Hypertension

Systemic hypertension (2022)

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Introduction

Systemic hypertension could be associated with environmental or situational stressors, occur secondary to other diseases or drugs (secondary hypertension) or to other unidentified potential causes (idiopathic hypertension). Secondary hypertension has been associated in dogs and cats with many different clinical situations such as kidney disease, hyperadrenocorticism (including use of glucocorticoids), hyperthyroidism, hypothyroidism, diabetes mellitus, obesity, pheochromocytoma or primary hyperaldosteronism. Idiopathic hypertension is more frequent in older cats (12.7% prevalence in apparently healthy cats ≥10 years of age; see Jepson et al., 2009) but it has also been described in dogs.

Target-organ damage to the kidney

Systemic hypertension is of concern because a chronically sustained increase in blood pressure produces injury to the kidneys, eyes, brain, and cardiovascular system. The rationale for treating hypertension in dogs and cats is to minimize or prevent this injury to these organs. Damage that results from the presence of sustained high blood pressure is referred to as end-organ or target-organ damage (TOD). In the kidney, TOD is generally manifest as a progression of kidney disease such as enhanced rate of decline of renal function, mortality, increased frequency of uremic crises, and/or increased magnitude of proteinuria. Hypertension may be present in any IRIS (International Renal Interest Society) stage of chronic kidney disease (CKD) or grade of acute kidney injury (AKI), as blood creatinine concentration is not directly correlated to blood pressure. In addition to the kidney disease progression, many dogs and cats with hypertension also have ocular, CNS, and/or cardiovascular TOD, so an effective treatment generally reduces the likelihood of further TOD in these tissues.

Measurement of systolic blood pressure (SBP)

Diagnosis and management of hypertension in dogs and cats with AKI or CKD should be based on repeated measurement of the patient's SBP. Published data suggest improved blood pressure monitoring in clinical practice may decrease the morbidity associated with hypertension. The choice of measurement device depends on operator experience and preference, although many veterinarians prefer Doppler devices for cats. Whatever method is used, it should be applied consistently following the same standard operating procedure if measurements for a given animal patient are to be compared from one measurement session to the next. Each practice should define persistent blood pressure measurements associated with ocular TOD. These are usually associated with IRIS classifications of severe hypertension or hypertension. This will help Veterinary practices to define their own reference ranges for blood pressure measured by their standard operating procedure. In general, the cuff width should be 30–40% of the circumference of the measurement site, which may be the tail, antebrachium, tarsus, or brachium but the cuff needs to be at the same level that heart. At least five measurements should be taken. The readings giving the highest and lowest value for SBP should be discarded with the result determined as the average of the remaining three or more values, if all SBP results are within 20 mm Hg of each other. If the remaining SBP readings differ by more than 20 mm Hg, the measurement session should be repeated. Results of all SBP measurements, rationale for

excluding values, the final (mean) result, and interpretation of the result by the veterinarian should be recorded. The animal's position and attitude, cuff size and site, cuff site circumference (cm), and the BP values obtained should be carefully considered and noted in the animal's record. Furthermore, the age, demeanor, sex, neuter status and clinical history should be taken into account when assessing systolic blood pressure in dogs and cats. It is customary to conduct at least two measurement sessions, normally separated by at least one week, before concluding that an animal needs antihypertensive therapy, particularly in cases where there is no evidence of TOD.

Interpretation of SBP

Approximately 20% of animals with CKD are hypertensive at the time of initial diagnosis and an additional 10-20% of initially normotensive animals will become hypertensive over time. The IRIS recommendation is that SBP should be measured, and CKD substage will be determined using the criteria shown in Table 1. Similar classification using SBP should be undertaken in dogs and cats with AKI or in those suspected of having systemic hypertension due to other underlying diseases or idiopathic.

Table 1: IRIS substage of SBP in dogs and cats based on risk for future TOD*

SBP (mm Hg)	Substage of SBP	Risk of future TOD
<140	Normotensive	Minimal
140 - 159	Prehypertensive	Low
160 - 179	Hypertensive	Moderate
≥180	Severely hypertensive	High

Treatment

The initial assessment of an animal suspected to have systemic hypertension should include recognizing conditions that may be contributing to an increase in SBP, identifying and characterizing TOD, and determining if there are any seemingly unrelated, concurrent conditions that may complicate antihypertensive therapy. Because hypertension is often a silent, slowly progressive condition requiring vigilance and life-long therapy, it is important to be "absolutely" certain about the diagnosis: a high SBP measurement in a dog or cat with CKD usually means systemic hypertension secondary to this disease. However, sometimes it could represent artifactual (anxiety-induced or "white-coat") hypertension or associated to other concomitant disease. White-coat hypertension is not an indication for treatment. A decision to use antihypertensive drugs should be based on the SBP substage (Table 1) and integration of all clinically available information.

Decision to institute treatment

In people, any reduction of SBP that does not produce overt hypotension lowers the risk of TOD. This finding remains to be confirmed in dogs and cats, but IRIS recommends that SBP be categorized based on risk of future TOD. Although interbreed differences in SBP exist in dogs, only the difference for Sight Hounds (20 mm Hg higher values for each category) mandates separate categorization at present.

The general consensus is to institute therapy in a patient with evidence of TOD, if reliable measurements of SBP exceed 160 mm Hg (that is, for hypertensive and severely hypertensive

patients - see Table 1) and in a patient with persistent hypertension. Animals with CKD are presumed to have TOD, even though it may not be clinically apparent.

Antihypertensive therapy

Antihypertensive therapy must be individualized to the patient and its concurrent conditions. Regardless of the initial SBP, the optimal goal of therapy should be to reduce the risk of future TOD to minimal (SBP<150 mm Hg). Some dogs and cats exhibit extreme elevations of SBP, and its reduction may be difficult. In these patients, an alternate goal is to reduce the risk for TOD by at least one substage (Table 1). In most circumstances SBP lowering should be achieved with a gradual, persistent reduction achieved over several weeks. The presence of severe CNS or ocular TOD justifies emergency management as a hypertensive crisis, with rapid lowering of SBP over several hours. Unfortunately, severe ocular damage (e.g., retinal detachment or marked intraocular hemorrhage) is usually associated with chronic retinal injury such that the animal may remain blind even if the antihypertensive regimen is effective.

While available evidence suggests sodium restriction alone generally does not reduce SBP, high salt intake may produce adverse consequences in some settings. Normal dogs and cats are apparently not as salt-sensitive as people or some inbred strains of rats, but it is likely that those with kidney disease, especially those with nephrotic syndrome, are salt sensitive. Furthermore, salt restriction enhances the antihypertensive efficacy of some antihypertensive drugs, particularly those that interfere with the renin-angiotensin-aldosterone system (RAAS). This evidence from laboratory studies of dogs and cats serves as the basis for the recommendation to feed a diet with reduced sodium chloride content to dogs and cats with CKD, regardless of IRIS stage.

In dogs with systemic hypertension, the initial therapeutic choice is often a drug that interferes with the RAAS, specifically angiotensin-converting enzyme inhibitors (ACEi) or angiotensin-receptor blockers (ARB). Clinical experience indicates that both classes of RAAS blockers reduce SBP slightly (~ 10–15%) and are antiproteinuric. The starting dosage should be adjusted to the individual patient based on the recommended range (Table 2). Caution should be exercised in azotemic dogs when dosage adjustments are made.

Table 2: Oral agents for antihypertensive therapy for dogs (D) and cats (C)

Note: some of the treatment recommendations are not authorized for use in all geographical regions and some may not be authorized for use in dogs and/or cats. Such recommended dose rates are therefore empirical. It is the treating veterinarian's duty to make a risk / benefit assessment for each patient prior to administering any treatment.

CLASS	DRUG	USUAL ORAL DOSAGE
ACEI /ARB:		
Angiotensin converting enzyme inhibitor	Benazepril	D: 0.5-2 mg/kg q 12 h C: 0.5-2 mg/kg q 24 h
	Enalapril	D: 0.5-2 mg/kg q 12 h C: 0.5-2 mg/kg q 24 h
	Ramipril	D/C: 0.25-1 mg/kg q 24 h
	Imidapril	D/C: 0.25-1 mg/kg q 24 h

Angiotensin receptor blocker	Telmisartan	D: 1-4 mg/kg q 24 h C: 2 mg/kg q 24 h
	Irbesartan	D: 1-5 mg/kg q 12-24 h
	Spironolactone	D/C: 1-2 mg/kg q 12-24 h
CCB:		
Calcium channel blocker	Amlodipine	D/C: 0.125-0.5 mg/kg q 24 h
OTHER AGENTS:		
β blocker	Atenolol	D: 0.25-1 mg/kg q 12 h C: 6.25-12.5 mg/cat q 12 h
	Labetalol	D: 1.1 (0.2-3.4) mg/kg/h CRI
α blocker	Prazosin	D: 0.5-2 mg/kg q 8-12 h C: 0.25-0.5 mg/cat q 24 h
	Phenoxybenzamine	D: 0.25 mg/kg q 8-12 h or 0.5 mg/kg q 24 h C: 2.5 mg/cat q 8-12 h or 5 mg/cat q 24 h
Direct vasodilator	Hydralazine	D: 0.5-2 mg/kg q 12 h (start at low end of range) C: 2.5 mg/cat q 12-24 h
	Acepromazine	D/C: 0.5-2 mg/kg q 8 h
DIURETICS:		
Thiazide diuretic	Hydrochlorothiazide	D/C: 2-4 mg/kg q 12-24 h
Loop diuretic	Furosemide	D/C: 1-4 mg/kg q 8-24 h

If an antihypertensive agent of choice is only partially effective, the usual approach is to increase the dosage before adding another drug. Thus, if a dog with CKD receiving an ACEi or an ARB remains hypertensive or severely hypertensive, upward adjustment of the dosage should be the first consideration. Many veterinarians start RAAS inhibitors at the lower limit of the recommended dosage (Table 2) and many experts will increase the ACEi dosage further, up to 2 mg/kg. Increasing an RAAS inhibitor beyond the suggested dosage range is not recommended. If an ACEi and/or an ARB is/are given at the upper end of the dosage ranges/range but the response is inadequate, the next step is to add a CCB to RAAS inhibition, typically 0.25–0.5 mg amlodipine/kg once daily. The CCB dosage may be increased to 0.75 mg/kg once daily but should not exceed this dose in dogs. While not ideal, some hypertensive dogs with significant hypertension will require more than two agents. There is no consensus as to which agent (ACEi, ARB, sympatholytic, or direct vasodilator) to add next. In human medicine several publications

have proposed that the combination of ACEi and ARB is more useful than with a single RAAS inhibitor at increasing dose rate to control systemic hypertension. However, combining ACEi and ARB has led to increasing adverse effects in humans and dogs (see Education article on ARBs for further details) and so is not recommended. In fact, certain disease conditions may be best addressed by adding specific classes of agents to the ACEi/ARB/CCB combination, such as alpha- and beta-blockers or surgical excision for pheochromocytoma; or for hypertension associated with hyperaldosteronism, either an aldosterone receptor blocker or surgical excision of the adrenal tumor. Diuretics are rarely used as antihypertensives in dogs and cats but may be useful in both with concurrent hypertension and chronic overhydration.

In cats with systemic hypertension, the principles are as above, although the initial therapeutic choice should be a CCB, specifically amlodipine, when SBP is ≥180 mm Hg or TOD is present. An alternative first choice agent, particularly in proteinuric cats, is telmisartan where recent clinical trials have demonstrated this ARB reduces SBP in hypertensive cats with similar efficacy to amlodipine (see education article on ARB for further details). Second choice agents would be drugs that interfere with the RAAS, specifically an ACEi. These agents could be co-administered (i.e., CCB and ACEi, CCB and ARB). Triple therapy is not usually required to control SBP in cats and the same caution should be exercised as mentioned for dogs when considering combining ARBs and ACEi.

An exception to the above gradual approach, where substantial time (weeks) is allowed between dosage adjustment, is animals classed as severely hypertensive with evidence of severe or progressing neural or ocular TOD. This generally constitutes an emergency, where combination therapy with a CCB plus a RAAS inhibitor is an appropriate first step in dogs, and a CCB will often be used alone in cats. When mentation is compromised, injectable or rectally administered medications should be initially used. In this critical situation, the goal in either species is to reduce SBP within hours, adjusting dosages within that time frame as necessary.

The benefit of lowering blood pressure on TOD within the kidney (where the damage is evident as a progressive decline in glomerular filtration rate) is directly dependent on the degree of proteinuria in people and cats, and there is presumably a similar relationship in proteinuric dogs. Thus, monitoring of the urine protein-to-creatinine ratio (UP/C) is important, with the goal of reducing it to the non-proteinuric range (Table 3) or at least by 50%. The CCB (amlodipine) in common use may be less antiproteinuric than RAAS inhibitors due to preferential dilation of the afferent arteriole. However, CCB often are anti-proteinuric in cats.

Table 3: IRIS substage of persistent renal proteinuria based on UP/C (in mass units) in cats and dogs

CATS (UP/C)	DOGS (UP/C)	PROTEINURIA SUBSTAGE
<0.2	<0.2	Nonproteinuric (NP)
0.2-0.4	0.2-0.5	Borderline Proteinuria (BP)
>0.4	>0.5	Proteinuric (P)

Monitoring antihypertensive therapy

Evident acute ocular and/or neural TOD constitute a hypertensive crisis, necessitating rapid lowering of SBP. In most other situations, hypertension is not an emergency and 3–4 weeks should be allowed between dosage adjustments. There has been some concern about acute exacerbation of azotemia with RAAS inhibition, though this is unusual and modest increases in

blood creatinine concentration (<30%) are generally tolerable. Nonetheless, a dog in IRIS Stage 1 or 2 should be evaluated 7–14 days after any change in antihypertensive therapy and this evaluation should include clinical assessment and measurement of blood creatinine, SBP and the UP/C. In unstable patients and those with IRIS Stage 3 or 4, this recheck should be conducted earlier, perhaps within 3–5 days. Patients deemed to be hypertensive emergencies and hospitalized, particularly those receiving fluid therapy or pharmacological agents with cardiovascular effects, should be assessed (clinical evaluation and assessment of blood creatinine and SBP) at least daily. The purpose of these short-term assessments is to identify findings that are unexpected (e.g., new or worsening TOD) or adverse (e.g., marked worsening of azotemia or systemic hypotension). Clinical findings of weakness or syncope with SBP <120 mm Hg indicates systemic hypotension and therapy should be adjusted accordingly.

Re-evaluation is appropriate at 1 to 4-month intervals, depending on stability (more frequent if SBP or other conditions are unstable) and degree of hypertension (more frequent if SBP remains ≥180 mm Hg). Follow-up evaluations to assess efficacy and adjust therapy should include assessment of SBP, blood creatinine concentration, urinalysis with UP/C, funduscopic examination, and any other specific evaluation depending on circumstances (e.g., TOD, causes of secondary hypertension, or concurrent conditions) of the patient. A key predictive indicator of antihypertensive efficacy is its effect on proteinuria: a benefit is predicted if the antihypertensive regimen is antiproteinuric (e.g., reduces UP/C at least by 50%). The frequency and nature of re-evaluations will vary depending on the SBP substage, stability of SBP, other aspects of the health of the patient, and frequency of dosage adjustment to antihypertensive therapy. Since signs of progression of TOD can be subtle, SBP should be closely monitored over time in patients receiving antihypertensive therapy, even when hypertension is seemingly well-controlled.

Further Reading

Acierno MJ, Brown S, Coleman AE, et al. ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. J Vet Intern Med 2018;32:1803-1822.

Bijsmans ES, Doig M, Jepson RE, et al. Factors influencing the relationship between the dose of amlodipine required for blood pressure control and change in blood pressure in hypertensive cats. J Vet Intern Med 2016;30:1939-1676.

Bodey AR, Sansom J. Epidemiological study of blood pressure in domestic cats. J Small Anim Pract 1998;39:567-573.

Brown CA, Elliott J, Schmiedt CW, et al. Chronic kidney disease in aged cats: Clinical features, morphology, and proposed pathogeneses. Vet Path 2016;53:309-326.

Brown SA, Brown CA, Jacobs G, et al. Effects of the angiotensin converting enzyme inhibitor benazepril in cats with induced renal insufficiency. Am J Vet Res 2001;62:375-383.

Cerna P, Archontakis PE, Cheuk HO, et al. Comparison of Doppler ultrasonic and oscillometric devices (with or without proprietary optimisations) for non-invasive blood pressure measurement in conscious cats. J Feline Med Surg 2021;23:121-130.

Chakrabarti S, Syme HM, Elliott J. Clinicopathological variables predicting progression of azotemia in cats with chronic kidney disease. J Vet Intern Med 2012;26:275-281.

Chetboul V, Lefebvre HP, Pinhas C, et al. Spontaneous feline hypertension: clinical and

echocardiographic abnormalities, and survival rate. J Vet Intern Med 2003;17:89-95.

Cole L, Jepson R, Humm K. Systemic hypertension in cats with acute kidney injury. J Small Anim Pract 2017;58:577-581.

Coleman AE, Brown SA, Traas AM, et al. Safety and efficacy of orally administered telmisartan for the treatment of systemic hypertension in cats: Results of a double-blind, placebo-controlled, randomized clinical trial. J Vet Intern Med 2019;33:478-488.

Conroy M, Chang YM, Brodbelt D, et al. Survival after diagnosis of hypertension in cats attending primary care practice in the United Kingdom. J Vet Intern Med 2018;32:1846-1855.

Elliott J, Watson ADJ. Chronic kidney disease: International Renal Interest Society staging and management. In: Bonagura JD, Twedt DC, eds. Kirk's Current Veterinary Therapy XV. Missouri: Elsevier Saunders; 2014:857-862.

Elliott J, Barber PJ, Syme HM, et al. Feline hypertension: clinical findings and response to antihypertensive treatment in 30 cases. J Small Anim Pract 2001;42:122-129.

Fowler BL, Stefanovski D, Hess RS, et al. Effect of telmisartan, angiotensin-converting enzyme inhibition, or both, on proteinuria and blood pressure in dogs. J Vet Intern Med 2021;35:1231-1237.

Geddes RF. Hypertension: Why Is It Critical? Vet Clin North Am Small Anim Pract 2020;50:1037-1052.

Glaus TM, Elliott J, Herberich E, et al. Efficacy of long-term oral telmisartan treatment in cats with hypertension: Results of a prospective European clinical trial. J Vet Intern Med 2019;33:413-422.

Henik RA, Snyder PS, Volk LM. Treatment of systemic hypertension in cats with amlodipine besylate. J Am Anim Hosp Assoc 1997;33:226-234.

Jacob F, Polzin DJ, Osborne CA, et al. Association between initial systolic blood pressure and risk of developing a uremic crisis or of dying in dogs with chronic renal failure. J Am Vet Med Assoc 2003;222:322-329.

Jacobs-Fohrman ZR, Barnes TS, McEwen MM, et al. Clinical evaluation of arterial blood pressure in anesthetized dogs by use of a veterinary-specific multiparameter monitor. Am J Vet Res 2020;81:635-641.

Jenkins TL, Coleman AE, Schmiedt CW, et al. Attenuation of the pressor response to exogenous angiotensin by angiotensin receptor blockers and benazepril hydrochloride in clinically normal cats. Am J Vet Res 2015;76:807-813.

Jepson RE, Brodbelt D, Elliott J, et al. Evaluation of the effects of control of systolic blood pressure on survival in cats with systemic hypertension. J Vet Intern Med 2007;21:402-409.

Jepson RE, Brodbelt D, Vallance C, et al. Evaluation of predictors of the development of azotemia in cats. J Vet Intern Med 2009;23:806-813.

Jepson RE, Syme HM, Elliott J. Plasma renin activity and aldosterone concentrations in

hypertensive cats with and without azotemia and in response to treatment with amlodipine besylate. J Vet Intern Med 2014;28:144-153.

Jepson RE. Feline systemic hypertension: Classification and pathogenesis. J Feline Med Surg 2011;13:25-34.

King JN, Gunn-Moore DA, Tasker S, et al. Tolerability and efficacy of benazepril in cats with chronic kidney disease. J Vet Intern Med 2006;20:1054-1064.

Lyberg M, Ljungvall I, Häggström J, et al. Impact of equipment and handling on systolic blood pressure measurements in conscious dogs in an animal hospital environment. J Vet Intern Med 2021;35:739-746.

Maggio F, DeFrancesco TC, Atkins CE, et al. Ocular lesions associated with systemic hypertension in cats: 69 cases (1985–1998). J Am Vet Med Assoc 2000;217:695-702.

Miyagawa Y, Akabane R, Sakatani A, et al. Effects of telmisartan on proteinuria and systolic blood pressure in dogs with chronic kidney disease. Res Vet Sci 2020;133:150-156.

Mizutani H, Koyama H, Watanabe T, et al. Evaluation of the clinical efficacy of benazepril in the treatment of chronic renal insufficiency in cats. J Vet Intern Med 2006;20:1074-1079.

Payne JR, Brodbelt DC, Luis Fuentes V. Blood Pressure Measurements in 780 Apparently Healthy Cats. J Vet Intern Med 2017;31:15-21.

Ray M, Carney HC, Boynton B, et al. 2021 AAFP Feline Senior Care Guidelines. J Feline Med Surg 2021;23:613-638.

Sansom J, Rogers K, Wood JL. Blood pressure assessment in healthy cats and cats with hypertensive retinopathy. Am J Vet Res 2004;65:245-252.

Syme HM, Barber PJ, Markwell PJ, et al. Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation. J Am Vet Med Assoc 2002;220:1799-1804.

Taylor SS, Sparkes AH, Briscoe K, et al. ISFM Consensus Guidelines on the Diagnosis and Management of Hypertension in Cats. J Feline Med Surg 2017;19:288-303.

Zublena F, De Gennaro C, Corletto F. Retrospective evaluation of labetalol as antihypertensive agent in dogs. BMC Vet Res 2020;16:256.