Commissioned paper*

Feline Endocrine Hypertension

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SUMMARY

Endocrine hypertension in cats is more prevalent than previously thought. Predominant causes are primary hyperaldosteronism (Conn's disease), hyperthyroidism and diabetes mellitus. Other endocrine disorders with an impact on blood pressure rarely occur in the cat. Reliable measurement of both systolic and diastolic blood pressure is vital in identifying hypertension associated with these disorders. An understanding of blood pressure regulation and of the pathophysiology of hypertension development facilitates appropriate diagnostic and therapeutic efforts. Even if other causes of hypertension in a patient are found such as chronic kidney disease, it is important to realize that an underlying endocrine disorder may have been precipitating the renal damage.

Key words: cats, hypertension, hyperaldosteronism, hyperthyroidism, diabetes mellitus, blood pressure Doppler flow meter, High Definition Oscillometry

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Introduction

With the advent of easier to use and more reliable non-invasive blood pressure monitors more routine screening of cats has been carried out and feline hypertension is increasingly recognized. Elevated blood pressure can be referred to as secondary hypertension if an underlying disease is present that is known to cause high blood pressure. Hypertension with no evident underlying disease should be termed idiopathic. As in human medicine, systemic hypertension can be subdivided into isolated systolic, isolated diastolic and combined hypertension and all three can cause target organ damage. Underlying causes of feline hypertension are mainly chronic kidney disease (CKD) and endocrine diseases such as hyperthyroidism, hyperaldosteronism, hyperadrenocorticism and diabetes mellitus.[8] With CKD hypertension is common and therefore is frequently screened for. When searching for endocrine causes of hypertension, hyperthyroidism is often the only disease considered. This leads to missed diagnoses such as hyperaldosteronism (Conn's disease) but also hyperadrenocorticism and diabetes mellitus.
Endocrine hypertension is also under-diagnosed as a result of the choice of diagnostic tools used. With the Doppler flow meter (Doppler), diastolic blood pressure usually cannot be reliably diagnosed. For this reason, and because systolic measurements often underestimate systolic pressure (closer to mean), studies performed with that technology may not reflect the true blood pressure situation. Understanding basic blood pressure regulation but also understanding the features and limitations of the technology in use, are as important as knowledge of symptoms of the possibly underlying disease and its diagnosis.

Regulation of blood pressure

Blood pressure is regulated by many mechanisms, including the central nervous system, the baro- and chemoreceptors, the sympathetic and parasympathetic nervous system, circulating hormones and local metabolites acting on vasodilation and vasoconstriction (see Table 1). This complex situation explains the variances in measurement even in a completely relaxed animal and supports the

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Table 1: Main influences on systemic vascular resistance (SVR) affecting blood pressure[26]

Source	Increase of SVR	Decrease of SVR
Neurohormonal	Increased activation of the sympathetic NS	Decreased activation of the sympathetic NS
Endothelium	Endothelin I, Thromboxane A2	Prostacyclin, nitric oxide
Circulating hormones	Epinephrine (adrenalin), norepinephrine (noradrenalin), angiotensin II, antidiuretic hormone	Atrial natriuretic peptide, kinins, histamine
Other factors	Decreased temperature	Increased temperature/K+/ lactate/ PaCO2/pH

need for a stress-free environment and procedure when measuring blood pressure.

Blood pressure (mean arterial pressure – MAP) is determined from cardiac output (CO) and total peripheral resistance (TPR):

MAP = CO x TPR

CO = stroke volume (SV) x heart rate (HR)

SV = diastolic filling x contractility

TPR is mainly affected by vascular status (systemic vascular resistance /SVR - vasolilation vs. vasoconstriction). Blood viscosity can further contribute but plays a minor role.

Hypertension occurs when the regulation of blood pressure lacks negative feedback after a compensatory up-regulation, initiated by direct or indirect hypovolaemia.

One of the most important mechanisms involved in the development of hypertension is the renin-angiotensin-aldosterone system (RAAS). Decreased arterial pressure, decreased tubular sodium/chloride and activation of the sympathetic nervous system lead to renin secretion, transforming angiotensinogen into angiotensin I and then via the angiotensin converting enzyme (ACE) activating angiotensin I to angiotensin II.

Angiotensin II effects are manifold, such as increasing sympathetic activity, tubular sodium and chloride reabsorption and consequently water retention accompanied by potassium excretion. It has an effect on the adrenal gland, leading to aldosterone secretion, further contributing to water retention. Aldosterone production can also be stimulated by increased potassium levels. Javadi et al. (2005) pointed out that aldosterone leads to glomerular sclerosis, tubular atrophy, arteriosclerosis and interstitial fibrosis, explaining the close relationship between hyperaldosteronism and CKD.[25]

Angiotensin II is also known to act as a very potent vasoconstrictor, directly affecting blood pressure. It increases ADH secretion via stimulation of the pituitary gland, stimulating water absorption in the collecting duct.

All these influences lead to an increase in blood pressure. Angiotensin II further acts on the podocytes of the basal membrane of the glomeruli leading to proteinuria. It is a growth factor and activates other growth factors (e.g. prostaglandin 2∝) resulting in glomerulosclerosis and arterial stiffening, which further increases SVR. Thus angiotensin II and aldosterone both have an effect on endothelial function.

Reliable blood pressure measurement

Since the American College of Veterinary Internal Medicine (ACVIM) Hypertension Consensus Panel published guidelines for the diagnosis and management of hypertension in dogs and cats[8], standards have been set up to evaluate non-invasive blood pressure units.

These guidelines require a unit to be tested against a true gold standard invasive technique. For a direct method to be considered a gold standard, the technique has to be performed properly with the system being calibrated statically but also dynamically and accuracy has to be verified if a water filled catheter with external transducer is used (determination of dynamic range and damping coefficient). Ideally the pressure transducer is placed inside the artery. Direct blood pressure is not a gold standard if not performed correctly and without an understanding of the limitations of this blood pressure measurement technique.[39,21]

ACVIM Guidelines[8]:

- Evaluation in comparison with invasive technology in conscious dogs and cats.
- Evaluation in compliance with adapted standards according to the Association for the Advancement of Medical Instrumentation (AAMI):
  - Mean difference (bias) of paired measurements ± 10 mmHg, standard deviation max. 15 mmHg
  - 50% of measurements within a deviation of max. 10 mmHg, 80% of measurements within a deviation of max. 20 mmHg

Table 2: HDO results compared to ACVIM guideline requirements[36]

Parameter	Bias (mmHg)	% of paired measurement within 10 mmHg	% of paired measurement within 20 mmHg
ACVIM guideline requirements	±10 mmHg	50%	80%
Martel al. (2013) [35]	-2.2 ± 1.1	88 % ± 3	96% ± 2

- Published in a peer reviewed journal

Neither Doppler flow meter nor conventional oscillometric devices (e.g. petMAP®, SurgiVet®, Cardell®) fulfilled these guidelines.[8,35,47,13] Very recent data even suggest that Doppler cannot be considered as a reliable technique in cats to determine blood pressure.[13]

Martel et al. (2013) compared high definition oscillometry (HDO) to a Data Sciences International™ implanted system and challenged blood pressure pharmacologically to reach hypotensive and hypertensive situations in conscious cats.[35] Systolic arterial pressure (SAP) showed a mean correlation coefficient of 0.92 ± 0.02 with individual correlation as high as 0.98 and for DAP 0.81 ± 0.02. The slightly lower correlation for diastolic arterial pressure (DAP) was discussed as being due to the difference of arterial wall structure in more central versus peripheral arteries.[35] In this study, ACVIM requirements have been fulfilled (Table 2). Similar results have been shown in dogs.[37,38]
In summary, the authors conclude that, 'HDO is the first and only validated non-invasive blood pressure device and, as such, it is the only non-invasive reference technique that should be used in future validation studies.'[35]

HDO non-invasive pulse wave analysis (PWA)

HDO is a patented new technology, allowing very sensitive and fast analysis of incoming signals and even real-time assessment of the pulse wave (Fig 1). Due to its speed it scans incoming signals and actually measures all 3 pressures: systolic, diastolic and mean arterial pressure compared to conventional oscillometry which only measures the strongest signal as mean arterial pressure, calculating systolic and diastolic pressure with an algorithm. This also allows for pulse pressure interpretation (pulse pressure = systolic – diastolic pressure), currently considered to be much more closely correlated to pressure induced arterial damage and remodelling than either systolic, diastolic or mean arterial pressure.[6,27]

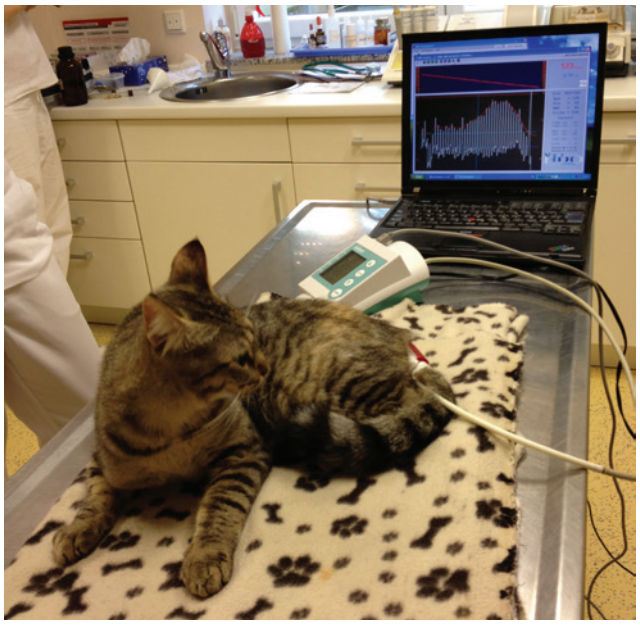

Fig 1. A feline patient linked up to a high definition oscillometry (HDO) device. Blood pressure is also being measured.

HDO visually displays the pulse waves in real time on screen, offering additional features to the practitioner:

1) Visualisation of the reading quality: identify a good reading and immediately realise if artefacts occur.
2) Rhythm information: similar to an ECG. The pulse wave-to-pulse wave interval is the same as R-R intervals on an ECG. Different intervals reflect an arrhythmic situation (Figs. 2a and b).
3) Information on arterial compliance (systemic vascular resistance /SVR): early presystolic amplitudes provide information on arterial compliance.[1,2,16] Main influence on arterial compliance can be expected with an increased activity of angiotensin II and in the case of arterial remodelling (angiotensin II and aldosterone mediated) being present. Impaired arterial compliance/ arterial stiffness can be identified in an increase in size of the pre-systolic amplitudes (Fig. 2c).
4) Information on stroke volume variances (SVV). In a stable cardiac output situation, pulse wave amplitudes increase and later decrease consistently beat by beat, whereas they differ in height if there is any impact on stroke volume, like arrhythmias, mitral regurgitation,

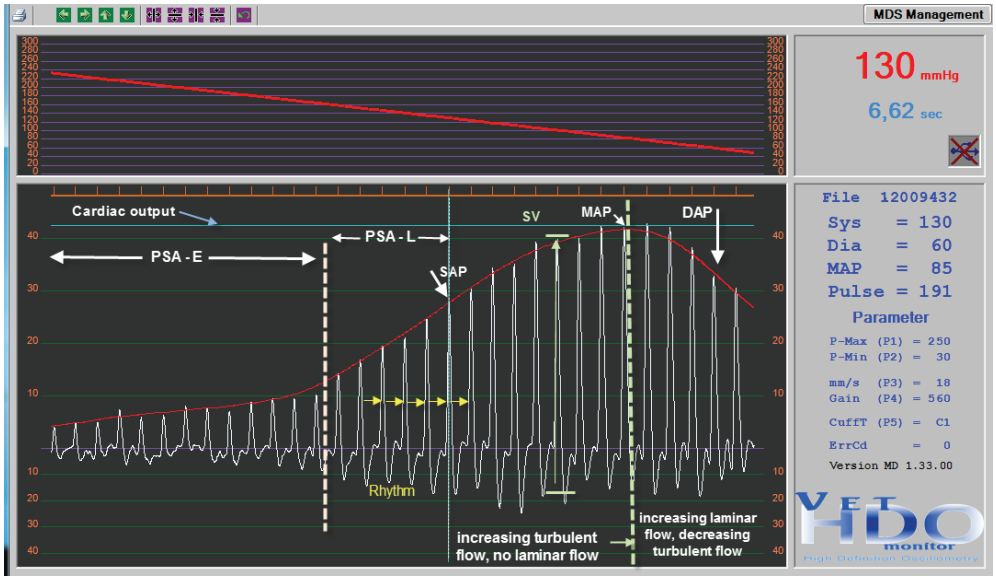

Fig. 2a. Normal HDO curve of a complete reading. From the right: pre-systolic amplitudes (PSA), followed - with continuous deflation of the cuff - by the opening behaviour of the artery (bell shape). Due initially to turbulent flow, amplitudes gradually increase up to a maximum: mean arterial pressure. At this stage, centrally laminar flow can be found resulting in decreasing amplitude height.

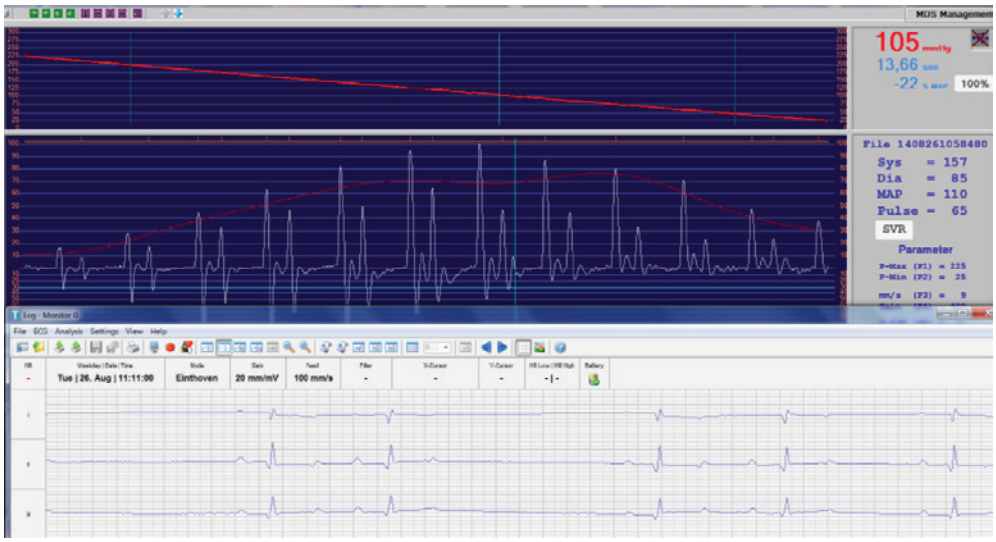

Fig. 2b. HDO curve with intermittent sinus arrest. Note the impact of the arrhythmia on stroke volume (SV) due to prolonged diastolic filling, increased contraction due to the Franck Starling law.

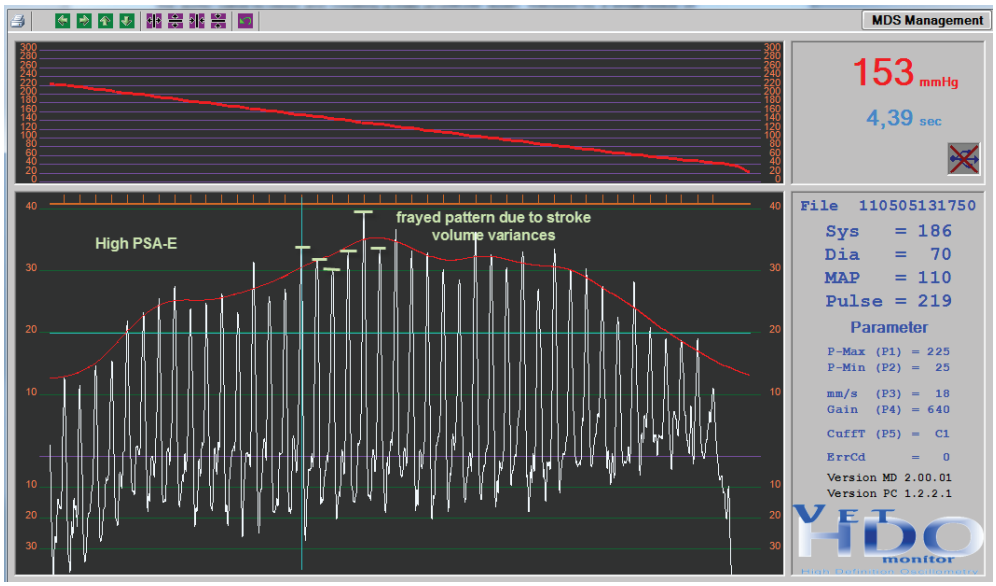

Fig. 2c. HDO curve of a cat with severe systolic hypertension. The first amplitudes - referred to as early Pre-Systolic Amplitudes (PSA - E) - are high, indicating increased systemic vascular resistance (SVR). Stroke volume beat-by-beat varies (height of single amplitudes).

aortic stenosis, myocardial disease etc. (Fig. 2c). SVV can be interpreted qualitatively to add information about the severity of the haemodynamic impact of such a situation and consequently, it may support the decision, how aggressively for e.g. an arrhythmia needs to be treated.

These additional features of the HDO technology might be particularly helpful in diagnosing endocrine hypertension and related cardio-vascular changes.

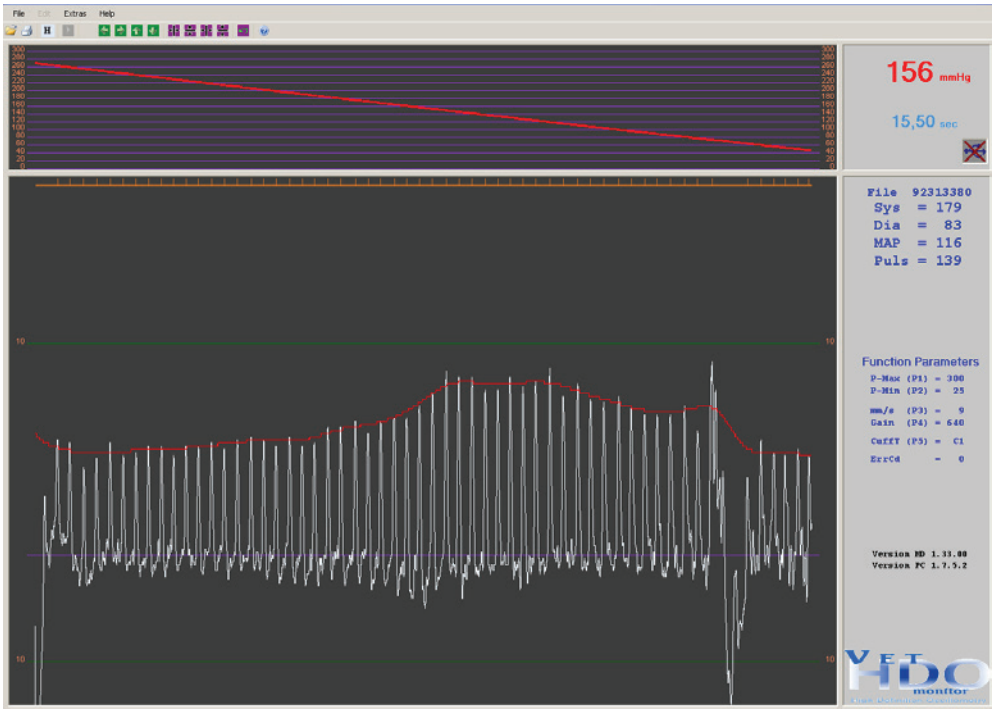

Fig. 2d. A cat with hypertensive left ventricular hypertrophy. High pre-systolic amplitudes (at the beginning of the trace) indicate impaired systemic vascular resistance, overall height of the bell shape curve is below 10% (10 at the left and right side of the window) indicating impaired cardiac output, single amplitude are more or less stable (no significant stroke volume variances). At the last part of the reading, an artefact appears.

Measuring blood pressure in a clinical environment

Blood pressure measurement today can be done easily and rapidly. Blood pressure is continuously influenced by different regulatory mechanisms so that it is possible to see considerable variation in sequential readings. Because of this, a minimum of three or better five consecutive readings should be performed and the average interpreted. With the right protocol, this only takes 2-3 minutes, which can easily be integrated into the normal physical examination of a patient. It is important to follow the ACVIM guidelines[8] for accurate measurement:

1) **Quiet environment.** This simply means: heavy traffic areas and sudden noises need to be avoided. In particular also one should ensure that nobody comes in or leaves the room while running a measurement (Fig 3).
2) **Observe the cat** while you obtain history details from the owner. The observation will give you important information regarding behaviour that can help you decide which position the cat might tolerate. Blood pressure measurement should ideally be at the beginning of a physical exam since taking of rectal temperature and blood sampling, can significantly influence blood pressure.[7] In general; the less an animal needs to be restrained, the better. Cats can be measured in their carrier, on the table (ideally on a blanket or towel) or on the owner's lap.
3) **Special attention should be paid to the animal.** During the measurement, they should be kept calm and reassured to avoid agitation and sudden movements. Watching the pulse waves and the animal during the measurement further aids in detecting artefact and determining its likely source. Readings should be taken one after another. As a single reading only takes 8-15 seconds in cats, the whole measurement cycle can be finished in 2-3 minutes.

Fig 3. A quiet, safe environment is essential for reliable blood pressure measurements in cats.

4) **Position the cuff at the same height as the base of the heart.** This is usually the case when the cuff is positioned on the tail or a limb when the animal is lying down. If an animal is standing this is usually only the case on the base of the tail. Tail measurements are less prone to artefacts even with some movement. Overall, tail measurements are easier, better tolerated and it is usually the fastest way to get 3-5 good readings.
5) **Score the environment and the patient** to better judge the possible influence of stress. Analyse the pulse waves for stress influence, too. This helps to differentiate true hypertension from stress induced or 'white coat' hypertension. Information given by the pulse waves can be: frayed pattern, due to the impact of catecholamines on stroke volume variances, mildly elevated pre-systolic amplitudes as a result of mild vasoconstriction due to catecholamines, and comparing the pulse waves of consecutive readings. With stress related changes, pre-systolic amplitudes should decrease with time (in contrast: hypertensive pulse waves reflect same situation over all readings).

Definition of Hypertension

In 2007, the ACVIM hypertension consensus panel published guidelines, which also included a classification system for hypertension which is widely accepted (Table 3).[8]
It is based on the risk for target organ damage (TOD) in relation to both systolic and diastolic blood pressure. ACVIM consensus guidelines do point out that it is important to evaluate both systolic and diastolic blood pressure.
Prevalence of hypertension in a large feline population was shown to be at least 31%.[11] Based on this, it is vital that blood pressure measurement be carried out in cats with symptoms for which hypertension cannot be excluded. As 84% of the affected cats in that study were older than 10 years, blood pressure should be measured as part of the routine physical examination of geriatric cats.[11] This is also reflected in the AAFP guidelines which recommend blood pressure measurement in all cats over 11 years of age.[54]

The kidney can be involved in hypertension as a target organ for damage but also as the source of hypertension. Kidney disease results in impaired auto-regulation, so that systemic hypertension can easily lead to glomerular hypertension, proteinuria and thus further damage to the kidney. In fact, up to 100% of cats with hypertension and TOD to the eyes show signs of chronic kidney disease.[45,34,32] As azotaemia is not always present in cats with early stages of kidney disease, blood pressure, urine specific gravity, UPC (Urine protein/creatinine ratio) and pulsewave analysis for detection of an increase in systemic vascular resistance (SVR) due to angiotensin II mediated vasoconstriction may increase suspicion of early CRD (Fig. 2d).

Endocrine hypertension in cats

Hyperthyroidism

The published prevalence of hypertension with hyperthyroidism is variable. Values range from 9% to 87%.[31,40,56] Part of this variation can be explained by differing blood pressure technologies, differing definitions of hypertension and variability caused by use of just systolic or systolic and diastolic pressures. In some studies additional criteria were used to define hypertension, especially with regard to the presence of hypertensive retinopathy or choroidopathy.

The pathophysiology of blood pressure related changes in hyperthyroidism has been thoroughly looked at in human medicine. The main trigger has been found to be the direct and indirect impact of tri-iodothyronine (T3). The T3 effect on vascular smooth muscle in combination with an increase of local vasodilators leads to a decrease in systemic vascular resistance (SVR). With an increase of vasodilatory influences, diastolic blood pressure drops, causing a reflex dependent increase in cardiac output due to an increase in stroke volume and heart rate. This

Table 3. ACVIM consensus guidelines for classification of elevated blood pressure[8]

Risk of TOD	Risk category	SBP mmHg	DBP mmHg
Minimal	I	<150	<95
Mild	II	150-159	95-99
Moderate	III	160-179	100-119
Severe	IV	>180	>120

TOD = target organ damage, SBP = systolic blood pressure, DBP = diastolic blood pressure

Table 4: Target organ damage in cats (video for examination for target organ damage to the eyes and to the heart)[17]

Target Organ	Symptoms	Prevalence	Reference
Eye	Hypertensive retinopathy/choroidopathy (tortuous retinal vessels, (punctate) retinal haemorrhage, focal bullous or complete retinal detachment and consequently sudden onset of blindness, hyphaema, mydriasis, anisocoria etc.	60-80% Most often reported with SBP >168 mmHg	Sansom et al. 1994, Syme et al. 2002, Elliott et al. 2001
Cardio-vascular	Left ventricular hypertrophy, Echo: mainly asymmetric concentric hypertrophy resulting in a functional mitral valve insufficiency and systolic murmur, gallop rhythm, arrhythmia, possible findings in EKG: wide QRS complexes, high R wave, wide P wave, deep S wave, X-Ray: wide/tortuous thoracic aorta, epistaxis	Over 70% - 85% If additionally retinal damage can be found, cardiac remodeling is more severe	Elliott et al. 2001, Snyder et al. 2001, Chetboul et al. 2003
CNS	Hypertensive encephalopathy, hyperplastic arteriosclerosis of cerebral vessels, oedema, (micro) haemorrhages and consequently increased intracranial pressure leading to CNS symptoms: ataxia, seizures, vocalization, head pressing, somnolence, sudden onset of aggression or other behavioral changes	29 - 46 % Mainly severe hypertension or sudden severe increase of blood pressure	Littman 1994, Maggio et al 2000 Brown et al. 2005
Kidney	Glomerular hypertrophy, glomerulosclerosis, interstitial fibrosis, development/progression of azotaemia, decrease of GFR, proteinuria, microalbuminuria	53% - 62%	Chetboul et al. 2003 Syme et al. 2006 Jepson et al. 2007

increase is mild and does not lead to a significant increase in systolic blood pressure. Still elevation in systolic blood pressure can be found in some hyperthyroid patients and may be a result of activation of the RAAS in response to a reduced renal perfusion due to vasodilation.[43,42,29,33] Also an up-regulation of RAAS in direct response to hyperthyroidism has been suggested by Williams et al. (2013), as levels became normal with treatment as a result of reaching euthyroidism.[56] Elevated blood pressure might also be attributed to a higher blood viscosity through stimulation of erythropoietin by T3.[33] Additionally, there is a direct effect of T3 on the heart. It upregulates ß-receptors in the myocardium leading to positive inotropy and chronotopy. Additionally, T3 mediated effects on alpha myosin and beta myosin as well as calcium-activated ATPase contribute to increased myocardial contractility.[20] This explains, why hypertension can be seen in some hyperthyroid patients independently of underlying kidney disease. If the unmasking of kidney disease occurs with treatment of hyperthyroidism, blood pressure can rise immediately, while in the absence of underlying kidney disease there was a median time of 5.3 months till blood pressure rose.[40] It is important to realize that initially normotensive cats with hyperthyroidism can develop hypertension with treatment initiation (23% in one study).[56] This supports the importance of implementing regular blood pressure measurements in cats with hyperthyroidism, both at initial diagnosis and during treatment.

What blood pressure-related information can be expected?

- Mild to moderate systolic hypertension
- Normal to decreased diastolic blood pressure
- Increased pulse pressure
- Increased heart rate
- Changes in HDO pulse wave analysis can include: frayed pattern due to stroke volume variances, tachycardia, changes in pre-systolic amplitudes due to effects on SVR

The measurement of cats with hyperthyroidism is not always easy. If a unit with automatic loop function and transfer of saved measurements to a PC for a later evaluation (e.g. HDO) is available, a measurement in a restraint cage could solve the problem. Animals in such a cage cannot turn around. The cuff should be placed around the base of the tail and hooked up outside the cage to the unit, which is set up to loop (automatic measurements, ideally every 1-2 minutes). Then the cat should be placed in a quiet room for 30 – 45 minutes while automatic measurements are taken. Readings can be transferred via Bluetooth to a computer outside the room or downloaded later for analysis. Generally, cats get used to this procedure and the last 10 – 20 readings are rarely affected by excitement. Effect of excitement can be identified in the pulse waves as mentioned above.

Diagnostic test for hyperthyroidism: total thyroxin concentration (TT4) above the reference range (> 55nmol/L; 4.26 µg/dL)

Hyperaldosteronism (HA)

Primary (PHA) and secondary hyperaldosteronism can occur in the cat and seem to be far more prevalent than previously thought. This is of increasing interest as PHA may lead to progression of CKD.[25] More recent studies point out that PHA may not be a rare cause of feline hypertension[25,5,14] and likely up to 20% of hypertensive cats may suffer from PHA.[44]

PHA or Conn's disease can result from hyperplasia or an aldosterone producing adenoma or carcinoma of the adrenal cortex. A familial predisposition may be present.[3,25] Keele et al (2009) reported adrenocortical hyperplasia in 95% of geriatric cats presented with CKD and hypertension.[28]

In comparison to secondary (often renal) hyperaldosteronism, an increased plasma aldosterone concentration (PAC)/plasma renin activation (PRA) ratio is seen with primary PHA.[28] This ratio is decreased in secondary HA.[25]

Normal values are considered to be PAC/PRA ratio 0.3 – 3.8.

Laboratory changes which might occur with PHA are:

- High PAC/PRA ratio
- Hypokalaemia
- Elevated creatinine kinase
- Hypernatraemia
- Increased BUN

Ultrasonographic changes indicating adrenal enlargement/hyperplasia or an adrenal mass may also be helpful.

Adrenal hyperplasia seems to contribute to a more significant increase in blood pressure than adrenal tumours. Hyperplasia also appears to be the more frequent cause of PHA. This may explain why typical symptoms of hypokalaemia, like muscle weakness, paresis and cervical ventroflexion are rather rare in cats with bilateral hyperplasia compared to hypertension. In a study on bilateral hyperplasia systolic blood pressures measured via Doppler were between 185-270 mmHg.[25]

Hypertension is mainly a result of increased blood volume due to aldosterone-mediated sodium retention, potassium diuresis and fluid retention. Extracellular volume increase leads to an increase in cardiac output. More recently, effects on vascular tone and vascular remodelling with resulting endothelial dysfunction have been documented. Arterial hypertension in primary hyperaldosteronism has to be looked at as a multifactorial process, influenced by increased extracellular volume, increased sympathetic activity and increased systemic vascular resistance (SVR).[52,23]

The prevalence of hypertension is high in primary hyperaldosteronism. Over 90% of cats with Conn's disease showed severely elevated systolic pressures.[25,5] It is also very possible that primary hyperaldosteronism has a higher incidence than currently diagnosed. It is one of the most common feline adrenocortical disorders.[14] Feline patients with hypertension may warrant testing for Conn's disease.

Symptoms of PHA: In a study of 11 cats diagnosed with primary hyperaldosteronism: hypokalaemia, paroxysmal flaccid paresis and retinal detachment/severe retinal haemorrhage were the most common presenting complaints (due to hypertension).[25]

Diagnostic tests for PHA include:

- Aldosterone: renin ratio (PAC/PRA)
- Urinary aldosterone-to-creatinine ratio (UACR)
- Oral fludrocortisone suppression test[14]
- Diagnostic imaging

Screening for PHA is recommended whenever a cat is presented with hypokalaemia or hypertension, especially when both are present concurrently. Mild azotaemia could also be an indication.

Treatment of Conn's disease includes potassium supplementation if hypokalaemia is present, amlodipine for blood pressure control and an aldosterone blocker (e.g. spironolactone).

Hyperadrenocorticism

Iatrogenic feline hyperadrenocorticism or Cushing's syndrome is rare. Spontaneous Cushing's disease can occur as a result of adrenal adenoma, carcinoma or pituitary adenoma which leads to an excessive secretion of cortisol. 80% of cats with hyperadrenocorticism are also diabetic.[41]

Symptoms are similar to Cushing's disease in the dog, but some are more specifically found in the cat,[55,24] and some are a result of the concurrent diabetes.

- Polyuria
- Polydipsia
- Polyphagia
- Lethargy
- Potbelly
- Central (mainly abdominal) obesity
- Muscle weakness
- Hepatomegaly
- Panting as a result of obesity, respiratory muscle weakness, decreased elasticity of airways
- Symmetric alopecia

- Secondary diabetes mellitus
- Immunosuppression
- Disturbances of haemostasis

Cutaneous atrophy (with or without open sores) and unregulated diabetes mellitus are specific symptoms in the cat.

The pathophysiology of hypertension in cats has not been investigated. In dogs and humans, RAAS activation may contribute to volume increase and vasoconstriction with increased SVR. Corticosteroids increase vascular sensitivity to catecholamines. Prostaglandin secretion is reduced suppressing vasodilation and thus supporting vasoconstriction and decreased arterial compliance. However effects on blood pressure are only mild to moderate.[30] Often, these cats have concurrent diabetes mellitus and/or glomerulosclerosis so that blood pressure elevation is likely the result of a complex interaction of various mechanisms.[12]

Phaeochromocytoma

Phaeochromocytoma is caused by a tumour of the chromaffin cells (phaeochromocytes) in the adrenal medulla, resulting in excessive but usually paroxysmal secretion of catecholamines. It is a very rare disease in cats but if present, very clinically significant. Phaeochromocytoma often causes episodic severe hypertension followed by normal blood pressure. Up to 325 mmHg systolic pressure has been reported.[44]
Other symptoms described are weight loss, anorexia, panting up to severe dyspnoea, lethargy and tachycardia as well as other cardiovascular symptoms like atrial fibrillation, ventricular fibrillation and pulmonary edema. [30] Hypertensive crisis can further lead to immediate onset of target organ damage, in particular of the eyes and the brain with the described symptoms.
Pathophysiology of hypertension is attributed to alpha and beta- receptor activation by catecholamines. Alpha receptor activation mainly leads to vasoconstrictive effects, leading to an increase of SVR and thus an increase of blood pressure.
Beta receptor activation is responsible for tachycardia but also increased contractility, increasing cardiac output. Both contribute to a substantial rise of blood pressure according to BP = CO x TPR.
Catecholamines further inhibit insulin and lead to a hypersecretion of renin. RAAS is activated as a result, which further contributes to hypertension.[30]
Diagnostic tests include repeated (ideally 24 hour) blood pressure measurements, diagnostic imaging and immunohistochemistry. Catecholamines can be measured in 24-hour urine samples, further laboratory testing should be focused on anaemia, leucocytosis with lymphocytopaenia, elevated alkaline phosphatase and alanine aminotransferase, and decreased levels of albumin.[30]
Treatment of the tumour requires surgical excision or irradiation. If not possible, blood pressure needs to be controlled primarily by using alpha blockers (like phenoxybenzamine or prazosin).[53]

Diabetes mellitus

Both type 1 and type 2 diabetes mellitus occur in the cat, with type 2 being most frequently found.
Diabetes mellitus can – rarely – be a result of Cushing's disease and as a consequence, in cats diagnosed with insulin resistant DM or with fragile, thin skin, testing for Cushing's disease should be considered.
In a large epidemiological study, 6% of hypertensive cats were diagnosed with hyperglycaemia (>200 mg/dL; reference range: 70 – 120 mg/dL[11]). Another study reported 9 out of 21 hypertensive cats to show increased serum glucose concentrations.[32]
Elevation in blood pressure can be partially attributed to an increase of catecholamine secretion as a result of insulin deficiency. Hypovolaemia and loss of sodium can lead to secondary hyperaldosteronism, contributing to hypertension. Diabetic microangiopathy and nephropathy are associated with impairment of arterial elasticity and vasoconstriction, which could predominantly effect diastolic blood pressure and SVR. Diastolic elevation has a clearly higher incidence than systolic hypertension in dogs with DM. Diastolic hypertension had a prevalence of 46% whereas only 12 out of 50 dogs showed systolic hypertension.[49] In humans, hypertension can be diagnosed in up to 60% of diabetic people. In human patients with Type 2 diabetes, blood pressure is often high at the time of diagnosis or even before, whereas in Type 1, hypertension usually develops later and often indicates development of diabetic nephropathy.[4] No study has looked at the importance of diastolic pressure in diabetic cats to date, most likely because most prior studies have been carried out with Doppler.
Given however that renal disease, diabetes and hypertension are intricately related, it is not possible to be certain which disease process is the causative process. When testing for diabetes, look for hyperglycaemia and glycosuria. Additionally, serum fructosamine might

be helpful. Transient diabetes may be present in cats secondary to pancreatitis and in obese cats.[30]
Specific treatment for hypertension is usually not necessary in diabetic cats, as blood pressure is only mildly elevated and treatment of diabetes usually normalizes blood pressure. If blood pressure is high or rises and is not affected by diabetes control, CKD might be the cause requiring antihypertensive medication. In any case, blood pressure should be monitored in diabetic cats.[30,11]

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