REVIEW ARTICLE

Systemic Hypertension in Companion Animals: A Review

Tanvika Sangwan*, Neetu Saini

Abstract

The lifestyle diseases are increasing in human beings and their companion animals due to rapid pace of urbanization, common life styles and feeding habits. Systemic hypertension, one of the most important lifestyle diseases is the most under-diagnosed disease due to its clinically quiescent nature. Secondary systemic hypertension due to the presence of underlying disease is the most prevalent form in companion animals with chronic kidney disease as the major underlying etiology. The persistently elevated systolic blood pressure causes damage to the various organs (kidney, eye, brain and heart) termed as target organ damage (TOD). The therapeutic management of the systemic hypertension includes treatment of primary etiology along with antihypertensive drugs. Angiotensin converting enzyme inhibitors (ACEi) are the initial antihypertensive drug of choice followed by calcium channel blockers (CCB).

Keywords: CKD, Dog, Heart, Systemic hypertension, Target Organ Damage.

Ind J Vet Sci and Biotech (2023): 10.48165/ijvsbt.19.4.01

Introduction

With the rapid pace of westernization, economic development and increasing pets as a member of nuclear families, human and companion animals do share a common sedentary behaviour and unhealthy feeding habits. These insalubrious habits predispose them to the lifestyle diseases also known as non-communicable chronic diseases which are increasing at an alarming rate in humans as well as in companion animals (Pappachan, 2011; Chandler *et al.,* 2017). These diseases include hypertension, obesity, diabetes mellitus and dyslipidemia, which are considered to be the major risk factors for cardiovascular diseases like myocardial ischemia and stroke in human beings (Pappachan, 2011). But, in contrast to humans, myocardial ischemia and stroke due to hypertension is very rare in dogs and cats (Elliott, 2020). Systemic hypertension also known as the silent killer in human medicine is a newly recognized disease in veterinary that affects the essence and survivability of companion animals (Dixon-Jimenez *et al.,* 2011; Elliott and Brown, 2020).

Systemic Hypertension and Blood Pressure

Blood pressure (BP) is the force exerted by blood against the walls of arteries (Creedon and Davis, 2012) which is the eventual function of cardiac output and total peripheral resistance (Acierno and Labato, 2004). Systemic arterial BP has three components systolic arterial BP, diastolic arterial BP and mean arterial BP (Skelding and Velverde, 2020). Out of all the three components of arterial BP, systolic BP is the most emphasized component in human and veterinary medicine as it is an important determinant of vascular and hypertensive damage resulting into cardiovascular morbidity and mortality (Mentari and Rahman, 2004; Brown *et al.,* 2007; Rahimi *et al.,* 2015).

Systemic hypertension is one of the most under-diagnosed disease because of its silent nature in clinical form (Acierno and Labato, 2004). Hypertension is the persistently elevated arterial systolic BP. The cut-off values for defining hypertension have been successively declining in humans from >160 mm Hg (Mahmood *et al.,* 2014) to 140 mm Hg (Syme, 2020). Similarly, it has been declined from >150 mm Hg (Brown *et al.,* 2007) to >140 mm Hg (Acierno *et al.,* 2018) in dogs and cats. Prehypertension is the new terminology introduced in humans and companion animals (Syme, 2020). According to latest American Council of Veterinary Internal Medicine (ACVIM) guidelines, hypertension is categorized on the basis of risk of target organ damage (TOD) and systolic BP into four types as presented in Table 1 (Acierno *et al.,* 2018).

Table 1: 2018 International Renal Interest Society (IRIS)/ ACVIM consensus statement regarding classification of dogs as per the systolic blood pressure (mm Hg) and risk of target organ damage (TOD)

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

Department of Veterinary Medicine, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana-141004, Punjab, India

Corresponding Author: Tanvika Sangwan, Department of Veterinary Medicine, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana-141004, Punjab, India, e-mail: tanvikasangwan1998@gmail.com

How to cite this article: Sangwan, T., & Saini, N. (2023). Systemic Hypertension in Companion Animals: A Review. Ind J Vet Sci and Biotech. 19(4), 1-6.

Source of support: Nil

Conflict of interest: None

Submitted: 16/05/2023 **Accepted:** 06/06/2023 **Published:** 10/07/2023

Classification of Systemic Hypertension

Hypertension can be classified into three types as i) situational hypertension ii) secondary hypertension iii) primary/ idiopathic hypertension (Acierno *et al.,* 2018).

Situational hypertension is the persistently elevated systolic BP measured in the clinical settings due to hospital environment anxiety in an otherwise normotensive animal. It is caused by the activation of autonomic nervous system due to release of stressors in the body while monitoring BP in an unaccustomed environment (Acierno *et al.,* 2018). It is also called white coat hypertension in human medicine (Syme, 2020). There is no rationale to treat situational hypertension in dogs and cats. There is wide variation in response of individual animal to different stressors. Some animal manifest marked increase in BP during in clinic BP monitoring as compared to at home BP monitoring (Marino *et al.,* 2011; Quimby *et al.,* 2011; Bragg *et al.,* 2015), while few animals show a decrease and no changes in BP (Kallet *et al.,* 1997). This type of hypertension can be resolved by allowing the animal to accustom at a quiet place in unfamiliar hospital environment for five to ten minutes and by monitoring BP at home (Belew *et al.,* 1999; Acierno *et al.,* 2018).

Secondary hypertension which constitutes only 5-10% of hypertensive cases in humans (Charles *et al.,* 2017), is the most common form of hypertension in canines (Acierno *et al.,* 2018; Syme, 2020). It is defined as the persistent pathologically elevated BP that is associated with the concurrent disease condition in the body. The most common diseases causing secondary hypertension in dogs are chronic kidney disease (CKD), acute kidney disease (AKD) followed by the various endocrinopathies like hyperadrenocorticism, pheochromocytoma and diabetes mellitus among the most common ones (Acierno *et al.,* 2018; Cole *et al.,* 2020; Syme, 2020). It is also associated with the ingestion of the toxicants like cocaine, 5-hydroxytryptophan, amphetamines (Thomas *et al.,* 2014; Appel *et al.,* 2015; Syme, 2020) and various therapeutic agents like glucocorticoids, mineralocorticoids and erythropoietin (Aceirno *et al.,* 2018; Syme, 2020). The prevalence of secondary hypertension is variable and constitutes about 80% of all hypertensive canine cases and has been described according to each underlying disease condition. In CKD, the hypertensive prevalence in dogs varies from 9 to 93% (Jacob *et al.,* 2003; Cortadellas *et al.,* 2006; Buranakarl *et al.,* 2007; Braga *et al.,* 2015).

Primary/essential/idiopathic hypertension in human medicine, is the most common form comprising about 90% of the hypertensive cases and the least common form in canine (Acierno and Labato, 2004; Acierno *et al.,* 2018). It is defined as the persistent pathologically elevated BP in the absence of any underlying disease condition in the body (Bovee *et al.,* 1989).

Target Organ Damage (TOD)

Systemic hypertension in animals is troublesome only when chronic elevation of BP causes tissue injury. The damage to different organs caused by chronically sustained high BP is termed as target organ damage (TOD). Different organs susceptible to TOD risk are kidney, heart & its vessels, eyes and brain (Acierno *et al.,* 2018).

Heart & its vessels as a target organ damage (TOD)

The significance of heart as a target organ of hypertension has been first recognized as hypertensive myocardial hypertrophy in renal human patient (Coleman and Brown, 2020). The cardiac manifestations associated with secondary hypertension in dogs are detected as systolic murmurs, gallop sounds and arrhythmia on physical examination in 67% of hypertensive animals (Misbach *et al.,* 2011). Also, the auscultative heart murmur in hypertensive patients does not always correlate with left ventricular hypertrophy (LVH) (Snyder *et al.,* 2001).

Radiographic changes include cardiomegaly (Misbach *et al.,* 2011) and an additional aortic undulation/tortuosity in hypertensive cats (Nelson *et al.,* 2002). In canine, Holland *et al.* (2022) and Sangwan *et al.* (2023) have found the dilated thoracic aorta, aortic knob presence on lateral radiographs and visualization of bowing of aorta on DV/VD radiographs of hypertensive dogs. Also, Sangwan *et al.* (2023) depicted the cut off value of 2.80±0.13 cm for the aortic knob in hypertensive dogs with 93.94% specificity and 55% sensitivity as compared to healthy dogs.

The possible electrocardiographic changes associated with left ventricular hypertrophy include peaked R waves, increased QRS complex duration and leftward shifting of mean electrical axis (Tilley, 1985). But, electrocardiography (ECG) is not specific and sensitive for detecting left ventricular hypertrophy (Coleman and Brown, 2020). The most common echocardiographic change in hypertensive dogs and cats is left ventricular hypertrophy, which is mostly symmetric diffuse concentric hypertrophy (72%) followed by asymmetric inter-ventricular septal hypertrophy (28%) and very rarely eccentric hypertrophy (Misbach *et al.,* 2011; Coleman and Brown, 2020). The diastolic dysfunction as measured by reverse Mitral E wave to A wave ratio usually precedes left ventricular hypertrophy and mild to moderate aortic valve regurgitation has been evaluated in dogs (Misbach *et al.,* 2011). Holland *et al.* (2021) revealed the asymmetry in the diameter of aortic cusps in hypertensive dogs. In hypertensive cats and dogs, aortic root dilatation at the level of proximal ascending aorta through left ventricular outflow tract view has been studied (Nelson *et al.,* 2002; Sangwan *et al.,* 2023). Also, the aortic dilatation due to hypertension has been studied in humans and various reference data regarding the effect of gender and age on the size of aorta is available (Lederle *et al.,* 1997; Hartshorn *et al.,* 2011). According to Holland *et al.* (2020) and Sangwan *et al.* (2023), the ratio of abdominal aorta and caudal venacava when measured through paralumbar region has been found to be increased in hypertensive dogs and this could be a novel method to diagnose hypertension.

Aorta dampens the pressure pulsations of left ventricular outflow of blood and revamps it into continuous flow because of the elastic properties of its wall (Sangwan et al., 2023). In

hypertension, there is abnormal functioning of aorta with breakdown of elastin causing dilatation and stiffening due to replacement of elastin by collagen fibers. Therefore, aortic stiffness and elasticity is the autonomous predictor of cardiovascular risk and mortality (Kamberi *et al.,* 2013). Corda *et al.* (2020) and Sangwan *et al.* (2023) conducted a study to determine the aortic elasticity and stiffness measured through abdominal paralumbar region in normotensive and systemically hypertensive dogs. They measured the aortic elasticity from the two different positions (one caudal to left renal artery and other cranial to emergence of external iliac artery) by taking percentage change in aortic diameter during systole and diastole. They have found the increased stiffness and decreased elasticity of aorta at both the levels in hypertensive dogs, but aortic elasticity measured cranial to iliac artery was not associated with age. This is due to the inverse relationship between age related arterial stiffness and distance from the heart (Corda *et al.,* 2020; Sangwan *et al.,* 2023).

Therefore, aorta could be considered as an important TOD of systemic hypertension in canine as depicted by a recent study conducted by Sangwan *et al.* (2023). They have depicted the dilatation of proximal ascending aorta along with the disparity in size and shape of thoracic aorta with decreased abdominal aortic elasticity and increased aortic-venacaval ratio in systemically hypertensive dogs as compared to the healthy dogs.

Kidney as a target organ

Renal diseases are the most common cause of secondary hypertension in canine (Acierno *et al.,* 2018). The prevalence of hypertension in renal disorders varies from 50-93% in dogs (Acierno and Labato, 2005 or 2004) and 19.4-61% in cats (Syme *et al.,* 2002; Acierno and Labato, 2005). In various studies of dogs and cats affected with CKD, it has been depicted that hypertensive patients are more plausibly proteinuric which in turn, is directly correlated with survival time and progression of renal diseases (Jacob *et al.,* 2005; Syme *et al.,* 2006; Jepson *et al.*, 2007; Chakrabarti *et al.,* 2012). But, this effect of hypertension on renal disease progression is not clear when animal is not proteinuric (Elliott, 2020). Also, it has been described that hypertension can occur at any stage of CKD and not directly linked to serum creatinine levels (Michell *et al.,* 1997; Stepien *et al.,* 2003; Acierno *et al.,* 2018) while, urine protein to creatinine ratio (UPC) had been reported to be positively correlated with systolic BP in various studies (Syme *et al.,* 2006; Chakrabarti *et al.,* 2012).

Eye as target organ

Ocular lesions associated with the hypertension have been described as hypertensive retinopathy and choroidopathy in dogs and cats. The prevalence of ocular lesions in hypertensive dogs is very sparse (Littman *et al.,* 1988; Bovee *et al.,* 1989; Sansom and Bodey, 1997) and nearly 100% in hypertensive cats (Littman, 1994; Maggio *et al.,* 2000). These lesions include exudative retinal detachment (Littman, 1994; Sansom *et al.,* 1994; Maggio *et al.,* 2000) as the most common finding in cats and retinal hemorrhages in dogs (LeBlanc *et al.,* 2011) alongwith papilledema, retinal vessel tortuosity, hyphema, glaucoma and retinal degeneration (Littman *et al.,* 1988; Bovee *et al.,* 1989; Chetboul *et al.,* 2003). The ocular changes have been detected at a minimum systolic BP of 168 mmHg (Sansom *et al.,* 2004) and the risk of injury increases when systolic BP is greater than 180 mm Hg (Chetboul *et al.,* 2003; Cortadellas *et al.,* 2006; Leblanc *et al.,* 2011).

Brain as a target organ

Hypertensive encephalopathy is the term used to describe the deadly complication of high BP in the form of central nervous system dysfunction like white matter edema and vascular lesions in human beings (Schwartz, 2002; Kletzmayr *et al.,* 2003) and in dogs and cats (Littman, 1994; Bagley, 2003; Church *et al.,* 2019). The prevalence of hypertensive encephalopathy in hypertensive cats varies between 29-46% (Maggio *et al.,* 2000). It has been associated with acute increase in systolic BP that exceeds 180 mm Hg in cats (Kyles *et al.,* 1999; Mathur *et al.,* 2002). The clinical signs associated with hypertensive encephalopathy include seizures, altered mentation, disorientation, altered behaviour, vestibular disturbances and focal neurological deficits (Acierno *et al.,* 2018).

Diagnosis and Management of Systemic Hypertension in Canines

The three main conditions that prompt the veterinarian to monitor the BP in dogs and cats are routine screening of healthy geriatric animals, patients having the signs of TOD and the presence of any disease condition or intoxication of substances that are known to increase BP. Once BP has been monitored in suspected patients, hypertension has to be classified into either of the categories as situational hypertension, secondary or primary hypertension (Spencer, 2020). In canines, the BP range at which the antihypertensive therapy needs to be started is still not clear. But the perusal of literature depicts that the therapy should be started whenever there is moderate or severe risk of TOD with systolic BP ≥ 160 mm Hg (Acierno *et al.,* 2018; Spencer, 2020).

The therapeutic management of the hypertension in dogs includes treatment of primary condition along with antihypertensive therapy depending on the degree of TOD (Acierno *et al.,* 2018). The goal of the therapy is to gradually decrease the systolic BP over a period of several weeks. Renin angiotensin aldosterone system (RAAS) inhibitors and calcium channel blockers are the most commonly used drugs to treat hypertension (Acierno *et al.,* 2018). RAAS inhibitors like angiotensin converting enzyme inhibitor (ACEi), angiotensin receptor blockers (ARB) and aldosterone antagonists are considered as the first line of treatment due to their anti-proteinuric effects where ACEi are most commonly studied in veterinary literature (Mathur *et al.,* 2002; Acierno *et al.,* 2018). Therefore, ACEi like enalapril/benazepril (0.5-2 mg/kg b.wt. q 12h) is the preferred initial drug of choice (Acierno *et*

al., 2018). This is followed by calcium channel blockers (CCB) like amlodipine (0.1-0.25 mg/kg b.w.t q24h) if the animal is refractory to ACEi (Brown and Henick, 1998).

Management of Hypertensive Crisis

The first choice of drug in hypertensive emergencies is selective dopamine-1 receptor agonist (fenoldopam). It works by increasing renal perfusion, glomerular filtration rate and sodium excretion (Kelly *et al.,* 2016). Due to its very short half life, fenoldopam is given as constant rate infusion (CRI) with initial loading dose rate of 0.1 µg/kg b.wt./min which is increased by 0.1 µg/kg b.wt./min every 15 min i.e at initial 0.1 µg/kg b.wt./min which followed by 0.2 µg/kg b.wt./min after 15 min, further followed by 0.3µg/kg b.wt./min after next 15 min and so on until desired BP is achieved (Acierno *et al.,* 2018).

Sodium nitroprusside has been established as an alternative to fenoldopam. As it works by reducing renal perfusion and causes direct vasodilation, it should not be used in patients affected with renal diseases. It should not be administered for more than one day to prevent thiocyanate and cyanide toxicity. The recommended dosage of sodium nitroprusside in the form of CRI is 0.5 µg/kg b.wt./min (maximum dose of 10 µg/kg/min) till required BP is achieved (Spencer, 2020).

The next suitable alternative to both of drugs mentioned above is oral or intravenous hydralazine. Although Kittelson and Hamlin (1983) described the prolonged effects of hydralazine in dogs but due to non-availability of alternative drugs, it has been recommended for use (Spencer, 2020).

Adverse Effects of Antihypertensive Therapy

Hypotension is one of the common complications associated with antihypertensive therapy. Whenever the BP falls below 110 mm Hg along with signs of lethargy and muscle weakness in a patient, antihypertensive therapy needs to be adjusted or discontinued. Amlodipine can cause reflex tachycardia in response to vasodilation and due to its metabolism through liver; it is contraindicated in hepatic dysfunction patients (Spencer, 2020). With the use of ACEi, various studies have implicated that there is no any potential adverse effects related to the use of these drugs in canines, except for small increase in creatinine values and thus azotemia as decribed in few studies (Brown *et al.,* 2003; Atkins *et al.,* 2007; Mishina and Watanabe, 2008; Konta *et al.,* 2018).

Dietary Therapy of Hypertension

Brown and Henik (1998) recommended the reduced salt intake as a good dietary method to manage hypertension in humans. In veterinary literature, there is still controversy over the dietary sodium role in hypertension. According to Krieger *et al.* (1990) and Lovern *et al.* (2001), salt restriction can cause RAAS activation and increased potassium excretion. While Acierno *et al.* (2018) recommended low salt diet in hypertensive dogs. Similarly many studies supported the phenomenon of salt sensitivity in renal patients therefore advised low sodium diet (Klosterman and Pressler, 2011).

With regard to obesity role in hypertension, there are various controversial studies. Bodey and Michell (1996), Brown and Henik (1998) and Montaya *et al.* (2006) recommended weight reduction in hypertensive obese dogs. While Mooney *et al.* (2017) reported no association of body weight on BP. Similarly Perez-Sanchez *et al.* (2015) reported the important role of underlying disease in controlling BP in spite of obesity.

Therefore, the therapeutic management of the hypertension in dogs includes treatment of primary condition along with antihypertensive therapy depending on the degree of TOD (Acierno *et al.,* 2018). The goal of the therapy is to gradually decrease the systolic BP over a period of several weeks. Renin angiotensin aldosterone system (RAAS) inhibitors and calcium channel blockers are the most commonly used drugs to treat hypertension (Acierno *et al.,* 2018). RAAS inhibitors like angiotensin converting enzyme inhibitor (ACEi), angiotensin receptor blockers (ARB) and aldosterone antagonists are considered as the first line of treatment due to their anti-proteinuric effects where ACEi are most commonly studied in veterinary literature (Acierno *et al.,* 2018). Therefore, ACEi like enalapril/benazepril (0.5-2 mg/kg bwt q 12h) is the preferred initial drug of choice (Acierno *et al.,* 2018). This is followed by calcium channel blockers (CCB) like amlodipine (0.1-0.25 mg/kg bwt q 24h) if the animal is refractory to ACEi (Brown and Henik, 1998).

References

Acierno, M.J., & Labato, M.A. (2004). Hypertension in dogs and cats. *Compendium on Continuing Education for the Practicing Veterinarian*, *26*(5), 336–345.

Acierno, M.J., Brown, S., Coleman, A.E., Jepson, R.E., Papich, M., Stepien, R.L., & Syme, H.M. (2018). ACVIM consensus statement: guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *Journal of Veterinary Internal Medicine, 32*(6), 1803-1822.

Appel, N.M., Li, S., Holmes, T.H., & Acri, J.B. (2015). *Dopamine D 3 Receptor Antagonist (GSK598809) Potentiates the Hypertensive Effects of Cocaine in Conscious, Freely-Moving Dogs*. *September*, 484-492.

Atkins, C.E., Rausch, W.P., Gardner, S.Y., Defrancesco, T.C., Keene, B.W., & Levine, J.F. (2007). The effect of amlodipine and the combination of amlodipine and enalapril on the rennin-angiotensin-aldosterone system in the dog. *Journal of Veterinary Pharmacology and Therapeutics*, *30*(5), 394-400.

Bagley, R.S. (2003). The brain as a target organ In: Egner B, Carr A, Brown S, eds. *Essential Facts of Blood Pressure in Dogs and Cats*. Babenhausen.

Belew, A.M., Barlett, T., & Brown, S.A. (1999). Evaluation of the white-coat effect in cats. *Journal of Veterinary Internal Medicine*, *13*(2), 134-142.

Bodey, A.R., & Michell, A.R. (1996). Epidemiological study of Blood Pressure in Domestic Dogs. *Journal of Small Animal Practice*, *37*(3), 116-125.

Bovee, K.C., Littman, M.P., Crabtree, B.J., & Aguirre, G. (1989). Essential hypertension in a dog. *Journal of American Veterinary Medical Association*, *195*(1), 81-86.

Braga, E.T., Leite, J.H.A.D.C., Rosa, F.A., Tivelli, P., Araújo, A.M., Almeida, B.F.M.D., & Marcondes, M. (2015).Hypertension and its correlation with renal lesions in dogs with leishmaniosis. *RevistaBrasileira de ParasitologiaVeterinária*, *24*, 45-51.

Bragg, R.F., Bennett, J.S., Cummings, A., & Quimby, J.M. (2015). Evaluation of the effects of hospital visit stress on physiologic variables in dogs. *Journal of the American Veterinary Medical Association*, *246*(2), 212-215.

Brown, S.A., & Henik, R.A. (1998). Diagnosis and treatment of systemic hypertension. *Veterinary Clinics: Small Animal Practice*, *28*(6), 1481-1494.

Brown, S.A., Finco, D.R., Brown, C.A., Crowell, W.A., Alva, R., Ericsson, G.F., & Cooper, T. (2003). Evaluation of the effects of inhibition of angiotensin converting enzyme with enalapril in dogs with induced chronic renal insufficiency. *American Journal of Veterinary Research*, *64*(3), 321-327.

Brown, S., Atkins, C., Bagley, R., Carr, A., Cowgill, L., Davidson, M., & Stepien, R. (2007). Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *Journal of Veterinary Internal Medicine*, *21*(3), 542-558.

Buranakarl, C., Ankanaporn, K., Thammacharoen, S., Trisiriroj, M., Maleeratmongkol, T., Thongchai, P., & Panasjaroen, S. (2007). Relationships between degree of azotaemia and blood pressure, urinary protein: creatinine ratio and fractional excretion of electrolytes in dogs with renal azotaemia. *Veterinary Research Communications*, *31*(3), 245-257.

Chakrabarti, S., Syme, H.M., & Elliott, J. (2012). Clinicopathological variables predicting progression of azotemia in cats with chronic kidney disease. *Journal of Veterinary Internal Medicine*, *26*(2), 275-281.

Chandler, M., Cunningham, S., Lund, E.M., Khanna, C., Naramore, R., Patel, A., & Day, M.J. (2017). Obesity and associated comorbidities in people and companion animals: a one health perspective. *Journal of Comparative Pathology*, *156*(4), 296-309.

Charles, L., Triscott, J., & Dobbs, B. (2017). Secondary hypertension: discovering the underlying cause. *American Family Physician*, *96*(7), 453-461.

Chetboul, V., Lefebvre, H.P., Pinhas, C., Clerc, B., Boussouf, M., & Pouchelon, J.L. (2003). Spontaneous feline hypertension: clinical and echocardiographic abnormalities, and survival rate. *Journal of Veterinary Internal Medicine*, *17*(1), 89-95.

Church, M.E., Turek, B.J., & Durham, A.C. (2019). Neuropathology of spontaneous hypertensive encephalopathy in cats. *Veterinary Pathology*, *56*(5), 778-782.

Cole, L.P., Jepson, R., Dawson, C., & Humm, K. (2020). Hypertension, retinopathy, and acute kidney injury in dogs: A prospective study. *Journal of Veterinary Internal Medicine*, *34*(5), 1940-1947.

Coleman, A.E., & Brown, S.A. (2020). Hypertension and the heart and vasculature. In: *Hypertension in the Dog and Cat* (pp. 187-215), Springer, Cham.

Corda, A., Corda, F., Caivano, D., Saderi, L., Sotgiu, G., Mollica, A., & Pinna Parpaglia, M.L. (2020). Ultrasonographic assessment of abdominal aortic elasticity in hypertensive dogs. *Journal of Veterinary Internal Medicine*, *34*(6), 2337-2344.

Cortadellas, O., del Palacio, M.J.F., Bayón, A., Albert, A., & Talavera, J. (2006). Systemic hypertension in dogs with leishmaniasis: prevalence and clinical consequences. *Journal of Veterinary Internal Medicine*, *20*(4), 941-947.

Creedon, J.M.B., & Davis, H. (Eds.) (2012). *Advanced monitoring and procedures for small animal emergency and critical care.* John Wiley & Sons.

Dixon-Jimenez, A., Rapoport, G., & Brown, S.A. (2011). Systemic Hypertension in Dogs & Cats. *Today›s Veterinary Practice, 1*(2), 20-26.

Elliott, J. (2020). Physiology of blood pressure regulation and pathophysiology of hypertension. In: *Hypertension in the Dog and Cat* (pp. 3-30), Springer, Cham.

Elliott, J., & Brown, C. (2020). Hypertension and the kidney. In: *Hypertension in the Dog and Cat* (pp. 171-185), Springer, Cham.

Hartshorne, T.C., McCollum, C.N., Earnshaw, J.J., Morris, J., & Nasim, A. (2011).Ultrasound measurement of aortic diameter in a national screening programme. *European Journal of Vascular and Endovascular Surgery*, *42*(2), 195-199.

Holland, M., Hofmeister, E., & Hudson, J. (2021). Echocardiographic changes in the shape and size of the aortic cusps in dogs with confirmed systemic hypertension. *Veterinary Radiology & Ultrasound*, *62*(6), 697-704.

Holland, M., Hudson, J., & Hofmeister, E. (2022). An observational thoracic radiographic study of aortic remodeling in dogs with confirmed systemic hypertension. *Veterinary Radiology & Ultrasound*, 63, 254-263

Holland, M., Hudson, J., Bao, Y., & Gaillard, P. (2020). Aortic to caudal vena cava ratio measurements using abdominal ultrasound are increased in dogs with confirmed systemic hypertension. *Veterinary Radiology & Ultrasound*, *61*(2), 206-214.

Jacob, F., Polzin, D.J., Osborne, C.A., Neaton, J.D., Lekcharoensuk, C., Allen, T.A., & Jepson, R.E. (2020). Measurement of Blood Pressure in Conscious Cats and Dogs. In: *Hypertension in the Dog and Cat* (pp. 31-65), Springer, Cham.

Jepson, R.E., Elliott, J., Brodbelt, D., & Syme, H.M. (2007).Effect of control of systolic blood pressure on survival in cats with systemic hypertension. *Journal of Veterinary Internal Medicine*, *21*(3), 402-409.

Kallet, A.J., Cowgill, L.D., & Kass, P.H. (1997). Comparison of blood pressure measurements obtained in dogs by use of indirect oscillometry in a veterinary clinic versus at home. *Journal of the American Veterinary Medical Association*, *210*(5), 651-654.

Kamberi, L.S., Gorani, D.R., Hoxha, T.F., & Zahiti, B.F. (2013). Aortic compliance and stiffness among severe longstanding hypertensive and non-hypertensive. *Acta Informatica Medica*, *21*(1), 12.

Kelly, K.L., Drobatz, K.J., & Foster, J.D. (2016). Effect of fenoldopam continuous infusion on glomerular filtration rate and fractional excretion of sodium in healthy dogs. *Journal of Veterinary Internal Medicine*, *30*(5), 1655-1660.

Kittleson, M.D., & Hamlin, R.L. (1983). Hydralazine pharmacodynamics in the dog. *American Journal of Veterinary Research*, *44*(8), 1501-1505.

Kletzmayr, J., Uffmann, M., & Schmaldienst, S. (2003). Severe but reversible hypertensive encephalopathy. *Wiener Klinische Wochenschrift*, *115*(12), 416-416.

Klosterman, E.S., & Pressler, B.M. (2011). Nephrotic syndrome in dogs: clinical features and evidence-based treatment considerations. *Topics in Companion Animal Medicine*, *26*(3), 135-142.

Konta, M., Nagakawa, M., Sakatani, A., Akabane, R., Miyagawa, Y., & Takemura, N. (2018). Evaluation of the inhibitory effects of telmisartan on drug-induced renin-angiotensin-aldosterone system activation in normal dogs. *Journal of Veterinary Cardiology*, *20*(5), 376-383.

Krieger, J.E., Liard, J.F., & Cowley Jr, A.W. (1990). Hemodynamics, fluid volume, and hormonal responses to chronic high-salt intake in dogs. *American Journal of Physiology-Heart and Circulatory Physiology*, *259*(6), H1629-H1636.

Kyles, A.E., Gregory, C.R., Wooldridge, J.D., Mathews, K.G., Aronson, L.R., Bernsteen, L., & Ilkiw, J.E. (1999). Management of hypertension controls postoperative neurologic disorders after renal transplantation in cats. *Veterinary Surgery*, *28*(6), 436-441.

LeBlanc, N.L., Stepien, R.L., & Bentley, E. (2011). Ocular lesions associated with systemic hypertension in dogs: 65 cases (2005-2007). *Journal of the American Veterinary Medical Association*, *238*(7), 915-921.

Lederle, F.A., Johnson, G.R., Wilson, S.E., Chute, E.P., Littooy, F.N., Bandyk, D., & Ballard, D.J. (1997). Prevalence and associations of abdominal aortic aneurysm detected through screening. *Annals of Internal Medicine*, *126*(6), 441-449.

Littman, M.P. (1994). Spontaneous systemic hypertension in 24 cats. *Journal of Veterinary Internal Medicine*, *8*(2), 79-86.

Littman, M.P., Robertson, J.L., & Bovee, K.C. (1988). Spontaneous systemic hypertension in dogs: five cases (1981-1983). *Journal of the American Veterinary Medical Association*, *193*(4), 486-494.

Lovern, C.S., Swecker, W.S., Lee, J.C., & Moon, M.L. (2001). Additive effects of a sodium chloride restricted diet and furosemide administration in healthy dogs. *American Journal of Veterinary Research*, *62*(11), 1793-1796.

Maggio, F., DeFrancesco, T.C., Atkins, C.E., Pizzirani, S., Gilger, B.C., & Davidson, M.G. (2000). Ocular lesions associated with systemic hypertension in cats: 69 cases (1985–1998). *Journal of the American Veterinary Medical Association*, *217*(5), 695-702.

Mahmood, S.S., Levy, D., Vasan, R.S., & Wang, T.J. (2014). The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *Lancet*, *383*(9921), 999-1008.

Marino, C.L., Cober, R.E., Iazbik, M.C., & Couto, C.G. (2011). White-coat effect on systemic blood pressure in retired racing greyhounds. *Journal of Veterinary Internal Medicine*, *25*(4), 861-865.

Mathur, S., Syme, H., Brown, C.A., Elliot, J., Moore, P.A., Newell, M.A., & Brown, S.A. (2002). Effects of the calcium channel antagonist amlodipine in cats with surgically induced hypertensive renal insufficiency. *American Journal of Veterinary Research*, *63*(6), 833-839.

Mentari, E., & Rahman, M. (2004). Blood pressure and progression of chronic kidney disease: importance of systolic, diastolic, or diurnal variation. *Current Hypertension Reports*, *6*(5), 400-404.

Michell, A.R., Bodey, A.R., & Gleadhill, A. (1997). Absence of hypertension in dogs with renal insufficiency. *Renal failure*, *19*(1), 61-68.

Misbach, C., Gouni, V., Tissier, R., Trehiou-Sechi, E., Petit, A.M.P., Carlos Sampedrano, C., & Chetboul, V. (2011). Echocardiographic and tissue Doppler imaging alterations associated with spontaneous canine systemic hypertension. *Journal of Veterinary Internal Medicine, 25*(5), 1025-1035.

Mishina, M., & Watanabe, T. (2008). Development of hypertension and effects of benazepril hydrochloride in a canine remnant kidney model of chronic renal failure. *Journal of Veterinary Medical Science*, *70*(5), 455-460.

Montoya, J.A., Morris, P.J., Bautista, I., Juste, M.C., SuárezRamírez, L., Pena, C., & Rawlings, J. (2006). Hypertension: a risk factor associated with weight status in dogs. *Journal of Nutrition*, *15*, 155-158.

Mooney, A.P., Mawby, D.I., Price, J.M., & Whittemore, J.C. (2017). Effects of various factors on Doppler flow ultrasonic radial and coccygeal artery systolic blood pressure measurements in privately-owned, conscious dogs. *PeerJ*, *5*, e3101.

Nelson, O.L., Reidesel, E., Ware, W.A., & Christensen, W.F. (2002). Echocardiographic and radiographic changes associated with systemic hypertension in cats. *Journal of Veterinary Internal Medicine*, *16*(4), 418-425.

Pappachan, M.J. (2011). Increasing prevalence of lifestyle diseases: high time for action. *The Indian Journal of Medical Research*, *134*(2), 143.

Perez-Sanchez, A.P., Del-Angel-Caraza, J., Quijano-Hernández, I.A., & Barbosa-Mireles, M.A. (2015). Obesity-hypertension and its relation to other diseases in dogs. *Veterinary Research Communications*, *39*(1), 45-51.

Quimby, J.M., Smith, M.L., & Lunn, K.F. (2011). Evaluation of the effects of hospital visit stress on physiologic parameters in the cat. *Journal of Feline Medicine and Surgery*, *13*(10), 733-737.

Rahimi, K., Emdin, C.A., & MacMahon, S. (2015). The epidemiology of blood pressure and its worldwide management. *Circulation Research*, *116*(6), 925-936.

Sangwan, T., Saini, N., Anand, A., & Bisla, A. (2023). Thoracic and abdominal aortic alterations in dogs affected with systemic hypertension. *Research in Veterinary Science, 159*, 133-145.

Sansom, J., & Bodey, A. (1997). Ocular signs in four dogs with hypertension.*Veterinary Record*, *140*(23), 593-598.

Sansom, J., Barnett, K.C., Dunn, K.A., Smith, K.C., & Dennis, R. (1994). Ocular disease associated with hypertension in 16 cats. *Journal of Small Animal Practice*, *35*(12), 604-611.

Sansom, J., Rogers, K., & Wood, J.L. (2004). Blood pressure assessment in healthy cats and cats with hypertensive retinopathy. *American Journal of Veterinary Research*, *65*(2), 245-252.

Schwartz, R.B. (2002). Hyperperfusion encephalopathies: hypertensive encephalopathy and related conditions. *The Neurologist*, *8*(1), 22-34.

Skelding, A., & Valverde, A. (2020). Non-invasive blood pressure measurement in animals: Part 1- Techniques for measurement and validation of non-invasive devices. *The Canadian Veterinary Journal*, *61*(4), 368.

Snyder, P.S., Sadek, D., & Jones, G.L. (2001).Effect of amlodipine on echocardiographic variables in cats with systemic hypertension. *Journal of Veterinary Internal Medicine*, *15*(1), 52-56.

Spencer, S. (2020). Management of Hypertension in Dogs. In *Hypertension in the Dog and Cat* (pp. 331-367), Springer, Cham.

Stepien, R.L., Rapoport, G.S., Henik, R.A., Wenholz, L., & Thomas, C.B. (2003). Comparative diagnostic test characteristics of oscillometric and Doppler ultrasonographic methods in the detection of systolic hypertension in dogs. *Journal of Veterinary Internal Medicine*, *17*(1), 65-72.

Syme, H.M. (2020). Epidemiology of Hypertension. In: *Hypertension in the Dog and Cat* (pp. 67-99), Springer, Cham.

Syme, H.M., Barber, P.J., Markwell, P.J., & Elliott, J. (2002). Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation. *Journal of the American Veterinary Medical Association*, *220*(12), 1799-1804.

Syme, H.M., Markwell, P.J., Pfeiffer, D., & Elliott, J. (2006). Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria. *Journal of Veterinary Internal Medicine*, *20*(3), 528-535

Thomas, E.K., Drobatz, K.J., & Mandell, D.C. (2014). Presumptive cocaine toxicosis in 19 dogs : 2004- 2012. *Journal of Veterinary Emergency and Critical Care, 24*(2), 201-207.

Tilley, L.P. (1985). *Essentials of canine and feline electrocardiography: interpretation and treatment* (2nd edn.), Lea & Febiger.