

ISFM Consensus Guidelines on the Diagnosis and Management of Hypertension in Cats

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Abstract

Practical relevance: Feline hypertension is a common disease in older cats that is frequently diagnosed in association with other diseases such as chronic kidney disease and hyperthyroidism (so-called secondary hypertension), although some cases of apparent primary hypertension are also reported. The clinical consequences of hypertension can be severe, related to ‘target organ damage’ (eye, heart and vasculature, brain and kidneys) and early diagnosis followed by appropriate therapeutic management should help reduce the morbidity associated with this condition.

Clinical challenges: Despite being a common disease, routine blood pressure monitoring is generally performed infrequently, probably leading to under-diagnosis of feline hypertension in clinical practice. There is a need to: (i) ensure blood pressure is measured as accurately as possible with a reproducible technique, (ii) identify and monitor patients at risk of developing hypertension, (iii) establish appropriate criteria for therapeutic intervention and (iv) establish appropriate therapeutic targets. Based on current data, amlodipine besylate is the treatment of choice to manage feline hypertension and is effective in the majority of cats, but the dose needed to successfully manage hypertension varies between individuals. Some cats may require long-term adjuvant therapy and, rarely, additional therapy may be necessary for emergency management of hypertensive crises.

Evidence base: These Guidelines are based on a comprehensive review of the currently available literature, and are aimed at providing practical recommendations to address the challenges of feline hypertension for veterinarians. There are many areas where more data is required which, in the future, will serve to confirm or modify some of the recommendations in these Guidelines.

Introduction

Systemic arterial hypertension (referred to simply as hypertension in this document) is a well-recognised condition in cats, but probably remains significantly under-diagnosed. The clinical consequences of hypertension can be severe, due to target organ damage (TOD) affecting the eyes, heart, brain and kidneys¹, and some damage may be irreversible. Unless marked TOD is detected, the presence of hypertension is unlikely to be immediately apparent. Therefore, more widespread routine monitoring of feline blood pressure (BP) would likely enable an earlier diagnosis of hypertension and facilitate the prompt provision of effective therapy to prevent TOD and hopefully reduce the morbidity associated with hypertension.

Indirect measurement of BP in cats can be readily performed, although care is needed with both the choice and use of the equipment to ensure meaningful and accurate results are obtained. Systolic blood pressure (SBP) has been shown to increase with age in cats² as does the risk of hypertension.³ The majority of cats diagnosed with hypertension have other systemic disease(s) which may cause or contribute to the hypertension^{3,4}, although in up to 20% of cases no underlying cause is found.⁵⁻⁷ Cats with an underlying disease are often referred to as having 'secondary hypertension' although the relationship between the hypertension and the underlying disease may not always be understood. When secondary hypertension is found, there is a need to manage both the hypertension and the underlying disease concurrently.

These Guidelines have been created to offer practitioners up to date information on the causes, clinical signs, diagnosis and management of feline hypertension, as well as practical advice on measurement of BP and interpretation of results. Where clinical studies and scientific data are not available, these Guidelines represent consensus opinion of this panel.

Regulation of blood pressure

Blood pressure (BP) is the product of cardiac output (CO), which in turn is the product of heart rate and stroke volume ($HR \times SV$), and systemic vascular resistance (SVR). Thus: $BP = HR \times SV \times SVR$.

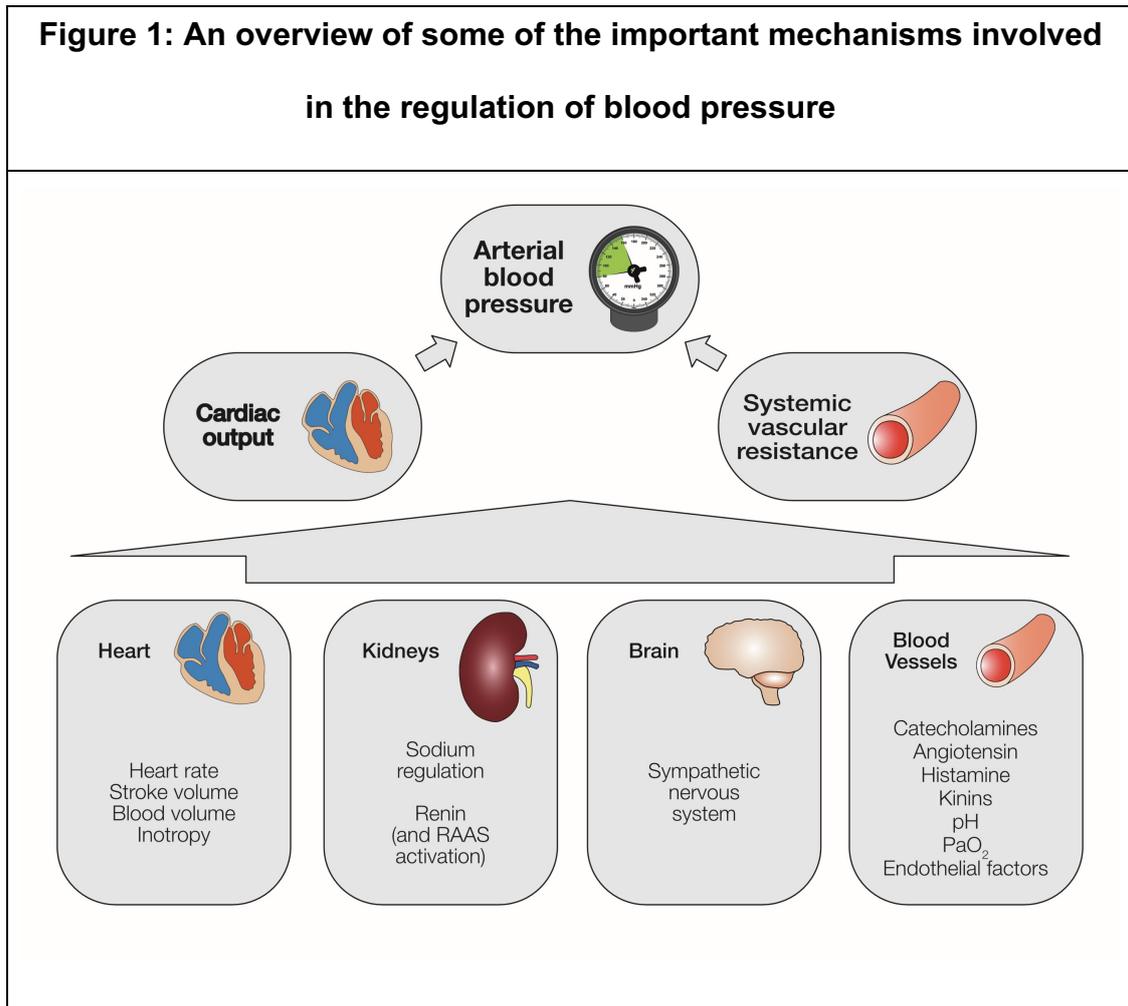
In health, despite potential changes to blood volume, CO and SVR, complex neural and hormonal homeostatic mechanisms involving the brain, heart, vasculature and kidneys, combine with local tissue factors to maintain BP within a relatively narrow range (Figure 1).

The predominant factor controlling SVR is arteriolar size, which is affected by many systemically circulating, local tissue and endothelial-derived factors (Figure 1).⁶ Blood volume is regulated by the kidneys, mainly through pressure natriuresis and the renin angiotensin aldosterone system (RAAS). Pressure natriuresis couples water and sodium excretion in response to changes in blood volume and CO (through alterations in renal perfusion) while RAAS directly affects SVR via the potent vasoconstrictor angiotensin II, and affects blood volume through renal reabsorption of sodium and water via aldosterone.

Some organs, including the kidney, have capacity to regulate their own BP ('autoregulation') to some extent. As a result, renal blood flow and glomerular filtration rate (GFR) are maintained over a range of SBPs (~80-160mmHg). Outside of these limits, and also when significant kidney disease is present, direct transfer of elevated pressures to the glomerular capillaries results in glomerular hypertension and the potential for glomerulosclerosis.

The pathogenesis of feline hypertension remains poorly understood and will vary with differing aetiologies. Altered renal function, RAAS activation and pressure natriuresis likely play a role, but local factors (including local [tissue-specific] RAAS activation) are increasingly recognised as possible contributors.⁸ The good response seen in many hypertensive cats to the use of the

vasodilator amlodipine^{5,6,9-15} suggests increased vascular tone may be a common component of feline hypertension.



Classification of feline hypertension

Hypertension is classified as:¹

- Idiopathic (or primary) where there is no apparent underlying disease, or
- Secondary (thought to be due to underlying diseases or the use of therapeutic agents).

‘White coat hypertension’ is the increase in BP that occurs as a consequence of excitement- or anxiety-related sympathetic activation. This is important in veterinary medicine as the neuro-hormonal changes associated with the stress and/or excitement surrounding a veterinary visit can create a temporary physiological increase in BP.^{16,17}

Idiopathic hypertension

Idiopathic hypertension is reported to occur in 13-20% of cats with hypertension.⁵⁻⁷ Further work is required to determine the degree to which non-azotaemic chronic kidney disease (CKD) might be a factor in some of these patients, and whether there are environmental factors or genetic predispositions as have been identified in humans with essential hypertension.¹⁸

Secondary hypertension

Secondary hypertension may be seen with many diseases including CKD, hyperthyroidism, primary hyperaldosteronism, hyperadrenocorticism, and phaeochromocytoma. Secondary hypertension is the most common form of hypertension seen in cats.

Chronic Kidney Disease

CKD is the most common condition associated with feline hypertension. Azotaemia has been found in up to 74% of hypertensive cats, and conversely between 19% and 65% of cats with CKD have

been found to be hypertensive.^{19–22} However, the prevalence and severity of hypertension does not appear to be related to the severity of the CKD.^{2,19,23}

In humans, factors such as sodium and water retention, activation of RAAS and the sympathetic nervous system, structural changes to arterioles, endothelial dysfunction, oxidative stress and genetics all play a role in the pathogenesis of CKD-associated hypertension.⁸

Less is known about the pathogenesis of hypertension in feline CKD, but the limited change in renin, aldosterone or BP in response to the use of angiotensin converting enzyme inhibitors (ACEi)^{24,25} suggests systemic RAAS activation is unlikely to be the major factor involved. Elevated aldosterone independent of RAAS activation is recognised in some hypertensive humans, and may also play a role in cats with hypertension.^{13,26} Some mechanisms worthy of investigation in cats with CKD-associated hypertension include local (tissue-specific) RAAS activation (independent of systemic RAAS), and impaired sodium handling by the tubules or collecting ducts^{18,27–29}, although there is limited evidence to suggest salt sensitive hypertension exists in cats.^{30–32} The profound response of cats with CKD-associated hypertension to amlodipine⁵ suggests that increased vascular tone may be particularly important, although this has not been specifically investigated.

Hyperthyroidism

Hypertension has been documented in 10–23% of cats with hyperthyroidism at the time of diagnosis^{21,33–35}, although some of these cats may also have had CKD. Additionally, nearly 25% of hyperthyroid cats normotensive at the time of diagnosis may develop hypertension after successful control of their hyperthyroidism.^{34–36}

The pathophysiology of hyperthyroid-associated hypertension remains poorly understood. Studies in other species suggest hyperthyroidism may increase cardiac sensitivity to circulating catecholamines, and thyroid hormones may also have direct effects on cardiac myocytes.³⁷

Hyperthyroidism may also decrease SVR (through direct and indirect effects on blood vessels) with subsequent stimulation of RAAS.³⁸ However, in studies of hyperthyroid cats, there is no evidence that RAAS activation causes hypertension, although RAAS dysfunction may be present in some cats that develop hypertension after treatment for their hyperthyroidism.³⁶

Primary hyperaldosteronism

Primary hyperaldosteronism (PHA) is an excess of aldosterone independent of its regulator, angiotensin II. Hypertension is reported in around 40-60% of cats with PHA^{39,40}, and could initially be the consequence of sodium retention and volume expansion leading to increased CO, but sustained hypertension should result in pressure natriuresis returning plasma volume to normal. This, together with the fact that not all cats with PHA develop hypertension, suggest that other mechanisms are involved⁴¹, potentially including effects on blood vessels, vascular tone, vascular remodelling and responses to sympathetic stimulation.⁴²⁻⁴⁴

Other diseases

Diabetes mellitus (DM) is a well-recognised risk factor for hypertension in humans, but there is little current evidence to show the same is true of cats, although further work is needed. Severe hypertension in cats with DM appears uncommon^{7,45}, and the prevalence of hypertension in cats with DM is typically low, but often confounded by the presence of concomitant conditions such as CKD.^{7,46} However, BP in cats with DM has been found to be higher than in healthy age-matched controls⁴⁷, and hypertensive ocular disease has occasionally been reported in diabetic cats with no other underlying cause identified⁷, suggesting a link could exist.

Phaeochromocytomas are rare tumours in cats⁴⁸⁻⁵² associated with excessive circulating catecholamines, which can result in sustained or paroxysmal bouts of hypertension. There is also a report of severe hypertension in a cat associated with hyperadrenocorticism (HAC)⁵³, although the prevalence of hypertension in cats with this disease is unknown.

Consequences and clinical signs of hypertension

Hypertension is most likely to cause disease in tissues with a rich arteriolar supply^{1,54}, and in the cardiovascular system as a result of increased SVR.^{1,54} The eyes, brain, kidneys and myocardium are thus particularly vulnerable and hypertensive injury to these tissues is known as ‘target organ damage’ (TOD).^{1,20,54} Clinical manifestations of TOD can be striking and may be the reason for presentation to the veterinarian.^{7,20,55} However, TOD is not always present and in some cats clinical signs of their underlying disease may predominate^{5,19,56}, or there may be no overt clinical signs.

Target organ damage: eyes

Hypertensive ocular changes have been reported in approximately 50% of hypertensive cats^{6,21,22,57}, and studies suggest that retinal changes can develop at a SBP of approximately 160 mmHg and above.^{58,59} However, the high prevalence of reported ocular lesions may reflect the relatively late diagnosis of hypertension in many studies.

The retina and choroid have separate blood supplies and both can suffer hypertensive damage⁶⁰, with an array of fundic lesions visible on ophthalmoscopy:^{7,61}

- Hypertensive retinopathy can manifest as haemorrhages of varying size and number^{21,55} (Figure 2)
- Hypertensive choroidopathy can cause changes in the appearance of the retinal vessels.⁷ Retinal oedema and breakdown of the blood-ocular barrier in the retinal pigment epithelium can create the impression that the vessels, particularly the arterioles, are narrowed⁶¹ (Figure 3)
- Hypertensive choroidopathy can also cause retinal detachment, which can appear bullous, flat, or may involve the whole retina⁶¹ (Figure 4), with the overlying retinal arterioles often

appearing more tortuous than normal.⁶¹ Photoreceptors often sustain irreversible damage from retinal detachment.⁶²

- Hypertensive optic neuropathy is diagnosed rarely in cats, possibly because the nerve head appears recessed, making pathology more difficult to appreciate⁶¹

Other ocular signs associated with hypertension include hyphaema and vitreal haemorrhage⁷, and hyphaema can lead to secondary glaucoma.⁵⁵

Many cats with severe hypertensive ocular damage present with blindness and bilateral mydriasis from complete retinal detachments and/or intraocular haemorrhage, with changes often irreversible.^{7,20,21} (Figure 5). Lesions that are not associated with impaired menace response or pupillary light deficits are much more amenable to antihypertensive treatment⁷, highlighting the importance of early diagnosis and management (Figure 6). Detection of early hypertensive ocular lesions requires an ocular examination to be performed on all cats at risk of developing lesions.

Target organ damage: brain

Hypertensive encephalopathy occurs when BP is high enough and sustained long enough to overcome the auto-regulatory ability of the cerebral vasculature.⁶³ Cerebral oedema and arteriosclerosis have been described in cats with hypertensive encephalopathy.^{64,65} Studies have reported neurological signs in 15–46% of hypertensive cats^{7,20,57,66,67} including disorientation, seizures, ataxia, depression and vestibular signs. Confirmation that clinical signs are due to hypertension is rarely achieved without advanced imaging, but a presumptive diagnosis can be made if signs improve following normalisation of BP.⁶⁵ Anecdotally, owners often report improvement in some behavioural signs (eg, depression, lethargy) after antihypertensive therapy.

Target organ damage: heart and vasculature

The elevated SVR associated with hypertension can increase left ventricular wall stress and result in concentric left ventricular hypertrophy (LVH). This may commonly produce auscultatory abnormalities such as gallop sounds, and perhaps less commonly murmurs and arrhythmias, in hypertensive cats.^{7,20,57} Echocardiography frequently reveals LVH^{57,68}, although the degree of hypertrophy does not correlate with the magnitude of hypertension.⁶⁹ Occasionally severe complications such as heart failure^{7,20}, or aortic dissection^{70,71} have been reported in affected cats.

Target organ damage: kidneys

A recent controlled study⁷² demonstrated increased glomerulosclerosis and arteriosclerosis in cats with higher BP, supporting the concept of kidney TOD in feline hypertension. However, such lesions are not only caused by hypertension, and as many cats with hypertension have concomitant CKD, the importance of hypertension in causing nephrosclerosis and in causing or contributing to the progression of CKD remains uncertain.⁷³

There is an association between the systolic BP and the magnitude of proteinuria in cats with CKD⁷⁴, and treatment with amlodipine reduces the proteinuria.⁶ This may be important as proteinuria has been linked to reduced survival in cats with either CKD^{74,75} or hypertension⁶, although managing hypertension has not yet been demonstrated to provide a survival benefit. In contrast, hypertension is recognised as both an important causal factor in human CKD, and a factor contributing to disease progression in human and canine CKD.^{8,76}

Patient groups benefiting from blood pressure measurement

Hypertension is much more common in older cats (>10 years old) with current studies suggesting a median age at diagnosis of 13 to 15 years^{6,7,57}, although it has been reported in cats as young as 5-7 years.^{7,12,20,22,53,59,65} As early diagnosis (and management) of hypertension is considered valuable to help prevent TOD, these data help provide a rationale for which cats should undergo routine BP assessment.

Additionally, as secondary hypertension is common in cats, individuals with recognised risk factors such as CKD, hyperthyroidism or PHA should undergo more frequent BP measurement. Further, the presence of any unexplained disease compatible with hypertensive TOD (eyes, brain, kidney and heart) warrants careful BP assessment.

Panel recommendations for monitoring BP in cats

Recommendations for monitoring of SBP	
Category	Frequency of SBP monitoring
Healthy adult cats (3-6 years of age)	Consider every 12 months*
Healthy senior cats (7-10 years of age)	At least every 12 months
Healthy geriatric cats (≥ 11 years of age)	At least every 6-12 months
Cats with recognised risk factors including: <ul style="list-style-type: none">• Underlying diseases: CKD, hyperthyroidism (including treated cats), PHA, HAC, pheochromocytoma, etc.• Drug therapy: e.g. erythropoietin^{77,78}• Evidence of TOD	Measure immediately and re-assess at least every 3-6 months

* The main purpose in this age group is to obtain baseline measurements for the individual cat. As few cats in this age category have hypertension, great care is needed in the interpretation of elevated BP measurements, especially in the absence of TOD or a clear underlying disease

Recommended equipment and procedures for measuring BP

Direct assessment of BP (via arterial cannulation) accurately measures systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP). Radio-telemetric implants allow direct BP measurements to be monitored over time in conscious animals, without direct intervention. However, this technique is not practical for clinical use in client-owned cats.^{54,79}

Equipment for routine clinical use

In clinical settings and with conscious cats, BP is usually measured using indirect techniques such as Doppler sphygmomanometry or oscillometry. The Doppler technique has been extensively used in feline medicine, with investigators demonstrating good correlation and accuracy compared with direct BP assessment.⁸⁰ It has been shown that traditional oscillometry is less accurate than Doppler in conscious cats, often underestimating BP at higher values, and there are many cats where it is difficult or impossible to achieve BP measurements with this equipment.⁸⁰⁻⁸⁵

Recently, high-definition oscillometry (HDO) equipment has been developed to overcome the problems with traditional oscillometry. Although there are fewer reports of its use in cats, it has been compared to direct BP assessment in conscious cats over a range of different BPs and shown to provide accurate results.⁸⁶ It also appears there are fewer cats where it is difficult to obtain a reading compared with traditional oscillometry.^{86,87} Notably, neither the Doppler nor HDO technique has been fully validated according to the ACVIM 2007 criteria.^{1,88} Although HDO equipment will generate figures for SBP, DBP and MAP, it has been shown that in conscious cats it is only the SBP value that has acceptable accuracy.⁸⁶ Further, although DBP can be measured with the Doppler equipment, this measurement also lacks acceptable accuracy and repeatability.^{80,89} However, systolic hypertension is generally thought to be the most clinically important form of hypertension, and although isolated diastolic hypertension may occur in cats¹, the limitations of

current measurement methodologies make this challenging to diagnose and any clinical significance uncertain.

As in other species, BP in cats is labile and varies considerably within and between individuals, depending in part on their level of arousal, activity or stress.^{16,79,90} Clinical assessment of SBP is also affected by many external variables including the operator, conditions, environment, equipment, position of the cat, size of the cuff, and site of measurement.^{16,17,80,81,87,89,91–94}

Panel recommendations on use of equipment and procedures

1. For assessment of BP and hypertension in conscious cats, either Doppler sphygmomanometry or HDO equipment should be used
2. Only SBP measurements should be used for clinical assessment (DBP and MAP readings are less accurate and should generally be ignored)
3. Use of standardised protocols (see box for panel recommendations) is imperative to improve the accuracy and reproducibility of measurements

Panel recommendations for standardised protocols to assess SBP in cats

1. Environment:

- The cat should be in a calm quiet room, away from other animals
- In a calm and quiet environment, SBP can sometimes be measured in hospitalised cats while they are in their cage
- Have the cat resting on its own bedding (with its own scent) and/or consider using a synthetic facial pheromone (Feliway®) in the environment or on the bedding which may help reduce stress⁹⁵

2. Acclimatisation:

- Allow the cat at least 5–10 minutes in the room to acclimatise¹⁷
- The cat should be free to explore the room and interact with people
- A cat carrier with a removable top will allow the cat to stay in the bottom of the carrier if it prefers

3. Personnel:

- Use the minimum number of people necessary (usually two)
- Having the owner present may be valuable if they are able to reassure the cat in a quiet, gentle way
- Having a trained, experienced individual measure SBP improves its reproducibility⁸⁹
- A nurse or technician who is empathetic with cats may often be the best person to measure SBP

4. Restraint and positioning of the cat:

- Using minimal and gentle restraint is vital
- Cats should be in a settled, relaxed, comfortable position
- If the cat becomes agitated, stop and let it settle rather than using firmer restraint
- Try to keep the cat in the same position throughout the procedure
- Avoid measuring BP while the cat is moving

5. Choice and position of cuff:

- The cuff width for cats should be 30–40% of the circumference of the limb/tail where it is used⁹³
- The site for BP measurement will depend partly on what is tolerated best by the cat, but the forelimb may be better for Doppler measurements⁹¹ while the tail is better for HDO⁸⁷
- Handle and manipulate limbs gently – older cats especially may suffer from osteoarthritis
- Where possible, the site of BP measurement should be roughly on the same horizontal plane as the heart
- Cuffs are usually secured with a Velcro fastener, fit them snugly but avoid restricting blood flow. A small piece of adhesive tape may also be used if necessary, but this should never be wrapped around the limb/tail

6. Using Doppler equipment

- Detection of blood flow requires good contact between the Doppler probe and the skin - this is best achieved with alcohol to dampen the hair and skin, and the use of plenty of ultrasound gel (figure)
- Clipping the hair at the site is not usually necessary. It may be considered if detection of blood flow is difficult, but use quiet clippers and allow the cat time to settle before measuring BP
- Ensure the inflatable portion of the cuff is positioned over the artery to be occluded
- Using headphones to avoid sound from the Doppler unit disturbing the cat is highly recommended; if not available ensure the volume is turned down when the procedure starts, and use the lowest volume needed to hear pulsatile blood flow
- Position the Doppler probe with gentle pressure to avoid restricting blood flow, and adjust the position slowly until pulsatile blood flow is heard
- Inflating and deflating the cuff a few times before making recordings helps the cat get used to the sensation
- Slowly inflate the cuff to 20–40 mmHg above the point where blood flow is no longer heard
- Allow air to slowly bleed from the cuff – SBP is the point when pulsatile blood flow is first detected

7. Using HDO equipment

- Patient movement can readily cause false SBP readings - using the tail and ensuring the cat is as still as possible helps to reduce this error^{86,87}
- The area where the inflation tube enters the cuff should be placed closest to the artery, as this maximises the sensitivity of the HDO equipment
- When the machine is activated, the cuff will automatically inflate and deflate at a constant rate, and BP values will be generated - **only** the SBP should be used
- The HDO should **always** be linked to a PC or tablet computer – this allows checking that the deflation of the cuff is steady and that the pulse waves are smooth, with an outline approximating a bell-shaped curve. If these criteria are not met, the reading should be discarded as unreliable (eg, due to movement artefact) (figure)

8. Measuring BP:

- The first SBP measurement is usually discarded, subsequently ideally 5–7 consecutive and consistent (<20% variability) measurements should be made and SBP calculated as the mean of these
- All readings should be recorded whether used to calculate SBP or not
- If there is a consistent downward (or upward) trend in readings or $\geq 20\%$ variation, further measurements should be made until consistent readings are achieved, using only the consistent readings to calculate the average SBP
- If there is doubt over SBP validity, the procedure should be repeated - either immediately, after further acclimatisation, or later. Consider also changing the placement of the cuff, and reassess the environment for causes of stress

9. Consistency:

- Careful records should be kept (Figure 7)
- For meaningful SBP comparisons in a cat, the assessment should be replicated using the same equipment, personnel and procedures as far as possible each time

International Cat Care have produced a set of videos (in various languages) on measuring blood pressure – these can be accessed by going to www.youtube.com/user/iCatCare and searching for ‘blood pressure’

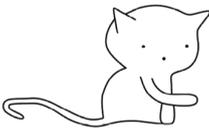
Figure: Example of a blood pressure assessment form



Blood pressure evaluation form

Date:	Cat's name:	Owner:	Clinician:
Age:	Sex:	Breed:	Time:

Position of the cat:


 Sitting


 Standing


 Sternal

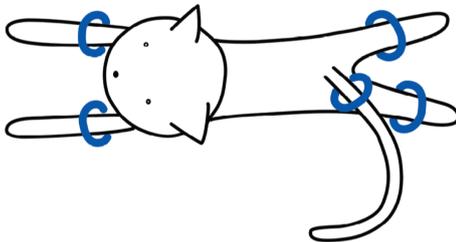

 Lateral

Other (specify):

Site of the cuff:

Right forelimb

 Left forelimb



Right hindlimb
 Tail
 Left hindlimb

Equipment used:	Size of cuff:
Location (room):	Others present:
Performed by:	

Subjective assessment of stress:

Relaxed Slightly tense Nervous Very nervous Aggitated

Record of all SBPs measured (mmHg):

1.	2.	3.	4.	5.
6.	7.	8.	9.	10.
11.	12.	13.	14.	15.

Mean Systolic Blood Pressure (mmHg):
Mean of stable values above (ignore outliers)

Defining normal blood pressure

Some studies have evaluated direct SBP, DBP and MAP in healthy cats using radio-telemetry (Table 1), the results of which were not dissimilar to other mammalian species, including humans.^{16,79,90,96} These studies also highlight the lability of feline BP in individual cats with one demonstrating up to 80 mmHg change in SBP in response to a simulated clinic visit¹⁶, showing the potential magnitude of ‘white-coat hypertension’ in healthy cats.

Table 1: Direct BP measurements (mmHg) in studies of healthy conscious cats			
Study and number of cats	SBP mean \pmSD	MAP mean \pmSD	DBP mean \pmSD
Brown et al (n=6) ⁹⁶	125 \pm 11	105 \pm 10	89 \pm 9
Belew et al (n=6) ¹⁶	126 \pm 9	106 \pm 10	91 \pm 11
Slingerland et al (n=21) ⁷⁹	132 \pm 9	115 \pm 8	96 \pm 8
Mishina et al (n=16) ⁹⁰	117 \pm 12	94 \pm 11	78 \pm 10

Establishing reference ranges of estimated SBP in healthy cats using Doppler or oscillometric equipment is fundamental to both the clinical diagnosis of hypertension, and also in determining therapeutic targets in affected cats. Results of studies in healthy cats are shown in Table 2, but it should be noted that there is a wide discrepancy between different studies reflecting, at least in part, the different populations examined, and differences in types of equipment used and the way equipment was used. Thus having a standardised technique is of paramount importance.

Unlike in humans, to date in feline medicine no gender or breed effects on BP have been identified^{56,94}, but similar to humans a recent large longitudinal study of cats established a small but significant increase in BP as cats age², equating to ~1-2 mmHg per annum for cats >9 years old. Humans with higher baseline BPs may be at higher risk for the future development of hypertension (termed pre-hypertension)⁹⁹⁻¹⁰¹, and there is evidence that the same may also be true of cats.²

Table 2: Indirect SBP (mmHg) measurements in studies of healthy conscious cats	
Equipment used and number of cats	SBP: mean (\pmSD)
Traditional oscillometric*	
Bodey & Sansom (n=104) ⁵⁶	139 (\pm 27)
Mishina et al (n=60) ⁹⁴	115 (\pm 10)
Curter et al (n=72) ⁹²	123
Morar et al (n=54) ⁹⁷	124
Haberman et al (n=13) ⁸⁰	133 (\pm 28)
Doppler sphygmomanometry	
Kobayashi et al (n=33) ¹⁹	118 (\pm 11)
Sparkes et al (n=50) ¹⁷	162 (\pm 19)
Lin et al (n=53) ⁹⁸	134 (\pm 16)
Bijsmans et al (n=124) ²	131
Conti et al (n=30) ⁹¹	135 (\pm 21)
Haberman et al (n=13) ⁸⁰	146 (\pm 50)
* Note traditional oscillometry not suitable for assessing clinical hypertension as it tends to under-estimate BP at higher values, and produces readings less reliably – see text	

The majority of cats reported in the literature to have TOD associated with hypertension have had indirect SBP measurements in excess of 160 mmHg^{5,7,14,20,22,53,55–57,59,64,65,71,102}, although there are occasional exceptions to this.⁵⁸ The International Renal Interest Society¹⁰³ (IRIS) has proposed four categories of BP in cats to help with the diagnosis of hypertension based on potential risk of TOD (Table 3). However, along with the lability of BP already noted, it is likely the TOD damage in hypertension will not only be related to the severity of the hypertension, but also to the duration and relative change in BP that occurs, thus strict categorisation is problematic.

Table 3: International Renal Interest Society staging for BP¹⁰³		
SBP (mmHg)	Category	Risk of TOD
<150	Normotensive	Minimal
150-159	Borderline hypertensive	Low
160-179	Hypertensive	Moderate
\geq 180	Severely hypertensive	High

Panel recommendations on criteria justifying anti-hypertensive therapy

While individual circumstances should always be carefully assessed, based on current knowledge the panel suggests that in general anti-hypertensive therapy is justified if SBP is measured carefully (see above) and when:

1. Indirect SBP is ≥ 150 mmHg on a single occasion, *and* there is clear evidence of ocular or neurological TOD. If clinical signs do not respond appropriately to adequate anti-hypertensive therapy, the diagnosis should be reassessed and other potential causes of the signs investigated
2. Indirect SBP is ≥ 160 mmHg on at least two separate occasions, *and* there is evidence of TOD including ocular, neurological, cardiac or kidney damage
3. Indirect SBP is ≥ 170 mmHg on at least two separate occasions, *and* the clinician does not consider 'white coat hypertension' is likely to be the cause
4. Indirect SBP is < 150 mmHg but where there is *clear* evidence of active ocular TOD. Cats should be monitored carefully – if there is any doubt about the diagnosis of hypertension the need for long-term therapy should be re-assessed by trial withdrawal of therapy once stable, and monitoring of BP and clinical signs.

Cats with evidence of potential TOD that have SBP < 150 mmHg should have their clinical signs and BP monitored carefully, and other potential causes of the signs investigated

Panel recommendations on investigation of hypertensive cats

Along with measuring SBP, when hypertension is diagnosed cats should be carefully evaluated for both TOD and the presence of underlying disease. Assessments should include:

- Complete physical examination (including thorough cardiac, neurological and ocular assessment, including indirect ophthalmoscopy) and thorough clinical history. Indirect ophthalmoscopy is a very valuable technique and readers are referred elsewhere for full details.¹⁰⁴
- Laboratory evaluation to identify any underlying disease(s):
 - Serum creatinine and/or SDMA
 - Urinalysis, including specific gravity and quantitative proteinuria assessment
 - Serum thyroxine
 - Serum sodium, potassium and chloride
- Additional investigations that may be of value include:
 - Diagnostic imaging (cardiac and abdominal imaging)
 - Serum aldosterone (ideally with measurement of renin or renin activity)
 - Further endocrine testing where appropriate (eg, dynamic adrenal function testing, glucose monitoring etc.)

Routine treatment of hypertension

Whenever hypertension is diagnosed, it is important to search for, and treat, underlying diseases as most cases of feline hypertension are secondary. However, treatment of underlying diseases is outside the scope of these guidelines, and does not obviate the need for appropriate anti-hypertensive therapy.

The goal of therapy for hypertension is to decrease the risk of TOD, and to help maintain or improve the health of the cat. This is generally achieved with an initial target SBP of <160mmHg¹, although the IRIS group¹⁰³ suggest the risk of TOD is minimal if SBP is <150 mmHg, and as some cats with TOD have pressures below 160 mmHg, a target of <150 mmHg may be an appropriate long-term goal.

Amlodipine besylate

Based on current data^{5,6,9,11,12,14,66}, the dihydropyridine calcium channel blocker amlodipine besylate is the drug of choice for the management of hypertension in cats, and there is now a product licensed for feline use in some countries.

Amlodipine is a potent peripheral arterial dilator that acts directly on vascular smooth muscle causing a reduction in SVR and BP with minimal cardiac effects.¹⁵ The reduction in SBP following treatment of hypertensive cats is generally around 30-70 mmHg^{5,6,11,12,14,66}, with 60%-100% of cats responding to amlodipine as a monotherapy, albeit with dose adjustment being needed in some.^{5,6,9,12,14} Amlodipine has also been shown to reduce the magnitude of proteinuria in hypertensive cats with CKD.^{6,74} Adverse events associated with amlodipine therapy appear uncommon.^{12,15} Although hypotension is a rare complication^{5,15}, monitoring of SBP is always recommended.¹⁵

Amlodipine has typically been used orally, at a starting dose of 0.625mg/cat (or 0.125mg/kg) q24h, with doubling of the dose if response is inadequate within 1-3 weeks.^{5,6,9,11,12,14,66} The reduction in SBP appears to be dose-related^{9,105}, and thus cats with a higher SBP (eg, ≥ 200 mmHg) may benefit from starting at the higher dose (1.25 mg/cat or 0.25 mg/kg q24h).^{9,105} Infrequently, higher doses (up to 2.5 mg/cat or 0.5 mg/kg q24h) of amlodipine may be needed¹², but compliance should be checked as few cats appear to require these doses.^{5,6,9,11,12,14,66} Transdermal amlodipine has also been used in cats⁶⁷, but may be less effective than oral therapy and further studies are required to determine optimum dosage and formulation.

Other treatments

Angiotensin converting enzyme inhibitors^{24,25,106-108}, angiotensin receptor blockers (ARB)¹⁰⁷ and beta-blockers⁴ have all been used to treat feline hypertension, but they appear to have poorer efficacy in reducing SBP than amlodipine (typically only a reduction in SBP of 10-20 mmHg^{24,25,106-109}), and fewer cats respond adequately to their use as monotherapy. These drugs are therefore best considered as second (or rarely third) agents to add in to therapy if treatment with amlodipine is not sufficient to control the SBP¹¹⁰ (Table 4), or if their use is dictated by any concurrent or underlying disease.

The choice of adjunctive therapy to help manage hypertension may in part be dictated by any concurrent or underlying disease. For example, ACEi or ARBs may be indicated in CKD patients to help manage proteinuria, atenolol may be indicated in some hyperthyroid cats to manage tachycardia, prazosin (an alpha adrenergic blocker) may be indicated in pheochromocytoma, and spironolactone in hyperaldosteronism. These drugs are usually combined with amlodipine and titrated to effect.

Table 4: Drugs used for management of hypertension		
Drug	Suggested dose	Comment
Amlodipine	0.625 – 1.25 mg/cat q24h PO or 0.125 – 0.25 mg/kg q24h PO	Calcium channel blocker and drug of first choice. Dose may be doubled if response is inadequate up to a maximum of 0.5 mg/kg or 2.5 mg/cat q24h ^{1,12}
Benazepril	0.5-1.0 mg/kg q24h PO	ACEi ^{24,25,108,110}
Enalapril	0.5 mg/kg q12-24h PO	ACEi ^{24,25}
Ramipril	0.125-0.25 mg/kg q24h PO	ACEi ¹¹¹
Telmisartan	1 mg/kg q24h PO (experimentally, a dose of 3 mg/kg exhibited a greater effect on blood pressure) ¹⁰⁷	ARB, licensed at 1mg/kg q24h in some regions for management of CKD-associated proteinuria. Not assessed clinically for managing feline hypertension but greater response than benazepril to angiotensin I-induced pressor response when given at 1-3 mg/kg ¹⁰⁷
Atenolol	1-2 mg/kg q12h PO	β-blocker ¹⁰⁹

Panel recommendations for routine therapy and monitoring

1. Routine treatment of cats with hypertension should commence with amlodipine at 0.625 mg/cat (or 0.125 mg/kg) q24h
2. For cats with a SBP \geq 200 mmHg, consideration should be given to commencing therapy at 1.25 mg/cat (or 0.25 mg/kg) q24h
3. Cats with evidence of TOD at the time of diagnosis and/or cats with SBP \geq 200 mmHg should have their BP and clinical signs monitored closely during the first 24-72 hours. For some cats (eg, those with overt hypertensive encephalopathy or severe cardiac complications) hospitalisation may be required to allow close monitoring and control of the SBP. In other cases, initial daily re-evaluation may be sufficient. See also ‘Emergency treatment of hypertension’ below.
4. Cats without evidence of TOD should initially have their SBP reassessed at least every 7-10 days (depending on severity, concomitant disease etc.), together with evaluation of clinical

signs (including thorough ocular examination). Re-evaluation of laboratory parameters may also be prudent at this time, depending on the presence and severity of concomitant disease.

5. If response to therapy is inadequate, amlodipine dose can be doubled up to a maximum of 2.5 mg/cat (or 0.5 mg/kg) q24h. Dose increases are generally made at intervals of 7 days or more, but may be shorter (eg, after 24 hours) if the SBP is high (≥ 200 mmHg) or there is ongoing TOD (see 'Emergency treatment of hypertension', below).
6. If response to amlodipine is inadequate, or if concomitant disease suggests another antihypertensive agent would be useful (eg, persistent proteinuria), a second drug can be added together with the amlodipine
7. The short-term (ideally within 1-2 weeks) aim of therapy should be to reduce SBP to < 160 mmHg. In the longer-term (weeks) aiming for a SBP of < 150 mmHg may be prudent to minimise any risk of TOD. A safe lower limit for indirectly measured SBP in cats on anti-hypertensive therapy has not been well established, but the panel recommend SBP should be kept above 110 mmHg.
8. Once BP is controlled in cats, SBP should be reassessed at least every 3 months. Along with SBP measurement, clinical signs of TOD should be monitored (ocular examination, neurological examination and cardiac auscultation \pm echocardiography); and laboratory tests re-evaluated (eg, serum creatinine and/or SDMA concentrations, urinalysis with UPC ratio, assessment of other parameters as indicated). Fundic examination with indirect ophthalmoscopy¹⁰⁴ provides the easiest way to monitor the progress of ocular TOD with antihypertensive treatment (Figures). Once SBP is controlled there should be no further progression of lesions, but existing fundic lesions may take weeks to months to show improvement (depending on the presenting severity of the lesions and the control of SBP). Mild fundic lesions (eg, retinal oedema and small bullous lesions) respond better to anti-

hypertensive treatment than advanced lesions do (eg, retinal detachment, severe retinal haemorrhage).^{7,58}

Emergency treatment of hypertension

Rationale for emergency treatment

Hypertension is generally a chronic condition, although some cats may present with an acute onset of severe clinical signs associated with TOD (usually ocular, neurological or cardiovascular). Acute elevations of BP may also be seen in some diseases such as acute kidney injury. Although hypertensive emergencies are not as clearly established as in humans¹¹², the severity of TOD may prompt more aggressive anti-hypertensive therapy^{1,113}, even though there is a lack of definitive evidence that this approach is any more beneficial, and the risks of adverse events could be greater.¹¹⁴

Emergency treatment is aimed at halting ongoing TOD and preventing further damage. In human medicine, the initial goal of emergency therapy is to smoothly reduce SBP by up to 25% in the first 1-2 hours, and then towards a level of 160 mmHg within a total of 6 hours.⁹⁹ Uncontrolled, abrupt reduction in SBP or development of hypotension can precipitate myocardial, cerebral, or renal ischemia and should be avoided.^{115,116}

Cats requiring emergency therapy should be hospitalised for close monitoring of BP and treatment adjustments. Where feasible, direct arterial pressure monitoring is preferred, to provide the most accurate measurement of BP. Generally, anti-hypertensive agents (especially parenteral agents) should be titrated upward to effect.^{117,118} Amlodipine monotherapy may still be effective in emergency situations and should be used whenever oral administration is possible, safe and likely to be adequate. Detailed pharmacokinetic data of amlodipine use in cats are lacking, in humans peak serum concentrations occur after 6-8 hours¹¹⁹ and data provided for licensing in cats suggests it has peak serum concentrations at 3-6 hours in this species, with a half-life of 53 hours.¹²⁰ It has also been reported to have a BP lowering effect within 4 hours and to last up to 30 hours in clinical

cases.¹⁰ Parenteral treatments may need to be considered if the oral route cannot be used, if response to oral therapy is inadequate, or if an underlying disease dictates their use.

Table 5: Parenteral drugs that can be used for emergency management of hypertension		
Drug	Suggested dose	Comment
Hydralazine	0.2-0.5 mg/cat SQ, repeat after 15 min if necessary	Direct arterial vasodilator. Add a β -blocker if reflex tachycardia occurs ^{1,102,113}
Acepromazine	50-100 μ g/cat IV or SC	Phenothiazine and alpha-blocker, non-specific vasodilator ^{102,118}
Nitroprusside	1 μ g/kg/min CRI; titrate up to 3 μ g/kg/min if needed	Nitric oxide donor, non-specific vasodilator ¹¹³
Labetolol	0.25 mg/kg IV over 2 min, repeat up to a total of 3.75 mg/kg, then 25 mg/kg/min as CRI	α and β -blocker ¹
Esmolol	50–100 mg/kg/min CRI	β -blocker ^{1,113}

Panel recommendations

1. Hypertensive emergencies are those cats with hypertension and evidence of (or at high risk of) acute, severe and progressive TOD
2. Affected cats should be hospitalised and their SBP should be monitored frequently and carefully (eg, every 4 hours until the target SBP is achieved and then 2-4 times daily until stable).
3. Whenever possible oral amlodipine should be administered immediately at a starting dose of 0.625-1.25 mg/cat (or 0.125-0.25 mg/kg), depending on the severity of both clinical signs and SBP.
4. The dose of amlodipine could be repeated after 4-8 hours if necessary, in increments up to a maximum of 2.5mg/cat in the first 24 hours

5. If oral amlodipine cannot be used or if additional therapy is required, short-acting parenteral anti-hypertensive drugs can be administered (Table 5)

6. Once the cat is stable, standard treatment should be instituted (see 'Panel recommendations for routine therapy and monitoring' above)

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