Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation

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**Objective**—To determine prevalence of systolic hypertension and associated risk factors in cats with chronic renal failure evaluated in first-opinion practice.

**Design**—Prospective study.

**Animals**—103 cats with chronic renal failure.

**Procedure**—Systolic arterial blood pressure (SABP) was measured with a noninvasive Doppler technique, and cats that had SABP > 175 mm Hg on 2 occasions or that had SABP > 175 mm Hg and compatible ocular lesions were classified as hypertensive. Information from the history (previous treatment for hyperthyroidism, age), physical examination (sex, body weight), routine plasma biochemical analyses (creatinine, cholesterol, potassium, sodium, chloride, and calcium concentrations), and thyroid status were evaluated as potential risk factors for systolic hypertension. Variables associated with systolic hypertension were evaluated by use of logistic regression.

**Results**—20 (19.4%; 95% confidence interval, 13 to 28%) cats had systolic hypertension. Plasma potassium concentration was significantly and inversely associated with systolic hypertension.

**Conclusions and Clinical Relevance**—Prevalence of systolic hypertension, although clinically important, was lower than that reported previously. The cause of the inverse association between systolic hypertension and plasma potassium concentration is not yet known. (J Am Vet Med Assoc 2002;220:1799–1804)

*Systemic hypertension in cats has been recognized in association with a variety of diseases, including hyperthyroidism, chronic anemia, primary hyperaldosteronism, hyperparathyroidism, diabetes mellitus, a primary hyperaldosteronism, primary hyperparathyroidism, diabetes mellitus, and chronic renal failure (CRF). The prevalence of hypertension in cats with CRF that are referred to university teaching hospitals has been reported to be as high as 61% to 65%. However, cats examined in a referral setting may not be representative of the feline population as a whole.

One difficulty in establishing the prevalence of hypertension in cats is in determining the criteria by which this condition is defined. Hypertension has been defined as indirect systolic arterial blood pressure (SABP) > 141 mm Hg or 160 mm Hg or 170 mm Hg or 185 mm Hg. These various definitions of systolic hypertension reflect different techniques for blood pressure measurement and methods for determining the reference range, as well as differences in the origin of the cats that were studied. For the purposes of our study, hypertension was defined as SABP > 175 mm Hg on multiple occasions (measured by use of Doppler techniques) or SABP > 175 mm Hg on a single occasion in association with compatible clinical signs. This cut off value was chosen on the basis of SABP measurements in clinically normal cats at our clinics' and our clinical experience relating to evaluation of cats with clinical signs of hypertensive retinopathy. We presently recommend antihypertensive drug therapy for cats in which these criteria are fulfilled. This recommendation is broadly in accordance with that of other authors.

In our study, no attempt was made to diagnose diastolic hypertension in the cats.

Variables including age; weight; and plasma creatinine, cholesterol, sodium, calcium, chloride, and potassium concentrations, in addition to a concurrent or previous diagnosis of hyperthyroidism, are of importance in development of hypertension in humans, dogs, and experimental models of hypertension. The purpose of the study reported here was to determine prevalence of systolic hypertension and associated risk factors in cats with CRF evaluated in first-opinion practices.

**Materials and Methods**

**Inclusion criteria**—Cats included in this study were evaluated for the first time at the Beaumont Animals Hospital of the Royal Veterinary College or the People's Dispensary for Sick Animals in Bow, London, between October 1997 and July 2000. Jugular blood samples and urine samples (collected by use of cystocentesis) were obtained from cats suspected to be in renal failure after obtaining informed consent of their owners. Cats were suspected to be in renal failure if the owners reported polyuria, polydipsia, weight loss, decreased appetite, or vomiting. Physical examination findings that were considered to be potentially associated with renal failure included abnormal results of renal palpation, a large urinary bladder in a cat that had urinated recently, and poor body con-
Cats with acute renal failure were excluded on the basis of their history and response to treatment. For all cats, blood pressure readings were made within 3 weeks of diagnosis of CRF and before any treatment had been instituted. Fundic examination was performed on all cats with SABP > 175 mm Hg. Direct or indirect fundoscopic methods were used according to the preference of the clinician performing the examination.

Plasma total thyroxine concentration was measured in cats only if hyperthyroidism was suspected because of historical (polyphagia, weight loss, vomiting, diarrhea), physical examination (poor body condition, palpable goiter, tachycardia), or plasma biochemical (high alanine aminotransferase or alkaline phosphatase activity) findings. Cats were classified into 4 groups: those with hyperthyroidism (plasma thyroxine concentration > 55 nmol/L, laboratory reference range, 10 to 55 nmol/L) and CRF simultaneously, those previously treated for hyperthyroidism that subsequently developed CRF; those suspected but not proven to have hyperthyroidism, and those that had not at any time been suspected to have hyperthyroidism. Cats were included in the suspected hyperthyroidism group if goiter was palpated or if plasma thyroxine concentration was > 35 nmol/L but < 55 nmol/L. Prevalence of hypertension in the group of cats with concurrent hyperthyroidism and CRF was compared with that of the group of cats that had not at any time been suspected to have hyperthyroidism.

Cats were excluded from the study if they were being treated with glucocorticoids, nonsteroidal anti-inflammatory drugs, anabolic steroids, antihypertensive medications, potassium supplements, erythropoietin, or IV fluid therapy.

Measurement of SABP—The SABP was measured by use of a Doppler flow detector with a 9.5-MHz probe as per a described protocol. Briefly, hair was clipped from the palmar aspect of the foot immediately distal to the carpal pad, and an inflatable 2.5- or 3.3-cm cuff was wrapped around the antebrachium midway between the carpal and elbow joints. The cuff with diameter closest to 40% of the circumference of the antebrachium was selected. The cats were allowed to adopt a comfortable position (most often a sitting position or sternal recumbency), and the cuff was connected to a sphygmomanometer. The Doppler probe was positioned over the clipped area of skin, and the position was adjusted until a clearly audible signal was obtained from the common digital artery. The cuff was inflated to 20 to 30 mm Hg above the point at which the Doppler signal was no longer audible. The cuff was slowly deflated, and the pressure at which a signal could again be detected was recorded. This process was repeated until consistent consecutive readings were obtained. The first measurement was disregarded. Five systolic blood pressure measurements were recorded from each cat on each occasion that it was examined, and the arithmetic mean of these measurements was used for subsequent data analysis.

Cats were tentatively classified as hypertensive if the SABP was > 175 mm Hg. Hypertension was confirmed by the presence of consistent ocular lesions or SABP > 175 mm Hg at a subsequent office visit, a maximum of 21 days later.

Ophthalmic and cardiovascular abnormalities in normotensive and hypertensive cats were compared. Results of cardiovascular examination were classified as abnormal if a murmur, dysrhythmia, or gallop rhythm was detected. Because a complete ophthalmic examination was performed only on cats that were suspected to be hypertensive, findings from the complete ophthalmologic examination were not included in the statistical analysis. Instead, the occurrence of ocular abnormalities that were detected during routine physical examination, such as hyphema or blindness, was compared between the 2 groups.

Statistical analyses—Computerized statistical software was used for all analyses. The association between categorical risk factors and dichotomized hypertension status was examined by use of Fisher exact tests. Continuous variables were initially compared in hypertensive and normotensive cats by use of the Mann-Whitney U-test. If an association (P < 0.10) with hypertension was evident in these analyses (Fisher exact test or Mann-Whitney U-test), the variable was included in a stepwise multivariable logistic regression in order to obtain odds ratio effect estimates. Variable inclusion into the final logistic regression model was made on the basis of P < 0.05.

The frequency of abnormal ophthalmic or cardiovascular findings was examined by means of a Fisher exact test. The SABP of hypertensive cats with and without ocular abnormalities were compared by use of the Mann-Whitney U-test. Data are reported as median values and interquartile (25th to 75th percentile) ranges.

Results

One hundred and three cats with CRF fulfilled the criteria for entry into this study. Ninety-seven of these cats had urine specific gravity < 1.035, detected either during the initial visit (91 cats) or during a subsequent visit (6 cats). During numerous visits, 3 cats had persistent azotemia as well as concentration of urine. In 3 cats, urine was not obtained at the initial visit, and the cats were never reexamined (2 cats died shortly after initial examination and 1 was lost to follow-up). All 3 of these cats had a history consistent with CRF and abnormal results of renal palpation.

Twenty of 103 (19.4%; 95% confidence interval [CI], 13 to 28%) cats were classified as hypertensive (Fig 1). One cat was classified as hypertensive, although
the initial SABP measurement was 174 mm Hg, because when the cat was reexamined 3 weeks later the SABP was 189 mm Hg, and 2 weeks after that evaluation the SABP was 220 mm Hg. We believed that classification of this cat as hypertensive was justified. Two cats that had SABP > 175 mm Hg when first examined subsequently had repeated SABP < 175 mm Hg and were categorized as normotensive.

Fourteen cats (9 normotensive, 5 hypertensive) were suspected but not proven to have hyperthyroidism. These cats had goiter, thyroxine concentration in the upper portion of the laboratory reference range (35 to 55 nmol/L), or both. Sixteen cats (14 normotensive, 2 hypertensive) had been treated for hyperthyroidism prior to the diagnosis of CRF (mean interval since initiation of successful treatment for hyperthyroidism, 130 days; range, 22 to 414 days). Ten cats (7 normotensive, 3 hypertensive) had CRF and hyperthyroidism simultaneously. Sixty-three cats (53 normotensive, 10 hypertensive) had CRF but no clinical signs of hyperthyroidism. There was no detectable difference in the prevalence of hypertension between the cats with concurrent hyperthyroidism and CRF and the cats with CRF in which hyperthyroidism was never suspected (P = 0.37). There was no association (P = 0.13) between hypertension and sex (15/20 hypertensive and 46/83 normotensive cats were male).

Plasma sodium, calcium, chloride, creatinine and cholesterol concentrations; age; and body weight were not different between hypertensive and normotensive cats when examined by the exact Mann-Whitney U-test (Fig 2). Hypertensive cats had lower (P = 0.036) plasma potassium concentrations, compared with normotensive cats; therefore, this was the only variable included in the final logistic regression analysis. Via logistic regression analysis, plasma potassium concentration had a significant (P = 0.021) inverse association with systemic hypertension (odds ratio, 0.39; 95% CI, 0.18 to 0.87).

Prevalence of cardiovascular abnormalities (murmurs, arrhythmias, or gallop rhythm) was significantly greater in hypertensive cats (65%), compared with normotensive cats (35%). Externally visible ocular hemorrhage or retinal detachment was only detected in hypertensive cats (50%; P < 0.001). In addition, retinal lesions were detected fundoscopically in 4 hypertensive cats in which no ocular abnormalities were evident during routine physical examination. There was no difference in the SABP in the hypertensive cats with and without ocular lesions (SABP, 200.4 mm Hg [range, 178.4 to 219.4 mm Hg] vs 196.5 mm Hg [range, 174.3 to 204.6 mm Hg]).

Discussion

The prevalence of hypertension depends on the composition of the study population and the criteria used to define the condition. In this study, prevalence of systolic hypertension (19.4%) in cats with CRF was lower than in previous reports. This, in part, reflects the higher SABP used to define hypertension in our study. However, Stiles et al measured SABP by use of
the same indirect Doppler method as we used and found that 15 of 23 (65%) cats had SABP > 160 mm Hg (which was their definition of hypertension). In our study, only 30 of 103 (29.1%) cats had SABP > 160 mm Hg. This suggests that the lower prevalence of hypertension in our study was not solely attributable to the SABP criterion defining hypertension.

The different prevalence of hypertension between these studies may be attributable to the different study populations. The cats in our study were primarily examined in first-opinion welfare clinics in an urban environment. There are likely to be a great number of demographic and environmental differences between these cats and cats included in previous studies. However, possibly most importantly, the cats reported by Stiles et al were being evaluated for enrollment in an ongoing intervention study. This may have influenced the study population, because cats were likely to be recruited only if their renal failure was judged to be relatively stable and the cats were voluntarily consuming food. Because our study included cats at the time of first diagnosis, it is possible some cats that had acutely decompensated renal function would have decreased SABP as a result. It was not possible to determine in our study, or from previous studies, whether chronicity of renal disease influenced development of hypertension. Prospective studies are required to address this issue.

Determination of diastolic blood pressure measurements in cats by use of the Doppler technique is difficult and subjective, and no attempt was made to measure diastolic blood pressure in this study. Accordingly, any cats with increased diastolic blood pressure without changes in systolic blood pressure would not have been recognized as hypertensive. Diastolic blood pressure measurements were recorded in the study of Stiles et al; however, none of the cats with CRF had isolated diastolic hypertension, so comparisons with results of our study are still legitimate.

Physical examination findings may indicate that hypertension is present in cats with CRF. Half the hypertensive cats (10/20) in this study had hyphema or retinal detachment that was sufficiently severe to cause vision loss. In addition, 4 cats had subtle retinal lesions that substantiated the diagnosis of hypertension. Thus, 70% of cats in this study had lesions compatible with hypertensive retinopathy. This finding is similar to results reported for previous studies. As has been reported elsewhere, prevalence of heart murmurs and arrhythmias in cats with CRF is high. However, as might be predicted, prevalence of cardiac abnormalities was higher in the hypertensive cats (65%) than in the normotensive cats (35%) in our study. Although cardiovascular and ocular changes may be indicators of hypertension, it is preferable to detect hypertension before these potentially irreversible pathologic changes have developed.

In our study, the severity of azotemia was not associated with the presence of hypertension. Other studies have also failed to document an increase in SABP in association with increasing severity of renal failure. There are several confounding factors that make the relationship between renal function and blood pressure particularly difficult to determine. The SABP may decrease in severely azotemic cats because of dehydration, and concurrently these cats may have prerenal increases in plasma creatinine concentration. Plasma creatinine concentration is also influenced by muscle mass. Studies of glomerular filtration rate are potentially of more value in examining the relationship between renal function and SABP, compared with studies of creatinine.

Attempts to examine the relationship between hypertension and severity of renal disease may be confounded by the different reasons owners have for seeking veterinary attention for their pets. Half (10/20) of the hypertensive cats in this study were evaluated at the veterinary clinic for blindness or hyphema. The owners had presumably either not noticed, or not considered important, any signs of renal failure. This may be the reason, at the time of first evaluation, that azotemia in many hypertensive cats is mild. It is also possible that hypertensive cats die because of causes other than progressive loss of renal function and therefore have mild azotemia. In 1 study of treated hypertensive cats, only 31% of cats died of renal disease. Cardiovascular disease was a significant cause of death in that study, particularly when the blood pressure was poorly controlled.

Obesity in dogs and humans causes increased blood pressure. In the study reported here, a significant difference in body weight of hypertensive and normotensive cats was not detected.

In humans, systolic blood pressure increases with age. Blood pressure has been found to increase with age in clinically normal cats in a previous study but not in others. The discrepancy in these results may reflect the larger size and, therefore, power of Bodey and Sansom’s study or may be because biochemical testing was not performed on all the cats in their study, so cats with CRF may have been erroneously included in the clinically normal group. Because CRF develops predominantly in old cats, this would have led to a false association between systolic blood pressure and age. Most clinical reports of hypertension have been from older cats, but this may simply reflect the population at greatest risk of developing associated diseases. In our study, increasing age was not a significant risk factor for developing hypertension.

Hyperthyroidism has been associated with development of systemic hypertension in cats, but there have been no reports of the prevalence of hypertension in cats with concurrent CRF and hyperthyroidism. An association between systolic hypertension and hyperthyroidism is well established in humans and in rats with experimentally induced disease. Case reports of hypertensive retinopathy in association with hyperthyroidism in cats have been published. However, in large retrospective studies of cats with hyperthyroidism, clinical signs associated with hypertension such as blindness or hyphema were not reported, suggesting that extreme increases in blood pressure are infrequent. In our study, there was no evidence of cumulative risk of hypertension in cats with CRF and hyperthyroidism, although the number of cats in this group was small (n = 10), and a real difference could
have been masked by subclinical thyrotoxicosis in the CRF-only group. Hyperthyroidism can be difficult to diagnose if CRF is present concurrently; it has been suggested that in as many as half the cats tested, thyroxine concentrations may be within reference range. In our study, thyroxine concentrations were only measured if hyperthyroidism was suspected on the basis of clinical findings, primarily polyphagia or weight loss in association with normal or increased appetite or palpable goiter. Goiter is reportedly palpable in 89% to 98% of cats with hyperthyroidism. Therefore, although goiter is not a definitive indication of hyperthyroidism, it was felt that using this criterion to aid in our clinical categorization of patients was preferable in determining a cat’s status solely by measuring thyroxine concentrations.

In the study reported here, no relationship between plasma sodium concentration and hypertension was found. It was not possible to determine dietary sodium intake of the cats accurately, but none were consuming high sodium-content prescription diets. Plasma sodium concentration is more influenced by changes in water balance than by dietary sodium intake. The cats in our study, particularly those that were severely azotemic, may have had volume contraction of the extracellular fluid because of dehydration. This would be expected to cause a decrease in SABP and an increase in plasma sodium concentration; however, no significant relationship between these variables was detected.

Plasma potassium concentration was significantly lower in the hypertensive cats than in the normotensive cats in our study. Hypokalemia is a relatively common complication of naturally occurring CRF in cats and develops in approximately 30% of clinical cases; however, an association with hypertension has not been previously reported. Although a lower plasma potassium concentration was a risk factor for hypertension in our study, the magnitude of the difference in potassium concentrations between hypertensive and normotensive cats was small, and overlap was evident between values for the 2 groups. Plasma potassium concentration is not, therefore, a useful discriminatory test for hypertension but may play a role in the pathophysiologic mechanisms associated with hypertension in cats with CRF.

The lower plasma potassium concentration in hypertensive cats, compared with normotensive cats, may reflect lower dietary intake. Low potassium intake may result from anorexia, low dietary potassium concentration, or decreased potassium availability. Because weight of the normotensive and hypertensive cats was not different, it is unlikely that the amount of food consumed was different in the 2 groups. Dietary potassium content and availability were not known, but blood samples were collected prior to the introduction of renal-care diets (which are typically supplemented with potassium) in all but 2 cats (1 hypertensive, 1 normotensive). Results in a study in humans indicate that a low potassium intake is associated with an increase in blood pressure and that this effect is most marked in patients at high risk for developing hypertension.

It is possible that the low potassium concentration in the hypertensive cats in our study was attributable to primary hyperaldosteronism in some of these cats. Primary hyperaldosteronism is detected in approximately 10% of humans with hypertension.

Hyperaldosteronism has also been detected in cats with and without hypertension. Most humans with primary hyperaldosteronism are not hypokalemic. Consequently, limiting evaluation for primary hyperaldosteronism to overtly hypokalemic cats may underestimate the prevalence of this potentially reversible cause of hypertension.

Results of a previous study suggest that a secondary increase in aldosterone secretion is the cause of hypertension in cats with CRF. The study has been criticized for comparing renin, angiotensin, and aldosterone concentrations in cats with CRF with values obtained from clinically normal cats. Other authors have compared results from normotensive and hypertensive patients with renal failure and have not been able to detect a difference in hormone concentrations, although only small numbers of cats were evaluated; consequently, the power of the study was limited.

References

11. Sparkes AH, Caney SM, King MC, et al. Inter- and intrain-