, and evidence for a causal relationship between exogenous corticosteroid administration in cats and thrombosis is scarce. In one retrospective observational study of 25 cats receiving exogenous corticosteroids, none developed evidence of thrombosis. In a study of 6 cats with PVT, 2 (33%) were receiving oral prednisolone at the time of presentation. However, all cats had underlying hepatic disease precluding the establishment of a clear association between corticosteroid administration and thrombosis. Similarly, in another study (LOE 5, good), 2/44 cats with distal ATE had received corticosteroids in the weeks preceding the thrombotic event, but these cats also had comorbidities considered high risk for thrombosis. In a retrospective study of 29 cats with PTE, 8 (27.6%) had received recent corticosteroids.

Given the lack of controlled studies in the current veterinary literature, no causal relationship can be determined between exogenous corticosteroids and an increased risk of thrombosis. However, based on the overall limited evidence supporting the PECO question with the corresponding high frequency of use of glucocorticoids, we suggest that antithrombotic therapy should not be routinely used in cats receiving this class of medication.

17  |  PECO QUESTION: INTRAVENOUS CATHETERS (DOGS)

In dogs (P), is the presence of an intravenous catheter (E), as opposed to no intravenous catheter (C), associated with the development of thrombosis (O)?

17.1  |  Guidelines

1.16 Intravenous catheters (dogs)

a. The risk of thrombosis associated with IV catheters in dogs is unknown.

b. We suggest that antithrombotic therapy should be considered in dogs with IV catheters only where other risk factors for thrombosis exist.

17.2  |  Evidence summary

A review of the literature yielded one report (LOE 2, fair quality) that was supportive of the PECO question. In that study, 50 dogs with cephalic peripheral catheters placed to enable repeated radiotherapy were monitored daily using vascular ultrasound. Eighteen dogs developed phlebitis, suggesting an incidence of 36%. Ten dogs with phlebitis developed evidence of local thrombosis (58%), suggesting an overall incidence of catheter-related thrombosis of 20% (10/50). Vascular ultrasound of the cephalic vein was performed in each dog prior to and soon after IV catheter placement and then at regular intervals, allowing the enrolled dogs to serve as their own controls.

Most identified studies were experimental and designed to evaluate the degree of catheter-related thrombus formation as opposed to systemic thrombosis; none were deemed good quality. Study designs varied, but most did not have a no-catheter control group and worked from an assumption that intravenous catheters are thrombogenic in dogs. Most studies compared catheter materials or designs, protocols for implantation or flushing, or methods of detecting thrombosis, such as radiolabeling of platelets or fibrinogen. The outcomes assessed were typically catheter function or the appearance and weight of catheter-associated thrombus postmortem. Assessments of the clinical relevance of thrombi are limited. Catheter-associated thrombosis was generally described as substantial and common, but methods of assessing this were limited. Two studies documented evidence of PTE, but most were not designed to evaluate the presence of systemic thrombosis. The short duration of most experiments suggests that catheter-associated thrombosis can occur rapidly in dogs.

Two experimental studies deemed neutral to the PECO question evaluated catheter patency as the only assessment of potential thrombosis, with equivocal results. Two studies, judged to oppose the PECO question, evaluated surgically implanted silicon-based central venous catheters. Both were conducted by the respective catheter manufacturers and were deemed at high risk of bias. Differences between catheter materials and designs were frequently detected but were inconsistent between studies. All catheter materials have been associated with some degree of thrombosis, and the only catheter designs that featured minimal thrombosis were experimental and are not commercially available. Most studies also employed surgically placed central catheters, which limits the generalizability of their findings to clinical practice.

Four case series were judged LOE 5 and in support of the PECO question. Two studies focused on IV catheter complications, and thrombosis was reported in both. A third described treatment of cases of fibrin sheaths formed on dialysis catheters, while another described cranial vena cava thrombosis and reported IV catheterization as a potential risk factor. Two case-control studies designed...
for other objectives also reported on cases with IV catheters and associated thrombosis. These were deemed LOE 5 for relevance to this PECO question. Four case reports documented thrombosis associated with IV catheters but were not controlled. One LOE 5 study that opposed the PECO question documented complications of long-term silicone central venous catheters and did not report any instances of thrombosis. However, that study relied on a retrospective review of medical records and was thus judged poor quality.

Overall, the literature suggests that IV catheters are likely thrombogenic in dogs, but the experimental nature of most studies and the lack of appropriate controls precludes determining the degree of risk. As such, it is difficult to make an evidence-based recommendation for widespread antithrombotic use in dogs with IV catheters. Overall, we feel it is reasonable to consider IV catheterization as an additional risk factor for thrombosis in dogs that warrants consideration as an indication for antithrombotic drugs, particularly where other risk factors for thrombosis exist. Reassessments of the need for IV catheters should be performed regularly, and catheters should be removed as soon as they are no longer needed.

### 18.1 Guidelines

1.17 Intravenous catheters (cats)

   a. The risk of thrombosis associated with IV catheters in cats is unknown.
   
   b. We suggest that antithrombotic therapy should be considered in cats with IV catheters only where other risk factors for thrombosis exist.

### 18.2 Evidence summary

Most studies evaluated thrombosis as a cause of catheter occlusion rather than assessing systemic thrombotic complications of catheter placement and thus did not directly address the PECO question. Four experimental (LOE 3) studies were identified that were considered relevant to the PECO question. In a report of polyethylene catheters surgically placed into the caudal vena cava, thrombosis was observed in 13/14 cats within 2.5 hours of placement. This study was deemed of poor quality but lacked a no-catheter control group, and the catheter material is no longer used. A second study compared long-term vascular access in 25 cats with surgically placed polyurethane jugular catheters with implanted vascular access ports (VAPs) in 42 cats featuring silicone catheters. Loss of catheter function was assumed to indicate thrombosis, which occurred in 12% of jugular catheters within 1 week. Another experimental study found no difference in coagulation test results between cats sampled via a jugular catheter and those sampled by jugular venipuncture, but this study did not investigate catheter-associated thrombosis and was deemed neutral to the PECO question. A final experimental study found no evidence of thrombosis in 48 catheterization episodes in 6 cats and therefore opposed the PECO question. However, observation for thrombosis was confined to evaluations of catheter patency, and the relevance to the PECO question was limited.

The remaining studies were case series or reports (LOE 5) that mostly supported the PECO question, although evidence quality and PECO question relevance were generally low. One case series documented complications of 100 polyurethane jugular central venous catheters in 12 cats and 81 dogs. Fourteen catheters failed to aspirate, suggesting possible catheter thrombosis, and 2 had evidence of venous thrombosis confirmed by palpation or ultrasound. This was the only clinical study to use standardized prospective data collection, but thrombosis was generally assumed from loss of catheter patency, and complications in cats were not separated from those in dogs. An older case series evaluated 300 polypropylene surgically placed jugular catheters in dogs and cats. Thrombosis formation was noted on 5/300 catheters (1.7%), but it is unclear how this was determined, and again, dogs and cats were not differentiated. Polypropylene catheters are no longer used; hence, this study is of limited applicability to current clinical practice. Thrombosis of dialysis catheters was described in a case series of 8 cats, but the associated risk cannot be estimated because there was no information provided about the total population at risk. Thus, it is not clear if thrombosis is a common or rare complication of dialysis catheter placement. In a case series of 29 cats with necropsy-confirmed PTE, IV catheterization was noted as a potential risk factor, with 21/29 cats having had IV catheters during the preceding hospitalization episode. However, the association between IV catheter placement and PTE is confounded by associations between the presence of an underlying disease (necessitating IV catheter placement) and thrombosis. A case report describes total parenteral nutrition extravasation from a polyurethane jugular central venous catheter after thrombosis of the jugular vein. However, it is not clear whether the thrombosis was associated with the catheter itself, parenteral nutrition infusion, or extravasation. A single clinical report was judged to oppose the PECO question, but this was a case series of 2 cats with long-term silicone jugular catheters that was uncontrolled and deemed of poor quality.

Overall, the available evidence indicates that thrombosis is a complication of IV catheterization in cats. However, the degree of risk for systemic complications of catheter-related thrombosis cannot be estimated from the current literature. It is likely that catheter placement technique, material, location, and dwell-time all affect the associated risk of thrombosis, but there is presently insufficient evidence to make evidence-based recommendations for widespread antithrombotic use in cats with IV catheters. As with dogs, IV catheters can be considered to represent an additional risk factor for thrombosis in cats but one that warrants consideration as an indication for antithrombotic drugs only where other risk factors for thrombosis exist. Regular determinations of the ongoing need for all catheters should be part of clinical
practice to reduce the risk of thrombosis by eliminating a potential risk factor.

19 | PECO QUESTION: ARTERIAL CATHETERS (DOGS)

In dogs (P), is the presence of an arterial catheter (E), as opposed to no arterial catheter (C), associated with the development of thrombosis (O)?

19.1 | Guidelines

1.18 Arterial catheters (dogs)

a. The risk of thrombosis associated with arterial catheterization in dogs appears to be low.

b. No evidence-based recommendations can be made regarding the use of antithrombotic therapy in dogs with arterial catheters.

c. We suggest that antithrombotic therapy should not be routinely used in dogs with arterial catheters.

19.2 | Evidence summary

Four studies (LOE 5, fair) were identified that evaluated the function of arterial catheters in dogs and reported subsequent complications such as thrombosis.\(^{308-311}\) None of these reports included a relevant control population (dogs without arterial catheters); hence, all 4 studies were considered neutral to the PECO question. Additionally, the complication defined as ‘catheter occlusion’ was not characterized in all cases to distinguish potential causes such as intraluminal thrombosis, catheter kinking, arterial spasm or thromboembolism. This precludes accurate determination of the association between arterial catheter placement and thrombosis or quantification of the resultant risk.

In 2 studies, arterial catheters were in place only during anesthetic procedures,\(^{310,311}\) while in the 2 remaining studies, some catheters remained in place postoperatively.\(^{308,309}\) The association between catheter dwell-time and complication rates was partially explored in 2 studies. The dwell time was median (min-max) 23.8 h (4.5-257) in dogs\(^{308}\) and median (min-max) 7.7 h (0.9-42.5) in dogs and cats.\(^{309}\) In dogs, no relationship between dwell time and complication rates was identified.

In a study of 267 arterial catheters placed in 213 dogs and 13 cats, 112 catheter sites were evaluated by an anesthesiologist after catheter removal.\(^{309}\) Most were removed in the ICU following anesthetic recovery (< 10 h dwell time). In 72/112, occurring at a median (min-max) of 16.7 h (2.3-124.3) after removal, no abnormalities were revealed. Although not explicitly stated, it is inferred that catheter sites were inspected for the presence of a pulse in 108 sites in dogs (dogs may have had more than 1 arterial catheter). No pulse was detected in 21 sites (inferred that all of these were in dogs). In 3 dogs, a knot was palpated on or under the skin, which likely (but not definitively) indicates thrombosis. No ischemic complications were noted in any patient.\(^{309}\)

In a study of 198 arterial catheters in dogs, complications were noted in 38 (19%),\(^{308}\) although in 59 (30%), the reason for catheter removal was “no longer aspirates/flushes.” Loss of catheter function was not noted as a complication in this study; rather, complications were categorized as pain on flush/aspirate, swollen paw, cold paw and site reaction. In dogs, there were 21 instances of swollen paws and 3 instances of cold paws. Taken together, the instances of loss of function, swollen paw and cold paw might all indicate thrombosis, but this cannot be confirmed.\(^{308}\)

Overall, the 4 identified studies were considered neutral to the PECO question due to a lack of contemporaneous unexposed controls with which to estimate risk, the heterogeneous nature of the clinical population and the lack of confirmation of thrombosis in many instances. Confounding of risk by the underlying disease process and the anesthetic and surgical procedures also impedes accurately attributing risk to the presence of the arterial catheter. As such, the current literature is insufficient to determine whether the use of arterial catheters predisposes dogs to thrombosis and hence precludes evidence-based recommendations for antithrombetics. Overall, the risk of thrombosis in dogs with arterial catheters is seemingly low, and hence, we recommend against routine use of antithrombotic agents for dogs with arterial catheters.

20 | PECO QUESTION: ARTERIAL CATHETERIZATION (CATS)

In cats (P), is the presence of an arterial catheter (E), as opposed to no arterial catheter (C), associated with the development of thrombosis (O)?

20.1 | Guidelines

1.20 Arterial catheters (cats)

a. The risk of thrombosis associated with arterial catheterization in cats appears to be low.

b. No evidence-based recommendations can be made regarding the use of antithrombotic therapy in cats with arterial catheters.

c. We suggest that antithrombotic therapy should not be routinely used in cats with arterial catheters.

20.2 | Evidence summary

Only 3 studies (LOE 5) were identified that specifically evaluated arterial catheters in cats and aimed to evaluate complications such as thrombosis.\(^{308,309,312}\) None of these studies included a control group without an arterial catheter; hence, all 3 were considered neutral to the PECO question. As with dogs, the complication ‘catheter occlusion’ was not further characterized to determine or differentiate the underlying cause. This lack of confirmation of thrombosis precludes
true determination of the risk of thrombosis posed by the use of arterial catheters. In most patients, arterial catheters were placed for monitoring arterial blood pressure during anesthesia with continued use postoperatively. The association between arterial catheters and dwell time was partially explored in these 3 studies. The dwell times were median (mix-max) 12 h (3.5-35),308 3 h (1-117),312 and 7.7 h (0.9-42.5, dogs and cats combined).309 Complication rates were related to dwell time, but the exact nature of the complications was not characterized.

In a study of 13 cats, arterial catheterization sites were checked following catheter removal in only 4 cats.309 In each case, a pulse was detected distally, indicating that the arteries remained patent, but the remaining catheter sites were not evaluated.

In a study that included 29 arterial catheters in cats, 2 catheters (7%) were removed due to a complication.308 Loss of catheter function where the catheter could not be flushed and failed to aspirate occurred 8 times (28%), while for 4 catheters (14%), a complication of “cold paw” was noted. Thrombosis is a possible cause for these various complications but was not confirmed.

The most likely occurrence of thrombosis associated with an arterial catheter in a cat was noted in the study by Mooshian et al. (LOE 5, poor), in which 1 cat suffered ischemic injury secondary to a coccygeal arterial catheter resulting in tail amputation.312 Histopathology was not conducted to confirm thrombosis; however, the underlying condition of this cat was not reported, which precludes assessment of the contribution of other risk factors.

One additional study identified arterial thrombosis in a cat associated with an infected arterial catheter.313 The infection was confirmed by bacterial culture, and thrombosis was confirmed by histopathology following amputation. However, in this case report, the relative contributions of the bacterial infection and the arterial catheter itself to the thrombosis cannot be determined. The case report demonstrates that arterial thrombosis can occur in association with arterial catheters in cats, but the comorbidity and the uncontrolled nature of the report means that this study must be considered neutral to the PECO question.

Overall, the 4 studies that were reviewed neither support nor oppose the PECO question. While a proportion of cats with arterial catheters may have developed thrombosis as a consequence of the catheter, the risk of thrombosis was not compared to a contemporaneous population of cats without arterial catheters, which precludes an assessment of relative risk. In cases where thrombosis did or may have occurred, it could not be discerned whether an underlying disease predisposed the cats to thrombosis or if the use of an arterial catheter augmented the risk. In conclusion, there are insufficient data to determine whether the use of arterial catheters predisposes cats to thrombosis; hence, no evidence-based recommendations can be made. Overall, the risk of thrombosis in cats with arterial catheters is seemingly low, and hence, we recommend against routine use of antithrombotics for cats with arterial catheters.

21  |  PECO QUESTION: VASCULAR ACCESS PORTS (DOGS)
In dogs (P), is the presence of a vascular access port (E), as opposed to no vascular access port (C), associated with the development of thrombosis (O)?

21.1  |  Guidelines

1.20 Vascular access ports (dogs)

a. There is insufficient evidence to determine whether the use of vascular access ports in dogs increases the risk of thrombosis.

b. No evidence-based recommendations can be made regarding the use of antithrombotic therapy in dogs with vascular access ports.

21.2  |  Evidence summary

Four studies (all LOE 5, poor) met the criteria for review. Given the small number and limited quality of the studies identified, there was insufficient evidence to support the PECO question. None of the studies had contemporaneous controls, and definitive causes of VAP failure were rarely identified. In instances where thrombosis was identified at the time of VAP removal, the potential that infection contributed to the thrombus could not be ruled out.314,315 Moreover, most dogs had VAPs implanted to enable the management of neoplasia (either for the administration of chemotherapy316 or sedation for radiation therapy,314,317) which may increase the inherent risk for thrombosis. Additionally, VAPs were typically functional for months, suggesting that the risk of developing complications related to thrombosis is relatively low. Three studies (LOE 5, poor) were considered neutral to the PECO question,314,315,317 whereas 1 report might be interpreted as being opposed to the PECO question since none of the dogs had any evidence of thrombosis.316 No study reported coagulation testing, and the impact of variation in animal size, underlying conditions, catheter materials and sizes, and device flushing protocols was not considered. Overall, there is insufficient evidence to make recommendations on the use of antithrombotic therapy in dogs with VAP in the absence of other risk factors for thrombosis.

22  |  PECO QUESTION: VASCULAR ACCESS PORTS (CATS)
In cats (P), is the presence of a vascular access port (E), as opposed to no vascular access port (C), associated with the development of thrombosis (O)?
22.1 Guidelines

1.21 Vascular access ports (cats)

a. There is no evidence that the use of vascular access ports in cats is associated with an increased risk of thrombosis.
b. We suggest that antithrombotic therapy should not be routinely used in cats with vascular access ports.

22.2 Evidence summary

Six studies describing the use of VAPs in cats were reviewed, the largest of which included 46 cats (and 126 dogs) receiving radiotherapy for various forms of neoplasia. Permanent loss of catheter patency was among the complications described, but the mechanism and species were not characterized, limiting the relevance of these data to the PECO question. Another study noted thrombotic complications in 2/6 cats with femoral vein VAPs. In 1 cat, a clinically silent thrombus distal to the catheter tip was identified that did not limit device utility. In the second cat, thrombosis was related to catheter kinking that necessitated removal. Another study described surgically placed VAPs in 42 healthy cats, 2 of which developed fatal pulmonary thromboembolism. An additional 3 studies including a total of 36 cats with implanted VAPs reported no thrombotic complications. The lower quality clinical studies (LOE 5, poor) that lacked a control group were considered neutral to the PECO question because the risk of thrombosis from VAP implantation was frequently confounded by underlying neoplasia. In the experimental studies (LOE 3 good-poor), involving healthy cats, no risk of thrombosis was apparent, and hence, these studies were assessed as opposing the PECO question. Only 1 study (LOE 3, fair) suggested an association between VAP implantation and thrombosis in cats, but another group of cats experienced no thrombotic complications, thereby limiting the strength of the association. Overall, we suggest that antithrombotic therapy not be routinely used in cats with VAP.

23 PECO QUESTION: EXTRACORPOREAL CIRCUITS (DOGS)

In dogs (P), is the use of an extracorporeal circuit (E), as opposed to no extracorporeal circuit (C), associated with the development of thrombosis (O)?

23.1 Guidelines

1.22 Extracorporeal circuits (dogs)

a. Extracorporeal circuits are associated with activation of coagulation and circuit thrombosis in dogs, necessitating use of systemic or regional anticoagulation during extracorporeal procedures unless otherwise contraindicated.

b. The risk of systemic thrombosis in dogs between extracorporeal therapy cycles appears low.
c. We suggest that antithrombotic therapy should not be routinely used between extracorporeal therapy cycles in dogs unless indicated by other risk factors for thrombosis.

23.2 Evidence summary

Extracorporeal circuits, specifically those used for hemodialysis and therapeutic apheresis, are associated with activation of platelets, neutrophil-platelet aggregation, and activation of coagulation. Extracorporeal circulation leads to reduced and turbulent blood flow within the circuit, high shear stress, and blood contact with both air and artificial surfaces (eg, filter membranes, tubing, IV catheter lumens). Platelet activation in response to shear stress leads to platelet-neutrophil aggregate formation, and a study utilizing radiolabeled canine platelets circulated through a dialyzer showed that platelets exposed to the circuit were significantly more thrombogenic than healthy control platelets. Leukocyte activation triggered by contact between blood and extracorporeal circuits contributes to a procoagulant state. In some instances, contact activation by the artificial membrane may also occur. Given these circuit-induced procoagulant effects, anticoagulation (systemic or regional) during extracorporeal therapy is required to avoid clotting within the circuit. We therefore recommend that anticoagulation (systemic or regional) be used during the procedure unless otherwise contraindicated.

Veterinary studies describing extracorporeal techniques consistently describe thrombotic complications related to the filter or the central venous catheter. However, across all studies reviewed, no systemic thrombotic complications were noted in dogs undergoing membrandialysis (n = 51), intermittent hemodialysis (n = 183), or centrifugal apheresis (n = 4). Anti-coagulation strategies, when used, were limited to the duration of the session and varied among the studies reviewed. The overall quality of evidence was judged to be low because of the retrospective nature of the studies and the lack of monitoring for systemic thrombosis. Several studies of cardiopulmonary bypass in dogs involving extracorporeal circulation reported thrombotic complications. However, all dogs in these reports had confounding factors for thrombosis, including underlying diseases, prosthetic vascular implants and cardiac surgical procedures.

Overall, despite the known procoagulant impact of the extracorporeal circuit, the risk of systemic thrombosis in dogs undergoing extracorporeal therapy appears to be low within and between cycles. We therefore suggest that antithrombotic therapy should not be routinely used between extracorporeal therapy cycles in dogs unless indicated by other risk factors for thrombosis. However, it should be recognized that no study in dogs directly addresses the PECO question because of the presence of confounding factors, including underlying disease and central venous catheters.
24 | PECO QUESTION: EXTRACORPOREAL CIRCUITS (CATS)

In cats (P), is the use of an extracorporeal circuit (E), as opposed to no extracorporeal circuit (C), associated with the development of thrombosis (O)?

24.1 | Guidelines

1.23 Extracorporeal circuits (cats)

a. Extracorporeal circuits are associated with activation of coagulation and circuit thrombosis in cats, necessitating the use of systemic or regional anticoagulation during extracorporeal procedures unless otherwise contraindicated.

b. No evidence-based recommendations can be made regarding the use of antithrombotic therapy between extracorporeal therapy cycles in cats.

24.2 | Evidence summary

Two studies investigating dialysis catheter performance in cats were reviewed. One report assessed patency of a nitric oxide releasing extracorporeal circuit using an in vivo feline model, and the second evaluated changes in blood flow rate through a dialysis catheter in response to tissue plasminogen activator in 17 dogs and 8 cats. Neither study was designed to investigate systemic thrombosis; hence, neither directly addressed the PECO question. Although the use of extracorporeal circuits in cats necessitates regional or systemic anticoagulation as it does in dogs, there is insufficient evidence upon which to base recommendations for the use of antithrombotics in cats between extracorporeal therapy cycles.

24.3 | Knowledge gaps

No studies were identified that directly addressed the PECO question, despite ample evidence supporting the high incidence of thrombosis in people undergoing extracorporeal circulation as opposed to those who do not.

25 | PECO QUESTION: TRANSVENOUS PACEMAKER (DOGS)

In dogs (P), is the presence of a transvenous pacemaker (E), as opposed to no transvenous pacemaker (C), associated with the development of thrombosis (O)?

25.1 | Guidelines

1.24 Transvenous pacemaker (dog)

a. The presence of a transvenous cardiac pacemaker is weakly associated with symptomatic thrombosis in dogs, while lead-associated thrombosis is more common.

b. We recommend the use of antithrombotic therapy in dogs following transvenous pacemaker implantation, where other risk factors for thrombosis exist.

c. We suggest that antithrombotic therapy be considered in all dogs following transvenous pacemaker implantation.

25.2 | Evidence summary

Thirty-five references that included ≥1 dog with transvenous pacemaker implantation were reviewed. Most were case series or single case reports (LOE 5), and 1240 dogs were described, of which 60 had suspected or confirmed thrombosis (5%). Two studies were experimental (LOE 3) but of poor quality. In most dogs, the thrombi caused no clinical signs, and the thrombi were identified at necropsy or noted using echocardiography. Only 17 dogs had clinically significant thrombi described (~1%).

Overall, 13 studies (1 LOE 3, 12 LOE 5) support the PECO question and suggest an association between transvenous pacemakers and thrombosis in dogs. The one LOE 3 report that supported the PECO question was a retrospective case series of 101 dogs that had polyurethane insulated transvenous pacemaker leads implanted. These pacemakers were in place for between 10 days and 13 years before euthanasia and postmortem examination. Thrombi were detected in 34/101 dogs, but no dogs showed clinical signs. Nine studies (LOE 5, fair) supported the PECO question, including 3 case series focused on pacemaker complications. In total, these three studies described thrombi in 7 dogs out of 426 dogs with sufficient follow-up to analyze complication rates. Thrombi occurred in the cranial vena cava, pulmonary arterial tree and aorta. It is unclear whether any of the dogs with thrombosis had additional predisposing comorbidities. The remaining supportive studies included 17 dogs with thrombosis following transvenous pacemaker implantation, typically in the cranial vena cava, some of which were fatal. Some studies reported comorbidities, including trauma, PLN and infection, that could have contributed to the risk of thrombosis. Four publications (LOE 5) were considered neutral to the PECO question either due to lack of follow-up, multiple possible causes for thrombosis, or reasons other than the presence of a pacemaker that were deemed likely to result in thrombosis (e.g., stenosis).

Eighteen studies (1 LOE 3 good, 17 LOE 5 good-fair) were judged to be neutral to the PECO question based on long-term follow-up of dogs after pacemaker implantation without reports of thrombotic complications. An experimental (LOE 3) study described 74 dogs with implanted pacemakers (≤180 days). A variety of complications were reported, but thrombosis did not occur. The other studies were focused on pacemaker complications and included large sample sizes (total n = 380), and thrombosis was not reported. One case series of dogs in which pacemakers were implanted for the management of suspected myocarditis described 74 dogs with prothrombotic comorbidities, including protein-losing disease, immune-mediated disease, the
presence of spontaneous echocontrast, hepatic disease, and hyperadrenocorticism. Thrombosis was not reported as a complication, with a median survival time of 1079 days.\textsuperscript{359}

Overall, the available literature suggests that the presence of a transvenous pacemaker in dogs is associated with the development of thrombosis, with an estimated overall prevalence of \textasciitilde 5% and an estimated prevalence of symptomatic thrombosis of \textasciitilde 1%. Cranial vena cava syndrome is the most commonly associated thrombotic complication of transvenous pacemakers in dogs, with outcomes ranging from resolution to death. The risk of thrombosis is not uniform, however, because some dogs with other comorbidities that might predispose to thrombosis did not develop thrombotic complications from their pacemaker. It seems reasonable, however, that all dogs with pacemakers and prothrombotic comorbidities should receive antithrombotic therapies for prophylaxis, while antithrombotic therapy can be considered in every dog following transvenous pacemaker implantation to minimize the risk of symptomatic thrombosis development.

25.3 Knowledge gap

Additional studies are needed to better characterize the role of comorbidities in the development of thrombosis in dogs with transvenous pacemakers.

26 PECO QUESTION: TRANSVENOUS PACEMAKER (CATS)

In cats (P), is the presence of a transvenous pacemaker (E), as opposed to no transvenous pacemaker (C), associated with the development of thrombosis (O)?

26.1 Guidelines

1.25 Transvenous pacemaker (cats)

a. No evidence-based recommendations can be made regarding the use of antithrombotic therapy in cats following transvenous cardiac pacemaker placement.

26.2 Evidence summary

Most studies of cardiac pacemaker implantation in cats describe epicardial lead placement only (total n = 52) and were not further evaluated. Five studies consisting of isolated case reports or small case series (LOE 5, fair) describing cats with implanted transvenous pacemakers were reviewed \textsuperscript{365-369} although 2 studies included cats with epicardial leads.\textsuperscript{366,367} Four studies were considered neutral to the worksheet question since thrombosis was not described, while 1 was considered neutral because chylothorax developed as a complication, and thrombosis could not be ruled out as the cause.\textsuperscript{369} The case report that was considered neutral to the PECO question described a cat with a three-week history of syncope due to third-degree atrioventricular block.\textsuperscript{369} A permanent transvenous pacemaker was placed in the left jugular vein, and the cat was asymptomatic for 3 months following implantation, when chylothorax was detected that required repeated thoracocentesis and ultimately prompted euthanasia. The cause of chylothorax was not determined, but thrombosis was a potential explanation. Overall, since most literature describes epicardial lead placement and there is no definitive evidence of thrombosis in cats following transvenous pacemaker placement, we were unable to make evidence-based recommendations on the use of antithrombotic medications for these cats.

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REFERENCES

1. 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. 2019;29(1):37-48.
2. Goggs R, Bacek L, Bianco D, et al. Consensus on the Rational Use of Antithrombotics in Veterinary Critical Care (CURATIVE): domain 2-Defining rational therapeutic usage. J Vet Emerg Crit Care. 2019;29(1):49-59.
3. 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. 2019;29(1):60-74.
4. Sharp CR, deLaforcade AM, Koenighof AM, et al. Consensus on the Rational Use of Antithrombotics in Veterinary Critical Care (CURATIVE): domain 4-Refining and monitoring antithrombotic therapies. J Vet Emerg Crit Care. 2019;29(1):75-87.
5. Brainard BM, Buriko Y, Good J, et al. Consensus on the Rational Use of Antithrombotics in Veterinary Critical Care (CURATIVE): domain 5-Discontinuation of anticoagulant therapy in small animals. J Vet Emerg Crit Care. 2019;29(1):88-97.
6. Hidaka Y, Hagio M, Murakami T, et al. Three dogs under 2 years of age with heartworm caval syndrome. J Vet Med Sci. 2003;65(10):1147-1149.
21. Savadelis MD, Coleman AE, Rapoport GS, et al. Clinical assessment of heartworm-infected dogs treated with the slow kill method. Vet Parasitol. 2017;244:35-38.

22. Boudreaux MK, Dillon AR, Suh SI, Hyn C. Evaluation of cardiac pulmonary and inflammatory markers in dogs with heartworm infection treated using the slow kill method. Vet Parasitol. 2017;244:35-38.

23. Tariq JH, Atwell RB. The role of Dirofilaria immitis antigen in the pathogenesis of pulmonary arteritis in the dog. J Vet Med Sci. 1992;54(5):897-904.

24. Hirano Y, Kitagawa H, Sasaki Y. Relationship between pulmonary artery pressure and pulmonary thromboembolism associated with dead worms in canine heartworm disease. J Vet Med Sci. 1992;54(5):897-904.

25. Panopoulos I, Specchi S, Soubasis N, et al. Multidetector computed tomographic pulmonary angiography in a cat with fatal heartworm disease. Vet Radiol Ultrasound. 2018;59(6):E71-75.

26. McCracken MD, Patton S. Pulmonary arterial changes in feline dirofilariasis. Vet Pathol. 1993;30(1):64-69.

27. Rawlings CA. Pulmonary arteriography and hemodynamics during feline heartworm disease. J Vet Intern Med. 1990;4(6):285-291.

28. Rawlings CA, Farrell RL, Mahood RM. Morphologic changes in the lungs of cats experimentally infected with Dirofilaria immitis but lacking adult heartworms in the heart and lungs. Am J Vet Res. 2005;66(9):1544-1549.

29. Norris CR, Griffey SM, Samii VF. Pulmonary thromboembolism in cats: 29 cases (1987-1997). J Am Vet Med Assoc. 1999;215(11):1650-1654.

30. Schermerhorn T, Pemberton-Corbett JR, Kornreich B. Pulmonary thromboembolism in cats. J Vet Intern Med. 2004;18(4):533-535.

31. Akiyoshi M, Hisaue M, Neo S, Akiyoshi M. Presumptive precursors of immuno-mediated anemia concurrent with gastrointestinal lymphoma in a cat. J Vet Med Sci. 2008;62(11):1570-1576.

32. Aucoin DP, Peterson ME, Hurvitz AI, et al. Propylthiouracil-induced immune-mediated disease in the cat. J Pharmacol Exp Ther. 1985;234(1):13-18.

33. Bacek LM, Macintire DK. Treatment of primary immune-mediated hemolytic anemia with mycophenolate mofetil in two cats. J Vet Emerg Crit Care. 2011;21(1):45-49.

34. Black V, Adamants S, Barfield D, Tasker S. Feline nonregenerative immune-mediated anemia: features and outcome in 15 cases. J Feline Med Surg. 2016;18(8):597-602.

35. Bolf P, Larson C, Peda A, et al. Thoracic and paraspinal extraembryonal hematopoiesis in a cat with chronic nonregenerative anemia. J Feline Med Surg Open Rep. 2018;4(2):2055161918798868.

36. Borgeat K, Wright J, Garrod O, et al. Arterial thromboembolism in 250 cats in general practice: 2004–2012. J Vet Intern Med. 2014;28(1):102-108.

37. Cain GR, Cain JL, Turrell JM, et al. Immune-mediated hemolytic anemia and thrombocytopenia in a cat after bone marrow transplantation. Vet Pathol. 1988;25(2):161-162.

38. Ceballos-Vasquez A. Concomitant feline immunodeficiency virus (FIV) and Mycoplasma hemofelis in a barn cat. Can J Vet. 2018;59(3):307-310.

39. Četin HS, Ecki O, Kuşçukyıldız F, et al. Response to doxycycline and oxytetracycline treatments in cats infected with Mycoplasma spp. and analysis of hemato-clinical findings and risk factors. Trop Biomed. 2021;38(2):149-158.

40. Contreras ET, Giger U, Malmberg JL, et al. Bcllrlubine encephalopathy in a Domestic Shorthair Cat With Increased Osmotic Fraility and Cholangiohepatitis. Vet Pathol. 2016;53(3):629-632.

41. de Oliveira Conrado F, Stern JK, Griffin FC. What is your diagnosis? Peripheral blood smear and splenic fine-needle aspirate from a cat. J Vet Clin Pathol. 2020;49(2):367-370.

42. Dunn JK, Searcy GP, Hirsch VM. The diagnostic significance of a positive direct antiglobulin test in anemic cats. Can J Comp Med. 1984;48(4):349-353.

43. Fathi E, Atiyabi N, Yazdi HS, Nassiri SM. Immune-mediated hemolytic anemia in cats referring to Veterinary Teaching Hospital of Tehran (2006-2007). Iran J Vet Res. 2009;10(4):373-377.

44. Hickey MC, Jandrey K, Farrell KS, Carlson-Bremer D. Concurrent diseases and conditions in cats with renal infarcts. J Vet Intern Med. 2014;28(2):319-323.

45. Horek N, Mekeli ML, Gönçzi E, et al. First molecular identification of Candidatus mycoplasma hemominutum` from a cat with fatal hemolytic anemia in Hungary. Acta Vet Hung. 2008;56(4):441-450.
47. Jones DR, Darke PG. Use of papain for the detection of incomplete erythrocyte autoantibodies in autoimmune hemolytic anemia of the dog and cat. J Vet Anim Pract. 1975;16(4):273-279.

48. Jordan HL, Grindem CB, Breitschwerdt EB. Thrombocytopenia in cats: a retrospective study of 41 cases. J Vet Intern Med. 1993;7(5):261-265.

49. Klaibart S, Kelmer E, Vidmayer B, et al. Peripheral and central venous blood glucose concentrations in dogs and cats with acute arterial thromboembolism. J Vet Intern Med. 2014;28(5):1513-1519.

50. Kohn B, Weingart C, Eckmann V, et al. Primary immune-mediated hemolytic anemia in 19 cats: diagnosis, therapy, and outcome (1998-2004). J Vet Intern Med. 2006;20(1):159-166.

51. Kopke MA, G allowance PEJ. Suspected hepatopathy and pancreatitis associated with mycoplasmal mocket in use with a cat in immune-mediated hemolytic anemia. J Fel Med Surg Open Rep. 2020;6(1):2055116920905038.

52. Kopke MA, Pemberton S, Ruaux CG. Presumed immune-mediated hemolytic anemia associated with pregnancy in a cat. J Fel Med Surg Open Rep. 2019;5(1):2055116919841689.

53. Korman RM, Hetzel N, Knowles TG, et al. A retrospective study of 180 anemic cats: features, etiologies and survival data. J Feline Med Surg. 2013;15(2):81-90.

54. Laste NJ, Harpsell NK. A retrospective study of 100 cases of feline distal aortic thromboembolism: 1977–1993. J Am Anim Hosp Assoc. 1995;31(6):492-500.

55. Limlenget P, Rungpipat A, Pusoonthornthum R. Application of Flow Cytometry for Early Diagnosis and Monitoring in Cats with Immune-mediated Hemolytic Anemia. Thai J Vet Med. 2011;41(2):185-191.

56. Merten N, Weingart C, Kohn B. Causes, diagnostics and course of disease in 194 cats with anemia. Berl Munch Tierarztl Wochenschr. 2007;124(9-10):1024-1027.

57. Mischke R. Cyclosporin A therapy in a cat with pure red cell aplasia. Berl Munch Tierarztl Wochenshr. 1998;111(11-12):432-437.

58. Mosca A, Bresciani L. Life-threatening hematological complication occurring in a cat after chronic carbimazole administration. J Feline Med Surg Open Rep. 2016;2(2):2055116916668198.

59. Norsworthy GD, de Faria VP. Retrobulbar thrombus in a cat with systemic hypertension. J Feline Med Surg. 2011;13(2):144-148.

60. Peterson JL, Couto CG, Wellman ML. Hemostatic disorders in cats: a retrospective study and review of the literature. J Vet Intern Med. 1995;9(5):298-303.

61. Peterson ME, Hurvitz AI, Leib MS, et al. Propylthiouracil-associated arterial thromboembolism occurring in a cat after chronic carbimazole administration. J Feline Med Surg Open Rep. 2020;6(1):2055116920905038.

62. Peterson JL, Couto CG, Wellman ML. Hemostatic disorders in cats: 6 cases (2001-2006).

63. Rogers CL, O’T oole TE, Keating JH, et al. Portal vein thrombosis in cats: 6 cases (2001-2006).

64. Schoeman T, Lobetti RG, Jacobson LS, Penzhorn BL. Feline babesiosis in cats: acute crisis in 127 cases (1992-2001) and long-term management with low-dose aspirin in 24 cases. J Vet Intern Med. 2003;17(1):73-83.

65. Smith CE, Rozanski EA, Freeman LM, et al. Peripheral and central venous blood glucose concentrations in dogs and cats with acute arterial thromboembolism. J Vet Intern Med. 2014;28(5):1513-1519.

66. Smith CE, Rozanski EA, Freeman LM, et al. Peripheral and central venous blood glucose concentrations in dogs and cats with acute arterial thromboembolism. J Vet Intern Med. 2014;28(5):1513-1519.

67. Sun P, Jeffery U. Decreased antithrombin activity and inflammation in cats. J Feline Med Surg. 2021;23(6):498-506.

68. Swann JW, Szladovits B, Glanemann B. Demographic characteristics, survival and Prognostic Factors for Mortality in Cats with Primary Immune-Mediated Hemolytic Anemia. J Vet Intern Med. 2016;30(1):147-156.

69. Tasker S, Murray JK, Knowles TG, Day MJ. Coombs’ hemolysa and retrovirus testing in feline anemia. J Am Anim Pract. 2010;51(4):192-199.

70. Utroska B. Autoimmune hemolytic anemia in sibling cats. Vet Med Small Anim Clin. 1980;75(11):1699-1701.

71. van Geffen C. Coinfection with Mycoplasma hemofelis and Candidatus Mycoplasma hemominutum in a cat with immune-mediated hemolytic anemia in Belgium. Vlaams Diergeneeskundig Tijdschrift. 2012;81(4):224-228.

72. VanSteenhous J, Taboada J, Dorfman MI. Hemobartonella felis infection with atypical hematological abnormalities. J Am Anim Hosp Assoc. 1995;31(2):165-169.

73. Viviano KR, Webb JL. Clinical use of cyclosporine as an adjunctive therapy in the management of feline idiopathic pure red cell aplasia. J Feline Med Surg. 2011;13(12):885-895.

74. Weingart C, Tasker S, Kohn B. Infection with hemoplasma species in 22 cats with anemia. J Feline Med Surg. 2016;18(2):129-136.

75. Weiss DJ. Differentiating benign and malignant causes of lymphocytosis in feline bone marrow. J Vet Intern Med. 2005;19(6):855-859.

76. Weiss DJ. Bone marrow pathology in dogs and cats with nonregenerative immune-mediated hemolytic anemia and pure red cell aplasia. J Comp Pathol. 2008;138(1):46-53.

77. Werner LL, Gormann NT. Immune-mediated disorders of cats. Vet Clin North Am Small Anim Pract. 1984;14(5):1039-1064.

78. Zeugswetter F, Hittmair KM, de Arespacochaga AG, et al. Eosinophilic polyarthritis associated with Mycoplasma gateae in a cat. J Feline Med Surg. 2007;9(3):226-231.

79. Zini E, Hauser B, Meli ML, et al. Immune-mediated erythroid and megakaryocytic aplasia in a cat. J Vet Med Assoc. 2007;230(7):1024-1027.

80. Zoia A, Drigo M. Association Between Pancreatitis and Immune-mediated Hemolytic Anemia in Cats: a Cross-sectional Study. J Comp Pathol. 2017;156(4):384-388.

81. Bishop SA, Lucke VM, Stokes CR, TJ G-J. Plasma and urine biochemical changes in cats with experimental immune complex glomerulonephritis. J Comp Pathol. 1991;104(1):65-76.

82. Nash AS, Wright NG, Spencer AJ, et al. Membranoproliferative glomerulonephritis in 19 cats: long-term clinical follow-up. Vet Rec. 1979;105(4):71-77.

83. Asano T, Tsukamoto A, Ohno K, et al. Membranoproliferative glomerulonephritis in a young cat. J Vet Med Sci. 2008;70(12):1373-1375.

84. Backlund B, Cianciolo RE, Cook AK. Minimal change glomerulonephritis in a cat. J Feline Med Surg. 2011;13(4):291-295.

85. Benson KK, Quimby JM, Shropshire SB, et al. Evaluation of platelet function in cats with and without kidney disease: a pilot study. J Feline Med Surg. 2020, 1098612

86. Bishop SA, Stokes CR, Lucke VM. Experimental proliferative glomerulonephritis in the cat. J Comp Pathol. 1992;106(4):49-60.

87. Bown P. A case of feline membranous glomerulonephritis. Vet Rec. 1971;89(21):557-558.

88. Cianciolo RE, Bishoff K, Ebel JG, et al. Clinicopathologic, histologic, and toxicologic findings in 70 cats inadvertently exposed to pet food
contaminated with melamine and cyanuric acid. J Am Vet Med Assoc. 2008;233(5):729-737.

94. Farrow BR, Huxtable CR. Membranous nephropathy and the nephrotic syndrome in the cat. J Comp Pathol. 1971;81(4):463-467.

95. Farrow BR, Huxtable CR, McGovern VJ. Nephrotic syndrome in the cat due to diffuse membranous glomerulonephritis. Pathology (Phil). 1969;1(1):67-72.

96. Giraldi M, Paltrinieri S, Piazza C, Scarpà P. Evaluation of Urinary Big Endothelin-1 in Feline Spontaneous CKD. Animals (Basel). 2020;10(11):2144.

97. Kamiie J, Haishima A, Inoue K, et al. Progression of glomerulonephritis to end-stage kidney disease in a cat with nephrotic syndrome. J Vet Med Sci. 2011;73(1):129-132.

98. Kuwahara Y, Ohba Y, Kitoh K, et al. Association of laboratory data and death within one month in cats with chronic renal failure. J Small Anim Pract. 2006;47(8):446-450.

99. Langston C, Eatroff A, Poeppel K. Use of tissue plasminogen activator in catheters used for extracorporeal renal replacement therapy. J Vet Intern Med. 2014;28(2):270-276.

100. Mardell EJ, Sparkes AH. Evaluation of a commercial in-house test kit for the semiquantitative assessment of microalbuminuria in cats. J Feline Med Surg. 2006;8(4):269-278.

101. Nash AS, Mohammed NA, Wright NG. Experimental immune complex glomerulonephritis and the nephrotic syndrome in cats immunized with cationised bovine serum albumin. Res Vet Sci. 1990;49(3):370-372.

102. Paepe D, Ghys LF, Smets P, et al. Routine kidney variables, glomerular filtration rate and urinary cystatin C in cats with diabetes mellitus, cats with chronic kidney disease and healthy cats. J Feline Med Surg. 2015;17(10):880-888.

103. Rayhel LH, Quimby JM, Cianciolo RE, et al. Clinopathologic and pathologic characteristics of feline proteinuric kidney disease. J Feline Med Surg. 2020;22(12):1219-1229.

104. Rossi F, Aresu L, Martini V, et al. Immune-complex glomerulonephritis in cats: a retrospective study based on clinico-pathological data, histopathology and ultrastructural features. BMC Vet Res. 2019;15(1):303.

105. Slauson DO, Russell SW, Schechter RD. Naturally occurring immune-complex glomerulonephritis in the cat. J Pathol. 1971;103(2):131-133.

106. Sugahara G, Hosaka S, Minshige T, et al. Clinical and histopathological features resembling those of human focal segmental glomerulosclerosis in a cat with nonimmune-mediated glomerulonephropathy. BMC Vet Res. 2015;11:251.

107. Syme HM, Markwell PJ, Pfeiffer D, Elliott J. Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria. J Vet Intern Med. 2006;20(3):528-535.

108. White JD, Norris JM, Baral RM, Malik R. Naturally occurring chronic renal disease in Australian cats: a prospective study of 184 cases. Aust Vet J. 2006;84(6):188-194.

109. White JD, Norris JM, Bosward KL, et al. Persistent hematuria and proteinuria due to glomerular disease in related Abyssinian cats. J Feline Med Surg. 2008;10(3):219-229.

110. Whittimore JC, Miyoshi Z, Jensen WA, et al. Association of microalbuminuria and the urine albumin-to-creatinine ratio with systemic disease in cats. J Am Vet Med Assoc. 2007;230(8):1165-1169.

111. Wipke M, O’Toole TE, Taeymans O, et al. Portal vein thrombosis in 33 dogs:1998-2011. J Vet Intern Med. 2012;26(2):230-237.

112. Laurenton K, Hopper K, Herrera MA, et al. Concurrent diseases and conditions in dogs with splenic vein thrombosis. J Vet Intern Med. 2010;24:1298-1304.

113. Van Winkle TJ, Bruce E. Thrombosis of the portal vein in eleven dogs. Vet Pathol. 1993;30:28-35.

114. Hardie EM, Vaden SL, Spaulding K, et al. Splenic infarction in 16 dogs: a retrospective study. J Vet Intern Med. 1995;9(3):141-148.

115. Johnson LR, Lappin MR, Baker DC. Pulmonary thromboembolism in 28 dogs: 1985-1995. J Vet Intern Med. 1999;13(4):338-345.
138. Yamada S, Hirao D, Miura N, et al. Comparison between blood coagulability in the intra-atrial and peripheral regions during the acute phase after rapid atrial pacing. Exp Anim. 2019;68(2):137-146.

139. Yamada S, Hirao D, Miura N, et al. Comparison of chronological changes in blood characteristics in the atrium and peripheral vessels after the development of nonvalvular atrial fibrillation. Thromb Res. 2018;171:31-37.

140. Louie EK, Liu D, Reynertson SI, et al. Stunning of the left atrium after spontaneous conversion of atrial fibrillation to sinus rhythm: demonstration by transesophageal Doppler techniques in a canine model. J Am Col Cardiol. 2018;32(7):2081-2086.

141. Cardin S, Libby E, Pelletier P, et al. Contrasting gene expression profiles in two canine models of atrial fibrillation. Circ Res. 2007;100(3):425-433.

142. Choi JI, Jung JS, Kim MK, Sim J, et al. Effects of angiotensin-II receptor blocker on inhibition of thrombogenicity in a canine atrial fibrillation model. Kor Circ J. 2016;46(3):335-342.

143. Nishida K, Chiba K, Iwasaki YK, Katsouras G, et al. Atrial fibrillation-associated remodeling does not promote atrial thrombus formation in canine models. Circ Arhyth Electrophys. 2012;5(6):1168-1175.

144. Usechak PJ, Bright JM, Day TK. Thrombotic complications associated with atrial fibrillation in three dogs. J Vet Cardiol. 2012;14(3):453-458.

145. Brownlie SE, Cobb MA. Observations on the development of congestive heart failure in Irish wolfhounds with dilated cardiomyopathy. J Sm Anim Pract. 1999;40(8):371-377.

146. Bauer N, Moritz A. Characterization of changes in the hemostasis system in dogs with thrombosis. J Sm Anim Pract. 2013;54(3):129-136.

147. Boswood A, Lamb CR, White RN. Aortic and iliac thrombosis in six dogs. J Sm Anim Pract. 2000;41(3):109-114.

148. Chow B, French A. Conversion of atrial fibrillation after levothyroxine therapy in dogs with thrombosis. J Vet Med Assoc. 2018;25(9):1025-1034.

149. Duesberg CA, Nelson RW, Feldman EC, Vaden SL, Scott-Moncrieff J. Adrenalectomy for treatment of hyperadrenocorticism in cats: 10 cases (1988-1992). J Am Vet Med Assoc. 1995;207(8):1066-1070.

150. Adams DJ, Demchur JA, Aronson LR. Renal cell carcinoma in a cat with polycystic kidney disease undergoing renal transplantation. J Feline Med Surg Open Rep. 2018;4(1):2055116918766152.

151. Klainbart S, Agi L, Bdolah-Abraham T, Kelmer E, Aroch I. Clinical, laboratory, and hemostatic findings in cats with naturally occurring sepsis. J Am Vet Med Assoc. 2017;251(9):1025-1034.

152. Dandrieux JR, Noble PJ, Scase TJ, et al. Comparison of a chlorambucil-prednisolone combination for treatment of chronic enteropathy with concurrent protein-losing enteropathy in dogs: 27 cases (2007-2010). J Am Vet Med Assoc. 2013;242(12):1705-1714.

153. Dixon A, Hall EJ, Adamantos S, et al. Hypercoagulability in dogs with chronic enteropathy and association with serum albumin concentration. J Vet Intern Med. 2021;35(2):860-866.

154. Engelmann N, Ondreka N, von Pückler K, et al. Applicability of (99m) Tc-Labeled Human Serum Albumin Scintigraphy in Dogs With Protein-Losing Enteropathy. J Vet Intern Med. 2017;31(2):365-370.

155. Finco DR, Duncan JR, Schall WD, et al. Chronic enteric disease and hypoproteinemia in 9 dogs. J Am Vet Med Assoc. 1973;163(3):262-271.

156. Fossum TW, Sherding RG, Zack PM, et al. Intestinal lymphangiectasia associated with chylothorax in two dogs. J Am Vet Med Assoc. 2008;49(4):178-184.

157. Garcia-Sancho M, Sainz A, Rodríguez-Franco F, et al. Pulmonary thromboembolism in a dog with inflammatory bowel disease. Revista Complutense de Ciencias Veterinarias. 2010(4):78-86.

158. 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.

159. Goodwin LV, Goggs R, Chan DL, Allen'spach K. Hypercoagulability in dogs with protein-losing enteropathy. J Vet Intern Med. 2011;25(2):273-277.

160. Jacinto AML, Ridyard AE, Aroch I, et al. Thromboembolism in Dogs with Protein-Losing Enteroportal with Non-Neoplastic Chronic Small Intestinal Disease. J Am Anim Hosp Assoc. 2017;53(3):185-192.

161. Kimmel SE, Waddell LS, Michel KE. Hypomagnesemia and hypocalcemia associated with protein-losing enteropathy in Yorkshire terriers: five cases (1992-1998). J Am Vet Med Assoc. 2000;217(5):703-706.

162. Landsverk T, Gamlem H. Intestinal lymphangiectasia in the Lunde-hund. Scanning electron microscopy of intestinal mucosa. Acta Pathol Microbiol Immunol Scand A. 1984;92(5):353-362.
219. Milstein M, Sanford SE. Intestinal lymphangiectasia in a dog. Can Vet J. 1977;18(5):127-130.
220. Moon ML, Biller DS, Armbrust LJ. Ultrasonographic appearance and etiology of corrugated small intestine. Vet Radiol Ultrasound. 2003;44(2):199-203.
221. Moser K, Mitze S, Teske E, et al. Correlation of clinical, diagnostic, and histopathological parameters in dogs with chronic lymphocytic-plasmacytic enteropathy. Tierarztl Prax Ausg K Kleintiere Heimtiere. 2018;46(1):15-20.
222. Münster M, Hörnau A, Bilzer T. Assessment of disease severity and outcome of dietary, antibiotic, and immunosuppressive interventions by use of the canine IBD activity index in 21 dogs with chronic inflammatory bowel disease. Berl Munch Tierarztl Wochenschr. 2006;119(11-12):493-505.
223. Münster M, Suchodolks JS, Bilzer T, et al. Influence of physiological disturbances on treatment success of dietary therapy in dogs with chronic enteropathies. Berl Munch Tierarztl Wochenschr. 2010;123(1-2):74-82.
224. Nagata N, Ohta H, Yokoyama N, et al. Clinical characteristics of dogs with food-responsive protein-losing enteropathy. J Vet Intern Med. 2020;34(2):659-668.
225. Nakashima K, Hiyoshi S, Ohno K, et al. Prognostic factors in dogs with protein-losing enteropathy. Vet J. 2015;205(1):28-32.
226. Ohno K, Konishi S, Kobayashi S, et al. Prognostic factors associated with survival in dogs with lymphocytic-plasmacytic enteritis. J Vet Med Sci. 2006;68(9):929-933.
227. Ohta H, Nagata N, Yokoyama N, et al. Prognostic value of small intestinal dilatation in dogs with protein-losing enteropathy. J Vet Med Sci. 2021;83(3):378-384.
228. Okanishi H, Yoshioka R, Kagawa Y, Watarai T. The clinical efficacy of dietary fat restriction in treatment of dogs with intestinal lymphangiectasia. J Vet Intern Med. 2014;28(3):809-817.
229. Olson NC, Zimmer JF. Protein-losing enteropathy secondary to intestinal lymphangiectasia in a dog. J Am Vet Med Assoc. 1978;173(3):271-274.
230. Palmer KG, King LG, Van Winkle TJ. Clinical manifestations and associated disease syndromes in dogs with cranial vena cava thrombosis: 17 cases (1989-1996). J Am Vet Med Assoc. 1998;213(2):220-224.
231. Ramsey CC, Burney DP, Macintire DK, Finn-Bodner S. Use of streptokinase in four dogs with thrombosis. J Am Vet Med Assoc. 1996;209(4):780-785.
232. Rodríguez-Alarcón CA, Beristain-Ruiz DM, Pérez-Casio F, et al. Protein-losing enteropathy in a dog with lymphangiectasia, lymphoplasmacytic enteritis and pancreatic exocrine insufficiency. Vet Q. 2012;32(3-4):193-197.
233. Rossi G, Cerquetella M, Antonelli E, et al. The importance of histologic parameters of lacteal involvement in cases of canine lymphoplasmacytic enteritis. Gastroenterol Hepatol Bed Bench. 2015;8(1):33-41.
234. Salavati Schmitz S, Gow A, Bommer N, et al. Diagnostic features, treatment, and outcome of dogs with inflammatory protein-losing enteropathy. J Vet Intern Med. 2019;33(5):2005-2013.
235. Schwartz-Porsche DM, Kasbohm C, Scholz A. [Enteral protein-losing syndrome in a dog]. Zentralbl Veterinarmed A. 1970;17(8):665-684.
236. Sobel KE, Williams JE. Pneumothorax secondary to pulmonary thromboembolism in a dog. J Vet Emerg Crit Care. 2009;19(1):120-126.
237. Sugita K, Shima A, Takahashi K, et al. Successful outcome after a single endoscopic fecal microbiota transplantation in a Shiba dog with nonresponsive enteropathy during the treatment with chlorambucil. J Vet Med Sci. 2021;83(6):984-989.
238. Thawley VJ, Sanchez MD, Drobotz KJ, King LG. Retrospective comparison of thromboelastography results to postmortem evidence of thrombosis in critically ill dogs: 39 cases (2005-2010). J Vet Emerg Crit Care. 2016;26(3):428-436.
239. Van Kroonenburg HJ, Lees GE, Hayden DW, et al. Lipogranulomatous lymphangitis in canine intestinal lymphangiectasia. Vet Pathol. 1984;21(4):377-383.
240. Volkmann M, Steiner JM, Fosgate GT, et al. Chronic Diarrhea in Dogs - Retrospective Study in 136 Cases. J Vet Intern Med. 2017;31(4):1043-1055.
241. Watson VE, Hobday MM, Durham AC. Focal intestinal lipogranulomatous lymphangitis in 6 dogs (2008-2011). J Vet Intern Med. 2014;28(1):48-51.
242. Willard MD, Zenger E, Mansell JL. Protein-losing enteropathy associated with cystic mucoid changes in the intestinal crypts of two dogs. J Am Anim Hosp Assoc. 2003;39(2):187-191.
243. Winter RL, Sedacca CD, Adams A, Orton EC. Aortic thrombosis in dogs: presentation, therapy, and outcome in 26 cases. J Vet Cardiol. 2012(14):333-342.
244. Yang VK, Cunningham SM, Rush JE, de Laforcade A. The use of rivaroxaban for the treatment of thrombotic complications in four dogs. J Vet Emerg Crit Care. 2016;26(5):729-736.
245. Yuki M, Sugimoto N, Takahashi K, et al. A case of protein-losing enteropathy treated with methrotexate in a dog. J Vet Med Sci. 2006;68(4):397-399.
246. Baez JL, Hendrick MJ, Walker LM, Washabau RJ. Radiographic, ultrasonographic, and endoscopic findings in cats with inflammatory bowel disease of the stomach and small intestine: 33 cases (1990-1997). J Am Vet Med Assoc. 1999;215(3):349-354.
247. Bailey S, Benigni L, Eastwood J, et al. Comparisons between cats with normal and increased fPLI concentrations in cats diagnosed with inflammatory bowel disease. J Small Anim Pract. 2010;51(9):484-489.
248. Burke KF, Broussard JD, Ruaux CG, et al. Evaluation of fecal α1-proteinase inhibitor concentrations in cats with idiopathic inflammatory bowel disease and cats with gastrointestinal neoplasia. Vet J. 2013;196(2):189-196.
249. Moon ML, Biller DS, Armbrust LJ. Ultrasonographic appearance and etiology of corrugated small intestine. Vet Radiol Ultrasound. 2003;44(2):199-203.
250. Center SA, Warner K, Corbett J, et al. Proteins invoked by vitamin K absence and clotting times in clinically ill cats. J Vet Intern Med. 2000;14(3):292-297.
251. Brown AL, Beatty JA, Lindsay SA, Barrs VR. Severe systemic hyper-tension in a cat with pituitary-dependent hyperadrenocorticism. J Sm Anim Pract. 2012;53(2):132-135.
252. Calsyn JD, Green RA, Davis GJ, Reilly CM. Adrenal pheochromocytoma with contralateral adrenocortical adenoma in a cat. J Am Anim Hosp Assoc. 2010;46(1):36-42.
253. Fracassi F, Mandrioli L, Diana A, Hilbe M, Grinwis G, Gandini G. Pituitary macroadenoma in a cat with diabetes mellitus, hypercortisolism and neurological signs. J Vet Med A Physiol Pathol Clin Med. 2007;54(7):359-363.
254. Guerios SD, Souza CHM, Bacon NJ. Adrenocortical tumor in a cat secreting more than one type of corticosteroid. J Fel Med Surg Open Rep. 2015;1(2):2055116915617970.
255. Immink WF, van Toor AJ, Vos JH, van der Linde-Sipman JS, Luibekker AA. Hyperadrenocorticism in four cats. Vet Q. 1992;14(3):81-85.
256. Lien YH, Huang HP, Chang PH. Iatrogenic hyperadrenocorticism in 12 cats. J Am Anim Hosp Assoc. 2006;42(6):414-423.
257. Mellett Keith AM, Bruyette D, Stanley S. Trilostane therapy for treatment of spontaneous hyperadrenocorticism in cats: 15 cases (2004-2012). J Vet Intern Med. 2013;27(6):1471-1477.
258. Moore LE, Biller DS, Olsen DE. Hyperadrenocorticism treated with metyrapone followed by bilateral adrenalectomy in a cat. J Am Vet Med Assoc. 2000;217(5):691-694, 673.
259. Neiger R, Witt AL, Noble A, et al. Trilostane therapy for treatment of pituitary-dependent hyperadrenocorticism in 5 cats. J Vet Intern Med. 2004;18(2):160-164.
260. Nelson RW, Feldman EC, Smith MC. Hyperadrenocorticism in cats: seven cases (1978-1987). J Am Vet Med Assoc. 1988;193(2):245-250.

261. Rossmeisl JH Jr, Scott-Moncrieff J, Siems J, et al. Hyperadrenocorticism and hyperprogesteronemia in a cat with an adenocortical adenocarcinoma. J Am Anim Hosp Assoc. 2000;36(6):512-517.

262. Skelly BJ, Petrus D, Nicholls PK. Use of triostanol for the treatment of pituitary-dependent hyperadrenocorticism in a cat. J Small Anim Pract. 2003;44(6):269-272.

263. Sohn J, Gruber T. Retrospective Study on the Effects of Long-Term Use of Methylprednisolone Acetate on the Blood Work of 25 Cats. J Am Anim Hosp Assoc. 2019;55(1):23-28.

264. Valentin SY, Cortright CC, Nelson RW, et al. Clinical findings, diagnostic test results, and treatment outcome in cats with spontaneous hyperadrenocorticism: 30 cases. J Vet Intern Med. 2014;28(2):481-487.

265. Watson PJ, Herrtage ME. Hyperadrenocorticism in six cats. J Small Anim Pract. 1998;39(4):175-184.

266. Zerbe CA, Nachreiner RF, Dunstan RW, et al. Hyperadrenocorticism in a cat. J Am Vet Med Assoc. 1987;190(5):559-563.

267. Schoeman JP. Feline Distal Aortic Thromboembolism: a Review of 44 Cases (1990–1998). J Fel Med Surg. 1999;1(4):221-231.

268. Gadzinska J, Leigh H, Parys M, et al. Vascular ultrasonographic findings in canine patients with clinically diagnosed phlebitis. Vet Radiol Ultra. 2019;60(6):745-752.

269. Bowor M, Crowley JG. Evaluation of central venous catheter thrombogenicity. Acta Anesthesiol Scand Suppl. 1985;29:59-64.

270. Dennis MB, Graham TC, Raff RF, et al. Implanted right atrial catheters for continuous infusion of solutions into dogs. J Invest Surg. 1993;6(5):461-467.

271. Litjert J, Mowat V. Common vascular changes in the jugular vein of saline controls in continuous infusion studies in the Beagle dog. Toxicol Pathol. 2004;32(6):694-700.

272. Wang LH, Wei F, Jia L, et al. Fibrin sheath formation and intimal thickening after catheter placement in dog model: role of hemodynamic wall shear stress. J Vasc Access. 2015;16(4):275-284.

273. Abrams-Ogg AC, Kruth SA, Carter RF, et al. The use of an implantable central venous (Hickman) catheter for long-term venous access in dogs undergoing bone marrow transplantation. Canad J Vet Res. 1992;56(4):382.

274. de Nies KS, Kruitwagen HS, van Straten G, et al. Innovative applications of an implantable venous access system in the portal vein: technique, the results and complications in three dogs. BMC Vet Res. 2019;15(1):1-8.

275. Gutowska A, Bae YH, Jacobs H, et al. Heparin release from thrombor sensitive polymer coatings: in vivo studies. J Biomed Mat Res. 1995;29(7):811-821.

276. Heyman PW, Cho CS, McRea JC, et al. Heparinized polyurethanes: in vitro and in vivo studies. J Biomed Mat Res. 1985;19(4):419-436.

277. Jacobsson B, Bergentz SE, Ljungqvist U. Platelet adhesion and thrombogenicity in vivo with indium-labeled platelets. J Biomed Mat Res. 1985;19(2):99-113.

278. Keogh JR, Wolf MF, Overend ME, et al. Biocompatibility of sulphonated polyurethane surfaces. Biomaterials. 1996;17(20):1987-1994.

279. Leach KR, Kurisu Y, Carlson JE, et al. Thrombogenicity of hydrophilically coated guide wires and catheters. Radiol. 1990;175(3):675-677.

280. Lewis J, Sweeney J, Baldini L, et al. Assessment of thromboreistance of intravenous cannulae by 125I-fibrinogen scanning. J Biomed Mat Res. 1985;19(2):99-113.

281. Libsack CV, Kollmeyer KR. Role of catheter surface morphology on intravascular thrombosis of plastic catheters. J Biomed Mat Res. 1979;13(3):459-466.

282. Lipton MJ, Doherty PW, Goodwin DA, et al. Evaluation of catheter thrombogenicity in vivo with indium-labeled platelets. Radiol. 1980;135(1):191-194.

283. Ngad MS, Klaper MA, Steggerda FR, et al. Clotting on the outer surfaces of vascular catheters. Radiol. 1968;91(2):248-250.

284. O’Connell JP, Dunn TS, Rumaks A, Williams JL. Detection of thrombus formation on intravascular catheters using 125I-fibrinogen. Thromb Res. 1981;21(1-2):111-120.

285. Sawyer PN, Ramsey W, Stanczewski B, et al. A comparative study of several polymers for use as intravascular catheters. Med Instrum. 1977;11(4):221-230.

286. Smith RS, Zhang Z, Bouchard M, et al. Vascular catheters with a noncoating poly-sulfo Betaine surface modification reduce thrombus formation and microbial attachment. Sci Transl Med. 2012;4(153):153ra132-153ra132.

287. Ueda Y, Odunayo A, Mann FA. Comparison of heparinized saline and 0.9% sodium chloride for maintaining peripheral intravenous catheter patency in dogs. J Vet Emerg Crit Care. 2013;23(5):517-522.

288. Welch GW, McKeel Jr DW, Silverstein P, et al. The role of catheter composition in the development of thrombophlebitis. Surg Gynecol Obstet. 1974;138(3):421-424.

289. Vos J, Odunayo A, Price J, et al. Comparison of heparinized saline and 0.9% sodium chloride for maintaining central venous catheter patency in healthy dogs. Peer J. 2019;7:e7072.

290. Wigness BD, Dorman FD, Rohde TD, et al. In vitro and in vivo testing of a new valved intravascular catheter design. ASAIO Trans. 1990;36(3):M355-358.

291. Mesfin GM, Higgins MJ, Brown WP, et al. Cardiovascular complications of chronic catheterization of the jugular vein in the dog. Vet Pathol. 1998;25(6):492-502.

292. Morris M, Phares K, Zaccardelli D, et al. A novel catheter system for totally implantable intravenous drug therapy: assessment of catheter function and patency with trepostinil therapy. J Vascular Access. 2008;9(1):20-27.

293. Adamamatos S, Brodbelt D, Moores AL. Prospective evaluation of complications associated with jugular venous catheter use in a veterinary hospital. J Sm Anim Pract. 2010;51(5):254-257.

294. Goodger WJ. Intravenous catheter placement for fluid therapy and for central venous pressure measurements in small animals. J Am Vet Med Assoc. 1973;162(2):121-122.

295. Otto CM, Rieser TM, Brooks MB, et al. Evidence of hypercoagulability in dogs with parvoviral enteritis. J Am Vet Med Assoc. 2000;217(10):1500-1504.

296. Song J, Drobatz KJ, Silverstein DC. Retrospective evaluation of shortened prothrombin time or activated partial thromboplastin time for the diagnosis of hypercoagulability in dogs: 25 cases (2006–2011). J Vet Emerg Crit Care. 2016;26(3):398-405.

297. Bliss SP, Bliss SK, Harvey HJ. Use of recombinant tissue-plasminogen activator in a dog with chylothorax secondary to catheter-associated thrombosis of the cranial vena cava. J Am Anim Hosp Assoc. 2002;38(5):431-435.

298. Bunch SE, Metcalf MR, Crane SW, et al. Idiopathic pleural effusion and pulmonary thromboembolism in a dog with autoimmune hemolytic anemia. J of the Am Vet Med Assoc. 1989;195(12):1748-1753.

299. Peterson SL. Postcaval thrombosis and delayed shunt migration after pleuro-peritoneal venous shunting for concurrent chylothorax and chylous ascites in a dog. Vet Surg. 1996;25(3):228-230.

300. Langston CE, Eatooff AE. Hemodialysis catheter-associated fibrin sheath in a dog. J Vet Emerg Crit Care. 2018;28(4):366-371.

301. Blaiset MA, Couto CG, Evans KL, et al. Complications of indwelling, silastic central venous access catheters in dogs and cats. J Am Anim Hosp Assoc. 1995;31(5):379-384.

302. Krichef II, Zucker MB, Tschopp TB, et al. Inhibition of thrombosis on vascular catheters in cats. Radiol. 1973;106(1):49-51.
304. Farrow HA, Rand JS, Burgess DM, et al. Jugular vascular access port implantation for frequent, long-term blood sampling in cats: methodology, assessment, and comparison with jugular catheters. Res Vet Sci. 2013;95(2):681-686.

305. Killingsworth CR, Weiss DJ, Eyster GE, et al. Screening coagulation tests in the cat: reference values based on direct venipuncture and catheterized samples. Vet Clin Path. 1985;14(3):19-23.

306. Albarellos GA, Bonafine RR, Kreil VE, et al. A nonsurgical jugular catheterization technique for multiple blood sampling in cats. Lab Anim. 2003;37(3):188-192. Jul 1.

307. Wasklags J, Schoeffler GL, Russell DS, et al. Extravasation injury associated with parenteral nutrition in a cat with presumptive gastroliths. J Vet Emerg Crit Care. 2011;21(4):375-381.

308. Hagley MJ, Hopper K, Epstein SE. Characteristics of arterial catheter use and related complications in dogs and cats in an intensive care unit. J Vet Emerg Crit Care. 2021;31(4):469-475.

309. Trim CM, Hofmeister EH, Quandt JE, et al. A survey of the use of arterial catheters in anesthetized dogs and cats: 267 cases. J Vet Emerg Crit Care. 2017;27(1):89-95.

310. Sasaki K, Shiga T, Gomez de Segura IA. Advantages of a novel device for arterial catheter securement in anesthetized dogs: a pilot randomized clinical trial. Front Vet Sci. 2019;6:171.

311. Sasaki K, Paredes GP, Shiga T. Heparinized saline solution vs. saline solution (0.9% Sodium Chloride) for the maintenance of dorsal pedal arterial catheter patency in dogs undergoing general anesthesia: a Pilot Study. Front Vet Sci. 2020;7:428.

312. Mooshanian S, Deitschel SJ, Haggy JM, et al. Incidence of arterial catheter complications: a retrospective study of 35 cats (2010-2014). J Fel Med Surg. 2019;21(2):173-177.

313. Bowit KL, Bortolami E, Harley R, et al. Ischemic distal limb necrosis and Klebsiella pneumoniae infection associated with arterial catheterisation in a cat. J Fel Med Surg. 2013;15(12):1165-1168.

314. Mayer MN, Grier CK, Yoshikawa H, et al. Complications associated with the use of vascular access ports in dogs receiving external beam radiation therapy. J Am Vet Med Assoc. 2008;233:96-103.

315. Cahalane AK, Rassnick KM, Flanders JA. Use of vascular access ports in femoral veins of dogs and cats with cancer. J Am Vet Med Assoc. 2007;231:1354-1360.

316. Valentini F, Fassone F, Pozzebon A, et al. Use of totally implantable vascular access port with mini-invasive Seldinger technique in 12 dogs undergoing chemotherapy. Res Vet Sci. 2013;94:152-157.

317. Culp WTN, Mayhew PD, Reese MS, et al. Complications associated with use of subcutaneous vascular access ports in cats and dogs undergoing fractionated radiotherapy: 172 cases (1996-2007). J Am Vet Med Assoc. 2010;236:1322-1327.

318. Aurbt I, Abrams-Ogg ACG, Sylvestre AM, et al. The use of vascular access ports for blood collection in feline blood donors. Can Vet J. 2011;75:25-34.

319. Morrison JA, Lauer SK, Baldwin CJ, et al. Evaluation of the use of subcutaneous implantable vascular access ports in feline blood donors. J Am Vet Med Assoc. 2007;230:885-861.

320. Henry CJ, Russell LE, Tyler JW, et al. Comparison of hematologic and biochemical values for blood samples obtained via jugular venipuncture and via vascular access ports in cats. J Am Vet Med Assoc. 2002;224(4):482-485.

321. Gawaz MP, Mujais SK, Schmidt B, et al. Platelet-leukocyte aggregates during hemodialysis: effect of membrane type. Artif Org. 1999;23(1):29-36.

322. Dewanee MK, Kapadavijwala M, Sanchez A, et al. Wuantitation of comparative thrombogenicity of dog, pig, and human platelets in a hemodialyzer. ASAIO J. 1992;38(2):88-90.

323. Gorbet MB, Sefton MV. Leukocyte activation and leukocyte procoagulant activities after blood contact with polystyrene and polyethylene glycol-immobilized polystyrene beads. J Lab Clin Med. 2001;137(5):345-355.

324. Franey T, Schweighauser A. Membrane-based therapeutic plasma exchange in dogs: prescription, anticoagulation, and metabolic response. J Vet Intern Med. 2019;33(4):1635-1645.

325. Franey T, Etter M, Schweighauser A. Evaluation of membrane-based therapeutic plasma exchange as adjunctive treatment for immune-mediated hematologic disorders in dogs. J Vet Intern Med. 2021;35(2):925-935.

326. Kopecky L, Palm CA, Naylor S, et al. Application of therapeutic plasma exchange in dogs with immune-mediated thrombocytopenia. J Vet Intern Med. 2020;24:1576-1581.

327. Franey T, Schweighauser A. Regional citrate anticoagulation for intermittent hemodialysis in dogs. J Vet Emerg Crit Care. 2017;32(1):147-156.

328. Teichmann-Knorrn S, Doerfelt S, et al. Retrospective evaluation of the use of hemodialysis in dogs with suspected metaldehyde poisoning (2012-2017): 11 cases. J Vet Emerg Crit Care. 2020;30(2):194-201.

329. Sekiguchi T, Vigan A, Ripoli A, et al. Clinical application of apheresis in very small dogs weighing <8 kg to pediatric patients. Ther Apher Dial. 2019;24(3):333-342.

330. Goudie MJ, Brainard BM, Schmidct CW, Handa H. Characterization of the use of citrate anticoagulation in dogs undergoing hemodialysis: a single center experience. J Vet Emerg Crit Care. 2020;30(2):194-201.

331. Lozada Miranda B, Walton R, Levine DN, et al. Use of rivaroxaban for treatment of cranial venous thromboembolism in three cats. J Vet Emerg Crit Care. 2017;27(1):25-34.

332. LeBlanc NL, Agarwal D, Menzen E, et al. Prevalence of major complications and procedural mortality in 336 dogs undergoing interventional cardiology procedures in a single academic center. J Vet Cardiol. 2019;23:45-57.

333. Garcia-Guasch L, Sa Borges C, Sousa P, et al. Identification and management of a subacute right ventricular perforation by an active-fixation permanent pacemaker lead in a dog. J Vet Cardiol. 2019;22:113-120.

334. Karlin ET, Rush JE, Nobrega EA. Synchronous diaphragmatic contraction associated with dual-chamber venous pacing in a dog. J Vet Cardiol. 2019;22:106-112.

335. Ward J, McLaughlin A, Burtsett R, et al. The effect of a surgical safety checklist on complication rates associated with permanent transvenous pacemaker implantation in dogs. J Vet Cardiol. 2019;22:72-83.

336. Swanson LE, Huibregtse BA, Scansen BA. A retrospective review of 146 active and passive fixation bradyarrhythmia implantations in 74 dogs undergoing pacemaker implantation in a research setting of short-term duration. BMC Vet Res. 2018;14(1):112.

337. Oyama MA, Hezzell MJ, Laughlin DS, et al. Anodal stimulation in two dogs with high-grade atrioventricular block performed during versus after normal business hours. J Vet Emerg Crit Care. 2016;18(4):398-404.

338. Djani DM, Coleman AE, Rapoport GS, et al. Congestive heart failure caused by transvenous pacemaker lead prolapse and associated right ventricular outflow tract obstruction in a dog. J Vet Cardiol. 2016;18(4):391-397.

339. st KE, Lebom BK. Long-term management of atrial myopathy in two dogs with single chamber permanent transvenous pacemakers. J Vet Cardiol. 2016;18(4):391-397.

340. Gunther-Harrington CT, Michel AO, et al. Acquired tricuspid valve stenosis due to intentionally redundant transvenous lead placement for VDD pacing in two small dogs. J Vet Cardiol. 2015;17(4):298-303.

341. Ward JL, DeFrancesco TC, Tou SP, et al. Complication rates associated with transvenous pacemaker implantation in dogs with high-grade atrioventricular block performed during versus after normal business hours. J Vet Emerg Crit Care. 2015;29(1):157-163.

342. LeBlanc N, Scollan K, Sisson D. Transvenous extraction of an abandoned endocardial pacemaker lead in a dog. J Vet Cardiol. 2014;16(1):51-57.
343. Burrage H. Sick sinus syndrome in a dog: treatment with dual-chambered pacemaker implantation. Can Vet J. 2012;53(5):565-568.
344. Mulz JM, Kraus MS, Thompson M, et al. Cranial vena caval syndrome secondary to central venous obstruction associated with a pacemaker lead in a dog. J Vet Cardiol. 2010;12(3):217-223.
345. Murray JD, O'Sullivan ML, Hawkes KC. Cranial vena caval thrombosis associated with endocardial pacing leads in three dogs. J Am Anim Hosp Assoc. 2010;46(3):186-192.
346. Stauthammer C, Tobias A, France M, et al. Caudal vena cava obstruction caused by redundant pacemaker lead in a dog. J Vet Cardiol. 2009;11(2):141-145.
347. Van De Wiele CM, Hogan DF. Cranial vena caval syndrome secondary to transvenous pacemaker implantation in two dogs. J Vet Cardiol. 2008;10(2):155-161.
348. Connolly DJ, Neiger-Aeschbacher G, Brockman DJ. Tricuspid valve stenosis caused by fibrous adhesions to an endocardial pacemaker lead in a dog. J Vet Cardiol. 2007;9(2):123-128.
349. Cunningham SM, Rush JE. Transvenous pacemaker placement in a dog with atrioventricular block and persistent left cranial vena cava. J Vet Cardiol. 2007;9(2):129.
350. Johnson MS, Martin MW, Henley W. The resultsof pacemaker implantation in 104 dogs. J Small Anim Pract. 2007;48(1):4-11.
351. Wess G, Thomas WP, Berger DM, et al. Applications, complications, and outcomes of transvenous pacemaker implantation in 105 dogs (1997-2002). J Vet Intern Med. 2006;20(4):877-884.
352. Domenecq O, Santilli R, Pradelli D, et al. The implantation of a permanent transvenous endocardial pacemaker in 42 dogs: a retrospective study. Med Sci Monit. 2005;11(6):BR168-75.
353. Kobayashi M, Hoshi K, Hirao H, et al. Implantation of permanent transvenous endocardial pacemaker in a dog with atrioventricular block. J Vet Med Sci. 2003;65(10):1101-1134.
354. Miura N, Fujiki M, Misumi K, et al. Successful use of an acceleration rate response pacemaker with a transvenous steroid-eluting screw-in lead for third-degree atrioventricular block in a labrador retriever. J Vet Med Sci. 2003;65(10):1101-1105.
355. Oyama MA, Sisson DD, Lehmkuhl LB. Practices and outcome of artificial cardiac pacing in 154 dogs. J Vet Intern Med. 2001;15(3):229-239.
356. Moneva-Jordan A, Corcoran BM, French A, et al. Sick sinus syndrome in nine West Highland white terriers. Vet Rec. 2001;148(5):142-147.
357. Noszczyk-Nowak A, Michalek M, Kapturska K, Janiszewski A, Paslawski R, Skrzypczak P, et al. Retrospective Analysis of Indications and Complications Related to Implantation of Permanent Pacemaker: 25 Years of Experience in 31 Dogs. J Vet Res. 2019;63(1):133-140.
358. Genovese DW, Estrada AH, Maisenbacher HW, et al. Procedure times, complication rates, and survival times associated with single-chamber versus dual-chamber pacemaker implantation in dogs with clinical signs of bradyarrhythmia: 54 cases (2004-2009). J Am Vet Med Assoc. 2013;242(2):230-236.
359. Wesselowski S, Cusack K, Gordon SG, et al. Artificial cardiac pacemaker placement in dogs with a cohort of myocarditis suspects and association of ultra-sensitive cardiac troponin I with survival. J Vet Cardiol. 2019;22:84-95.
360. Hildebrandt N, Stertmann WA, Wehner M, et al. Dual chamber pacemaker implantation in dogs with atrioventricular block. J Vet Intern Med. 2009;23(1):31-38.
361. Stokes K, Anderson J, McVenes R, et al. The encapsulation of polyurethane-insulated transvenous cardiac pacemaker leads. Cardiovasc Pathol. 1995;4(3):163-171.
362. Cunningham SM, Ames MK, Rush JE, et al. Successful treatment of pacemaker-induced stricture and thrombosis of the cranial vena cava in two dogs by use of anticoagulants and balloon venoplasty. J Am Vet Med Assoc. 2009;235(12):1467-1473.
363. Sisson D, Thomas WP, Woodfield J, et al. Permanent transvenous pacemaker implantation in forty dogs. J Vet Intern Med. 1991;5(6):322-331.
364. Ciavarella A, Nimmo J, Hambrok L. Pacemaker lead perforation of the right ventricle associated with Moraxella phenylpyruvica infection in a dog. Aust Vet J. 2016;94(4):101-106.
365. Darke PG, McAreavey D, Been M. Transvenous cardiac pacing in 19 dogs and one cat. J Small Anim Pract. 1989;30(9):491-499.
366. Fox PR, Moise NS, Woodfield JA, et al. Techniques and complications of pacemaker implantation in four cats. J Am Vet Med Assoc. 1991;199(12):1742-1753.
367. Stamoulis ME, Bond BR, Fox PR. Permanent pacemaker implantation for treatment of symptomatic bradycardia in two cats. J Vet Emerg Crit Care. 1992;2(2):67-72.
368. Forterre S, Nurnberg JH, Forterre F, et al. Transvenous demand pacemaker treatment for intermittent complete heart block in a cat. J Vet Cardiol. 2001;3(2):21-26.
369. Ferasin L, van de Stad M, Rudorf H, et al. Syncope associated with paroxysmal atrioventricular block and ventricular standstill in a cat. J Small Anim Pract. 2002;43(3):124-128.

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How to cite this article: deLaforcade A, Bacek L, Boyd C, et al. 2022 Update of the Consensus on the Rational Use of Antithrombotics and Thrombolytics in Veterinary Critical Care (CURATIVE) Domain 1- Defining populations at risk. J Vet Emerg Crit Care. 2022;32:289–314 https://doi.org/10.1111/vec.13204.