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ORIGINAL RESEARCH

Clinical findings associated with N-terminal pro-B-type natriuretic peptide measurement in dogs and cats attending first opinion veterinary practices

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Abstract

Background: Clinical findings associated with N-terminal pro-B-type natriuretic peptide (NT-proBNP) measurement in dogs and cats in primary practice, and their relevance to published measurement indications, have not been described.

Methods: Using electronic health record data collected by the Small Animal Veterinary Surveillance Network, appointments in which NT-proBNP was measured were identified using keyword-based text filtering. For these appointments, clinical findings were manually identified from each patient's clinical narrative (CN) and their frequencies described.

Results: CNs of 3510 appointments (357 dogs and 257 cats) from 99practices were evaluated. The most frequently recorded clinical findings in dogs were: heart murmur (*n* = 147, 41.2% (95% confidence interval (CI) = 36.1%–46.3%), coughing (*n* = 83, 23.2% (95% CI = 18.8%–27.6%)) and panting (*n* = 58, 16.2% (95% CI = 12.4%–20.0%)) and in cats: heart murmur (*n* = 143, 55.6% (95% CI = 49.5%–61.7%)), suspected thromboembolism (*n* = 88, 34.2% (95% CI = 28.4%–40.0%)) and weight loss (*n* = 53, 20.6% (95% CI = 15.7%–25.5%)). Dyspnoea and tachypnoea were infrequently reported in dogs (*n* = 29, 8.1% (95% CI = 5.3%–10.9%) and *n* = 21, 5.9% (95% CI = 3.5%–8.3%), respectively) and cats (*n* = 26, 10.1% (95% CI = 6.4%–13.8%) and *n* = 36, 14.0% (95% CI = 9.8%–18.2%), respectively).

Conclusion: Clinical findings referable to cardiac disease were recorded contemporaneously with NT-proBNP measurement and suggested both published and other indications (coughing (in dogs and cats), and serial measurements and thromboembolism (in cats)) for testing.

INTRODUCTION

Cardiac disease is an important cause of morbidity and mortality in dogs and cats and is particularly prevalent in certain breeds. For example, myxomatous mitral valve disease (MMVD) is reported to affect 100% of cavalier King Charles spaniels (CKCS) over 11 years old,[1] dilated cardiomyopathy (DCM) affects approximately 44% of dobermanns over six years old,[2] and hypertrophic cardiomyopathy (HCM) affects approximately 15% of cats during their lifetime.[3]

N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a biomarker of a myocardial stretch, and circulating concentrations increase with the increasing cardiac filling pressures that occur in most cardiac diseases, including MMVD, DCM and HCM.[4–8] Echocardiography, although the most clinically valuable single test for the diagnosis of cardiac disease in dogs and cats, requires expensive equipment and technical expertise and therefore is not universally available or affordable. The potential utility of cardiac biomarkers to provide a readily available and relatively affordable complementary or alternative diagnostic test to echocardiography is, therefore, undoubtedly appealing. The clinical utility of NT-proBNP measurement has been investigated in a variety of samples that can be relatively easily acquired, including plasma,[9–12]

TABLE 1 A summary of the available evidence to support clinical indications for N-terminal pro-B-type natriuretic peptide (NT-proBNP) measurement during the study period

Indication		Species	Reference
1. Differentiation of cardiac from non-cardiac causes of respiratory distress or pleural effusion	Respiratory distress	Cats	Fox et al. (2009), Connolly et al. (2009)
		Dogs	Fine et al. (2008), Oyama et al. (2009), Boswood et al. (2008), Fox et al. (2015)
	Pleural effusion	Cats	Humm et al. (2013), Hassdenteufel et al. (2013), Hezzell et al. (2016)
2. Screening for occult cardiomyopathy		Cats	Fox et.al. (2011), Machen (2014)
3. Prediction of the first onset of congestive heart failure (CHF) and/ or mortality in dogs with myxomatous mitral valve disease (MMVD)	First onset of CHFMortality	DogsDogs	Reynolds et al. (2012)Hezzell et al. (2012)
4. Serial measurements for disease monitoring in MMVD		Dogs	Hezzell et al. (2012), Reynolds et al. (2012)
5. Detection of occult dilated cardiomyopathy in dobermanns		Dogs	Singletary et al. (2012)

serum,[13–15] pleural fluid [16,17] and urine;[16] measurement in plasma samples is associated with the greatest diagnostic accuracy.[16] Quantitative ELISAs are available for both canine and feline samples: CardiopetCanine pro-BNP and Cardiopet Feline pro-BNP, respectively (IDEXX Laboratories Inc.). Samples for these assays must be submitted to a reference laboratory, and same-day results are not available. A semi-quantitative point-of-care ELISA is also available for feline samples: SNAP Feline proBNP (IDEXX Laboratories Inc.).

Indications for circulating NT-proBNP measurement in dogs and cats, based on published studies, are summarised in Table 1. The most frequently investigated indication for NT-proBNP measurement is for differentiation between cardiac and non-cardiac causes of respiratory distress in dogs[14,15,18,19] and cats[8,10] although diagnostic sensitivity and specificity vary according to species, sample type and the test used. A subset of these studies specifically focussed on measurement of NT-proBNP in cats presenting with respiratory distress due to pleural effusion.[16,17,20] Two prospective, multi-centre studies support the use of plasma NT-proBNP measurement for the screening of cats with suspected occult cardiac disease.[9,21] Other uses reported in the literature include the stratification of dogs with MMVD with respect to risk of congestive heart failure (CHF) or death[6,22] and identification of dobermanns most likely to have occult DCM, when used in combination with Holter 24-h ECG recordings.[23] Serial measurements may be useful for monitoring MMVD in dogs.[6,22] However, there is little evidence to support its use beyond these indications.

The clinical scenarios in which NT-proBNP is measured by primary practitioners remain unknown. As NT-proBNP measurement is more accessible and affordable, compared to other cardiac diagnostic tests, there is potential for less discriminate patient selection. This may be further compounded by a lack of clear consensus regarding indications for use in veterinary patients. This is of interest, as the diagnostic accuracy of any test is influenced by the pre-test probability of the patient having the disease in question. For example, a middle-aged, small breed dog with no audible heart murmur is very unlikely to have significant heart disease; a high NT-proBNP measurement is, therefore, most likely to represent a false positive result or could be seen in a healthy individual whose NT-proBNP value naturally falls outside the 95% reference interval. However, in this same clinical scenario, the probability that a patient with a negative test result is truly free from the disease will be high, so although a positive test may not accurately rule in heart disease, a negative test can effectively rule it out when the pre-test probability is low.

The aims of the present study were to (1) report the signalment, presenting signs and physical examination findings recorded in the electronic patient records of dogs and cats in which circulating NT-proBNP was measured in UK primary practices and (2) compare reported clinical findings with published indications for NT-proBNP measurement.

MATERIALS AND METHODS

Data were collected from volunteering veterinary practices using compatible versions of practice management software (Vet Solutions Ltd.) by the Small Animal Veterinary Surveillance Network (SAVSNET) at the University of Liverpool (ethical approval reference RETH000964). Each electronic healthcare record (EHR) contained a range of data pertaining to signalment (breed, sex, neutering status and date of birth), the geographic region of the practice (postal district code, county and country) and the clinical narratives (CNs) for each appointment. The CN, a free text component of the EHR completed by the attending veterinary professional, contained information pertaining to clinical history (including presenting clinical signs), physical examination findings and management plans. Additionally, each EHR contained a practice-defined product description field describing products charged for at the time of each appointment (e.g., vaccinations, medications, diagnostic tests, etc.). This latter field was scrutinised via the use of a simple regular expression (cardiop|bnp|idexx cardi[oa]|cardio prof|(canine|feline) cardia|cardiac screen) to identify product descriptions and hence appointments during which an NT-proBNP test was ordered.

The available clinical history of each animal in which at least one NT-proBNP measurement was performed was then extracted and manually analysed, including access to all records and fields from every recorded appointment for which the animal's owner did not opt-out of data provision (the SAVSNET data collection protocol has previously been described[24]). This allowed valuable additional information to be collected in the following circumstances: (1) where a separate appointment was made for blood to be drawn for NT-proBNP testing (in these situations the clinical findings were recorded in the CN of the preceding appointment, typically within 24 h of the blood draw) and (2) where a specific cardiac diagnosis had been made (e.g., on echocardiography) before NT-proBNP measurement.

The CN contemporaneous with NT-proBNP measurement was manually reviewed and the following clinical findings recorded:

1. Signalment–age at the time of appointment, breed and sex. Any age > 25 years was assumed to be inaccurate.
2. Presenting signs–coughing, panting, weight loss, exercise intolerance, dyspnoea, episodes of collapse and lethargy.
3. Physical examination findings and additional information–presence of a cardiac murmur, murmur grade, arrhythmia, gallop sound, tachycardia (recorded in the CN as 'tachycardia', or heart rate > 200 beats per min), tachypnoea (recorded in the CN as 'tachypnoea', or respiratory rate > 30 breaths/min in dogs or > 40 breaths/min in cats), abnormal lung auscultation findings.
4. Other–pre-anaesthetic assessment, whether the test was requested by the owner, whether echocardiography was mentioned and any financial incentive for testing and, for cats, suspected thromboembolic disease, diagnosis of hyperthyroidism and/or chronic kidney disease.

For each animal, each non-signalment clinical finding was assigned to one of four categories based on all information available from the CN at the time of NT-proBNP measurement by one author (IC) and checked for accuracy by a second author (MJH). These categories comprised:

1. Reported in CN as present–the finding was recorded in the CN as being present (e.g., 'Grade 3 murmur heard')
2. Reported in CN as absent–the finding was recorded in the CN as being absent (e.g., 'no murmur detected')
3. Not reported in CN–no mention of this finding in the CN (i.e., presence or absence not recorded).
4. Reported but unclear–the finding was mentioned in the CN, but its presence or absence could not be clearly determined (e.g., 'not sure whether murmur present due to growling').

The frequencies of each category were reported for each non-signalment clinical finding for both dogs and cats. Where not specified in the CN, numerical murmur grades (e.g. 'Grade 3 murmur') were assumed to have used the Levine scale (I–VI).[25] For animals in which NT-proBNP was measured more than once, only the clinical findings reported at the time of the first measurement were reported (i.e., clinical findings were reported once per individual animal).

Assumptions were made to enable categorisation of clinical findings according to published indications for NT-proBNP measurement. Five indications were thereby categorised as follows:

1. Differentiation of cardiac from non-cardiac causes of respiratory distress or pleural effusion in dogs and cats; dyspnoea and/or tachypnoea were recorded in the CN.
2. Screening for occult cardiomyopathies in cats; the detection of a heart murmur, gallop sound or arrhythmia and/or health screening before general anaesthesia were recorded in the CN.
3. Prediction of the onset of CHF and/or mortality in dogs with MMVD; the presence of a heart murmur was recorded in the CN, ideally with evidence of echocardiographic confirmation of a diagnosis of MMVD.
4. Serial measurements for disease monitoring in MMVD; at least two measurements of NT-proBNP were recorded, ideally with evidence of echocardiographic confirmation of a diagnosis of MMVD.
5. Screening for occult DCM in dobermanns; measurement of NT-proBNP for this indication would be reasonable in any adult dobermann, and clinical suspicion of disease would increase following detection of a heart murmur, arrhythmia or gallop sound.

Statistical analysis

Statistical analysis was performed using commercially available software (SPSS v24, IBM Inc.). Continuous data were assessed for normality graphically and by use of the Kolmogorov-Smirnov test. Continuous data are reported as median (minimum, maximum) and categorical data as number and percentage of the total number. Ninety-five percent confidence intervals (CIs) for percentages were calculated using the total number of dogs and cats for which data were available for analysis.

RESULTS

Data from 1,630,505 canine appointments, pertaining to 571,409 unique dogs, and 649,872 feline appointments, pertaining to 303,803 unique cats, undertaken

TABLE 2 A summary of signalment for dogs in which measurement of NT-proBNP was recorded. For all variables, $n = 357$

Variable	Number (%)	Median (minimum, maximum)
Age at time of NT-proBNP measurement (years)[a]		9.6 (0.3 to 16.4)
Breed:		
Cavalier King Charles spaniel	51 (14.3%)	
Crossbreed	44 (12.3%)	
Labrador retriever	36 (10.1%)	
Cocker spaniel	18 (5.0%)	
Springer spaniel	18 (5.0%)	
Boxer	15 (4.0%)	
Jack Russell terrier	13 (3.6%)	
Dobermann	8 (2.2%)	
German shepherd dog	8 (2.2%)	
Golden retriever	8 (2.2%)	
Total top 10 breeds	219 (61.3%)	
Other breeds	135 (37.8%)	
Breed not recorded	3 (0.8%)	
Sex:		
Female entire	30 (8.4%)	
Female neutered	133 (37.3%)	
Male entire	60 (16.8%)	
Male neutered	134 (37.5%)	

[a]For dogs in which NT-proBNP was measured more than once, age is that at the time of the first recorded measurement.

between April 2014 and March 2017 were searched from 215 veterinary practices (460 sites) across Great Britain. Full data were available for 2,372,699 appointments across all species; owners opted out of data collection for 266,173 of these appointments (11.2%). At least one measurement of NT-proBNP was identified in the EHRs of 357 (0.06%) dogs and 257 (0.08%) cats, originating from 99 veterinary practices (46.0% (95% CI 41.7%–50.3%; 158 sites (34.3%)). The postcodes of these practices were distributed widely across England, Wales and Scotland. The median number of NT-proBNP measurements per practice was 2.0 (minimum 1, maximum 25) for canine samples (number of practices = 77) and 2.0 (minimum 1, maximum 27) for feline samples (number of practices = 64). In total, CNs pertaining to 3510 individual appointments (0.2% of 1,630,505 appointments searched (95% CI = 0.2%–0.2%)) were analysed for these 614 animals.

NT-proBNP measurements in dogs

Data from dogs included 367 NT-proBNP measurements from 357 dogs at 77 practices (102 sites). Signalment information is presented in Table 2. The median age was 9.6 years (minimum 0.3 years, maximum 16.4 years); the age of one dog was 36.4 years and was considered inaccurate. Dogs of 70 breeds were included, with the five most frequently represented: the CKCS, crossbreeds, Labrador retriever, cocker spaniel and springer spaniel. One hundred and ninety-four dogs were male and 163 female.

Presenting signs, physical examination findings and additional information from the CN are presented in Table 3. The most frequently reported finding in dogs in which NT-proBNP was measured was a heart murmur (n = 147, 41.2% of dogs (95% (CI) = 36.1%–46.3%)). In 35 dogs (9.8%, 95% CI = 6.7%–12.9%), the presence of a heart murmur was the only presenting sign or physical examination finding recorded in the CN.

The second most frequently reported finding was coughing (n = 83, 23.2% of dogs (95% CI = 18.8%–27.6%)). In 52 of these dogs (62.7% (95% CI = 57.7%–67.7%)), a heart murmur was also recorded, while in 10 of these dogs (12.0% (95% CI = 5.0%–19.0%)), coughing was the only finding recorded in the CN. Other frequently reported findings included panting (n = 58, 16.2% of dogs (95% CI = 12.4%–20.0%)) and weight loss (n = 38, 10.6% of dogs (95% CI = 7.4%–13.8%)). Dyspnoea, tachypnoea and abnormal lung auscultation findings were recorded in 8.1% (95% CI = 5.3%–10.9%), 5.9% (95% CI = 3.5%–8.3%) and 4.2% (95% CI = 2.1%–6.3%) of dogs, respectively.

Echocardiography was mentioned in the CN of 90 dogs, as a diagnostic test either performed or recommended to the client (25.2% (95% CI = 20.7%–29.7%)). A specific cardiac disease and/or echocardiographic findings were reported in the CNs of 17 dogs. In three dogs (0.8% (95% CI = −0.1%–1.7%), two CKCS and one labradoodle), echocardiography was performed contemporaneously with NT-proBNP measurement and a diagnosis of MMVD recorded. One dog (0.3% (95% CI = −0.3%–0.9%), a lurcher) underwent echocardiography subsequent to NT-proBNP measurement, and a diagnosis of MMVD was recorded. In two dogs (0.6% (95% CI = −0.2%–1.4%), both CKCS), a presumptive diagnosis of MMVD was made, which was not echocardiographically confirmed. In four dogs (1.1% (95% CI = 0.0%–2.2%), one cocker spaniel, one Irish wolfhound, one springer spaniel and one dobermann), echocardiography was performed contemporaneously with NT-proBNP measurement, and a diagnosis of DCM was recorded. In six dogs (1.6% (95% CI = 0.3%–2.9%), two cocker spaniels, one crossbreed, one dobermann, one poodle and one dog in which the breed was not recorded), NT-proBNP measurement was used as an initial screening test for suspected DCM; the diagnosis was not echocardiographically confirmed in any of these six dogs. In one dog (0.3% (95% CI = −0.3%–0.9%), a cocker spaniel), echocardiography was performed contemporaneously with NT-proBNP measurement, but no cardiac diagnosis was recorded.

In 70 dogs (19.6% (95% CI = 15.5%–23.7%)), a financial discount was applied to the NT-proBNP measurement: free test (n = 26, 37.1% (95% CI = 25.8%–48.4%)), unspecified discount (n = 21, 30.0% (95% CI = 19.3%–40.7%)), research study (n = 12, 17.1% (95% CI = 8.3%–25.9%)) or health care plan (n = 11,

TABLE 3 A summary of contemporaneous presenting signs, physical examination findings and additional information from the clinical narrative (CN) for dogs in which measurement of NT-proBNP was recorded ($n = 357$)

A: Presenting signs contemporaneous with NT-proBNP measurement.

Presenting sign	Reported in CN as present (number, percentage (95% confidence interval (CI)))	Reported in CN as absent (number, percentage (95% CI))	Not reported in CN (number, percentage (95% CI))	Reported but unclear (number, percentage (95% CI))
Coughing	83, 23.2% (18.8–27.6)	39, 10.9% (7.7–14.1)	233, 65.3% (60.4–70.2)	2, 0.6% (−0.2–1.4)
Panting	58, 16.2% (12.4–20.0)	3, 0.8% (−0.1–1.7)	296, 82.9% (79.0–86.8)	0, 0% (0–0)
Weight loss	38, 10.6% (7.4–13.8)	86, 24.1% (19.7–28.5)	233, 65.3% (60.4–70.2)	0, 0% (0–0)
Exercise intolerance	31, 8.7% (5.8–11.6)	34, 9.5% (6.5–12.5)	287, 80.4% 76.3–84.5)	5, 1.4% (0.2–2.6)
Dyspnoea	29, 8.1% (5.3–10.9)	28, 7.8% (5.0–10.6)	296, 82.9% (79.0–86.8)	4, 1.1% (0.0–2.2)
Episodes of collapse	26, 7.3% (4.6–10.0)	3, 0.8% (−0.1–1.7)	324, 90.8% (87.8–93.8)	4, 1.1% (0.0–2.2)
Lethargy	5, 1.4% (0.2–2.6)	0, 0% (0–0)	352, 98.6% (97.4–99.8)	0, 0% (0–0)

B: Physical examination findings and additional information recorded in the CN contemporaneous with NT-proBNP measurement.

Physical examination finding/additional information	Reported in CN as present (number, percentage (95% CI))		Reported in CN as absent (number, percentage (95% CI))	Not reported in CN (number, percentage (95% CI))	Reported but unclear (number, percentage (95% CI))
Heart murmur	147, 41.2% (36.1–46.3)		33, 9.2% (6.2–12.2)	166, 46.5% (41.3–51.7)	11[f], 3.1% (1.3–4.9)
Murmur grade ($n = 147$)	I/VI	11, 7.8% (3.5–12.1)	N/A	N/A	N/A
	II/VI	20, 13.6% (8.1–19.1)			
	III/VI	28, 19.0% (12.7–25.3)			
	IV/VI	24, 16.3% (10.3–22.3)			
	V/VI	16, 10.9% (5.7–15.9)			
	VI/VI	3, 2.0% (−0.3–4.3)			
	Range stated:				
	I-II/VI	4, 2.7% (0.1–5.3)			
	II-III/VI	4, 2.7% (0.1–5.3)			
	III-IV/VI	10, 6.8% (2.7–10.9)			
	IV-V/VI	7, 4.8% (1.3–8.3)			
	V-VI/VI	3, 2.0% (−0.3–4.3)			
	Murmur present but not graded:	17, 11.6% (6.4–16.8)			
Arrhythmia	18, 5.0% (2.7–7.3)		62, 17.4% (13.5–21.3)	276, 77.3% (73.0–81.7)	1, 0.3% (−0.3–0.9)
Gallop sound	3, 0.8% (−0.1–1.7)		0, 0% (0-0)	354, 99.2% (98.3–100.1)	0, 0% (0–0)
Tachycardia (heart rate > 200 bpm)	15, 4.2% (2.1–6.3)		144, 40.3% (35.2–45.4)	197, 55.2% (50.0–60.4)	1, 0.3% (−0.3–0.9)
Tachypnoea	21, 5.9% (3.5–8.3)		49, 13.7% (10.1–17.3)	285, 79.8% (75.6–84.0)	2, 0.6% (−0.2–1.4)
Abnormal lung auscultation	15, 4.2% (2.1–6.3)		144, 40.3% (35.2–45.4)	197, 55.2% (50.0–60.4)	1, 0.3% (−0.3–0.9)

15.7% (95% CI = 7.2%–24.2%)). In 36/70 (51.4% (95% CI = 39.7%–63.1%)) dogs in which a discount was mentioned, no presenting signs or physical examination findings were recorded.

NT-proBNP was measured twice in six dogs and three times in two dogs. In one dog, a CKCS, with echocardiographically confirmed MMVD, NT-proBNP was measured three times. In one dog, in which the breed was not recorded, NT-proBNP was measured twice, and the CN states that DCM was suspected, although not echocardiographically confirmed. In one dog, a Lhasa apso, NT-proBNP was measured twice, and the CN states that the purpose of measurement was 'monitoring of heart disease'; however, no specific cardiac diagnosis was recorded. No specific cardiac diagnosis was recorded as being suspected or confirmed in any of the remaining five dogs.

TABLE 3 Continued.

C: Other information recorded in the CN contemporaneous with NT-proBNP measurement.				
Other information	**Reported in CN as present (number, percentage (95% CI))**	**Reported in CN as absent (number, percentage (95% CI))**	**Not reported in CN (number, percentage (95% CI))**	**Reported but unclear (number, percentage (95% CI))**
Echocardiography mentioned	90, 25.2% (20.7–29.7)	0, 0% (0–0)	264, 73.9% (69.3–78.5)	3, 0.8% (−0.1–1.7)
Financial incentive for testing	70, 19.6% (15.5–23.7)	0, 0% (0–0)	287, 80.4% (76.3–84.5)	0, 0% (0–0)
Pre-anaesthetic assessment	21, 5.9% (3.5–8.3)	22, 6.2% (3.7–8.7)	313, 87.7% (84.3–91.1)	1, 0.3% (−0.3–0.9)
Test requested by owner	20, 5.6% (3.2–8.0)	1, 0.3% (−0.3–0.9)	335, 93.8% (91.3–96.3)	1, 0.3% (−0.3–0.9)

[b]Reported in CN as present–recorded as being present in the CN (e.g., "Grade 2 murmur detected").
[c]Reported in CN as absent–recorded as being absent in the CN (e.g., "no murmur detected").
[d]Not reported in CN–no mention of this finding in the CN (i.e., presence or absence not recorded).
[e]Reported but unclear–mentioned in the CN, but the presence or absence could not clearly be determined (e.g., "not sure whether murmur present due to growling").
[f]Murmur grade unclear: heard previously but not on the day of blood sampling ($n = 7$), auscultation challenging due to shaking/panting/growling ($n = 4$).

TABLE 4 A summary of signalment for cats in which measurement of NT-proBNP was recorded. For all variables, $n = 257$

Variable	Number (%)	Median (minimum, maximum)
Age at time of NT-proBNP measurement (years)[g]		10.4 (0.1 to 21.7)
Breed:		
Domestic shorthair	179 (69.6%)	
Domestic longhair	32 (12.5%)	
Siamese	7 (2.7%)	
Maine coon	6 (2.3%)	
Burmese	4 (1.6%)	
Domestic medium hair	4 (1.6%)	
Top six breeds	232 (90.3%)	
Other breeds	18 (7.0%)	
Breed not recorded	7 (2.7%)	
Sex:		
Female entire	19 (7.4%)	
Female neutered	97 (37.7%)	
Male entire	12 (4.7%)	
Male neutered	129 (50.2%)	

[g]For cats in which NT-proBNP was measured more than once, age is that at the time of the first recorded measurement.

NT-proBNP measurements in cats

Data from cats included 271 NT-proBNP measurements from 257 cats at 64 practices (85 sites). Signalment information is presented in Table 4. The median age was 10.4 years (minimum 0.1 years, maximum 21.7 years); the age of one cat was 36.0 years and was considered inaccurate. Cats of 19 breeds were included, with the three most frequently represented the domestic shorthair, domestic longhair and Siamese. One hundred and forty-one cats were male and 116 female.

Presenting signs, physical examination findings and additional information from the CN are presented in Table 5. The most frequently reported finding in cats in which NT-proBNP was measured was a heart murmur ($n = 143$, 55.6% of cats (95% CI = 49.5%–61.7%)). In 46 cats (17.9% (95% CI = 13.2%–22.6%)), the presence of a heart murmur was the only presenting sign or physical examination finding recorded in the CN.

The second most frequently reported scenario was suspected thromboembolic disease ($n = 88$, 34.2% of cats (95% CI = 28.4%–40.0%)); in five of these cats (5.7% (95% CI = 0.9%–10.5%)), no other findings compatible with possible cardiac disease were recorded in the CN. Other reported findings included weight loss ($n = 53$, 20.6% of cats (95% CI = 15.7%–25.5%)), tachypnoea ($n = 36$, 14.0% of cats (95% CI = 9.8%–18.2%)), tachycardia ($n = 34$, 13.2% of cats (95% CI = 9.1%–17.3%)) and dyspnoea ($n = 26$, 10.1% of cats (95% CI = 6.4%–13.8%)). Abnormal lung auscultation findings were recorded in 8.9% of cats (95% CI = 5.4%–12.4%). Concurrent diagnoses of hyperthyroidism and chronic kidney disease were recorded in 16 (6.2% (95% CI = 3.3%–9.2%)) and 11 (4.3% (95% CI = 1.8%–6.8%)) cats, respectively.

Echocardiography was mentioned in the CN of five cats, as a diagnostic test either performed or recommended to the client (1.9% (95% CI = 0.2%–3.6%)). A diagnosis of specific cardiac disease and/or echocardiographic findings were reported in the CNs of 10 cats, including: HCM ($n = 4$, 1.6% of cats (95% CI = 0.1%–3.1%)), echocardiographic findings reported but no clear diagnosis recorded ($n = 6$, 2.3% of cats (95% CI = 0.5%–4.1%)). In one cat (0.4% (95% CI = −0.4%–1.2%)), a domestic shorthair cat, echocardiography was performed one year before NT-proBNP measurement, but no cardiac diagnosis was recorded. In two cats (0.8% (95% CI = −0.3%–1.9%)), both domestic shorthair cats, echocardiography was performed contemporaneously with NT-proBNP measurement and a diagnosis of HCM was recorded. Two cats (0.8% (95% CI = −0.3%–1.9%)), both domestic shorthair cats underwent echocardiography subsequent to NT-proBNP measurement, and a diagnosis of HCM was recorded. In five cats (1.9% (95% CI = 0.2%–3.6%)), one Siamese and four domestic shorthair cats,

TABLE 5 A summary of contemporaneous presenting signs, physical examination findings and additional information from the CN for cats in which measurement of NT-proBNP was recorded ($n = 257$)

A: Presenting signs contemporaneous with NT-proBNP measurement.

Presenting sign	Reported in CN as present (number, percentage (95% CI))	Reported in CN as absent (number, percentage (95% CI))	Not reported in CN (number, percentage (95% CI))	Reported but unclear (number, percentage (95% CI))
Weight loss	53, 20.6% (15.7–25.5)	43, 16.7% (12.1-21.3)	160, 62.3% (56.4-68.2)	1, 0.4% (−0.4-1.2)
Dyspnoea	26, 10.1% (6.4–13.8)	19, 7.4% (4.2–10.6)	211, 82.1% (77.4–86.8)	1, 0.4% (−0.4–1.2)
Coughing	25, 9.7% (6.1–13.3)	16, 6.2% (3.3–9.2)	216, 84.0% (80.0–88.5)	0, 0% (0-0)
Lethargy	17, 6.6% (3.6–9.6)	5, 1.9% (0.2–3.6)	232, 90.3% (86.7–93.9)	3, 1.2% (−0.1–2.5)
Episodes of collapse	4, 1.6% (0.1–3.1)	4, 1.6% (0.1–3.1)	249, 96.9% (94.8–99.0)	0, 0% (0–0)
Exercise intolerance	4, 1.6% (0.1–3.1)	3, 1.2% (−0.1–2.5)	249, 96.9% (94.8–99.0)	1, 0.4% (−0.4–1.2)
Panting	3, 1.2% (−0.1–2.5)	2, 0.8% (−0.3–1.9)	252, 98.1% (96.4–99.8)	0, 0% (0–0)

Table 5B: Physical examination findings and additional information recorded in the CN contemporaneous with NT-proBNP measurement.

Physical examination finding	Reported in CN as present (number, percentage (95% CI))		Reported in CN as absent (number, percentage (95% CI))	Not reported in CN (number, percentage (95% CI))	Reported but unclear (number, percentage (95% CI))
Heart murmur	143, 55.6% (49.5–61.7)		22, 8.6% (5.2–12.0)	79, 30.7% (25.1–36.4)	13,[l] 5.1% (2.4–7.8)
Murmur grade ($n = 143$)	I/VI	3, 2.1% (−0.3–4.5)	N/A	N/A	N/A
	II/VI	48, 33.6% (25.7–41.3)			
	III/VI	43, 30.1% (22.6–37.6)			
	IV/VI	9, 6.3% (2.3–10.3)			
	Range stated:				
	II-III/VI	13, 9.1% (4.4–13.8)			
	III-IV/VI	10, 7.0% (2.8–11.2)			
	IV-V/VI	3, 2.1% (−0.3–4.5)			
	Murmur present but not graded	14, 9.8% (4.9–14.7)			
Tachypnoea	36, 14.0% (9.8–18.2)		29, 11.3% (7.4–15.2)	192, 74.7% (69.4–80.0)	0, 0% (0–0)
Tachycardia (heart rate > 200 bpm)	34, 13.2% (9.1–17.3)		132, 51.4% (45.3–57.5)	91, 35.4% (29.6–41.3)	0, 0% (0–0)
Abnormal lung auscultation	23, 8.9% (5.4–12.4)		56, 21.8% (16.8–26.9)	177, 68.9% (63.2–74.6)	1, 0.4% (−0.4–1.2)
Gallop sound	13, 5.1% (2.4–7.8)		8, 3.1% (1.0–5.2)	236, 91.8% (88.5–95.2)	0, 0% (0–0)
Arrhythmia	12, 4.7% (2.1–7.3)		40, 15.6% (11.2–20.0)	205, 79.8% (74.9–84.7)	0, 0% (0–0)

C: Other information recorded in the CN contemporaneous with NT-proBNP measurement.

Other information	Reported in CN as present (number, percentage (95% CI))	Reported in CN as absent (number, percentage (95% CI))	Not reported in CN (number, percentage (95% CI))	Reported but unclear (number, percentage (95% CI))
Suspected thromboembolic disease	88, 34.2% (28.4–40.0)	6, 2.3% (0.5–4.1)	161, 62.6% (56.7–68.5)	2, 0.8% (−0.3–1.9)
Pre-anaesthetic assessment	33, 12.8% (8.7–16.9)	1, 0.4% (−0.4–1.2)	221, 86.0% (81.8–90.2)	2, 0.8% (−0.3–1.9)
Diagnosis of hyperthryoidism	16, 6.2% (3.3–9.2)	2, 0.8% (−0.3–1.9)	239, 93.0% (89.9–96.1)	0, 0% (0–0)
Financial incentive for testing	13, 5.1% (2.4–7.8)	1, 0.4% (−0.4–1.2)	243, 94.6% (91.8–97.4)	0, 0% (0–0)
Test requested by owner	11, 4.3% (1.8–6.8)	0, 0% (0–0)	245, 95.3% (92.7–97.9)	1, 0.4% (−0.4–1.2)
Chronic kidney disease	11, 4.3% (1.8–6.8)	1, 0.4% (−0.4–1.2)	244, 94.9% (92.2–97.6)	1, 0.4% (−0.4–1.2)
Echocardiography mentioned	10, 3.9% (1.5–6.3)	0, 0% (0–0)	243, 94.6% (91.8–97.4)	4, 1.6% (0.1–3.1)

[h]Reported in CN as present–recorded as being present in the CN (e.g., "Grade 2 murmur detected").
[i]Reported in CN as absent–recorded as being absent in the CN (e.g., "no murmur detected").
[j]Not reported in CN–no mention of this finding in the CN (i.e., presence or absence not recorded).
[k]Reported but unclear–mentioned in the CN, but the presence or absence could not clearly be determined (e.g., "hyperthyroid?" with no record of confirmatory blood test results).
[l]Murmur grade unclear: heard previously but not on the day of blood sampling ($n = 10$), heard previously but purring on day of sampling ($n = 2$), inconsistent recording of murmur grade, so true grade unclear ($n = 1$).

echocardiography was performed subsequent to NT-proBNP measurement, and no cardiac diagnosis was recorded.

In 13 cats, a financial discount was applied to the NT-proBNP measurement: all health care plan (5.1% of cats (95% CI = 2.4%–7.8%)). In all 13 cats, at least one other presenting sign or physical examination finding was recorded in the CN.

NT-proBNP was measured twice in eight cats and three times in three cats. In one cat, a domestic shorthair, with echocardiographically confirmed HCM, NT-proBNP was measured three times. In one cat, a domestic shorthair, NT-proBNP was measured twice and echocardiography was performed; however, no specific cardiac diagnosis was recorded. No specific cardiac diagnosis was recorded as being suspected or confirmed in any of the remaining nine cats.

DISCUSSION

The findings of this study reveal that information recorded in the CNs of EHRs can provide insight into the clinical findings associated with NT-proBNP measurement in dogs and cats in veterinary primary practice. The median age of measurement was consistent with typical ages of onset of acquired canine and feline cardiac disease. Measurement was also performed in some puppies and kittens, possibly reflecting investigation for congenital cardiac disease (although no specific diagnoses of congenital cardiac diseases were recorded in either dogs or cats). The most frequently represented dog breeds include the CKCS, in which MMVD is almost ubiquitous, and the Labrador retriever, which is consistently one of the most popular breeds in the United Kingdom. Cocker and springer spaniels are also popular breeds and are predisposed to acquired cardiac disease. The most frequently represented cat breeds include the domestic shorthair, which is both the most common type of cat in the United Kingdom and commonly affected by HCM, and the domestic longhair, for which the situation is similar. The frequency with which measurement was performed in Siamese cats is harder to explain, as this breed is not among those predisposed to HCM (e.g., Maine coon and ragdoll cats), nor is this breed among the most frequently registered with the Cat Fanciers' Association.

Overall, a heart murmur was the most common clinical finding reported at the time of NT-proBNP measurement in both dogs and cats. In dogs, coughing and panting were also commonly reported, whereas in cats, suspected thromboembolic disease and weight loss were also commonly reported.

Five categories of indication for NT-proBNP measurement in dogs and cats were considered, based on previously published studies. The first was the use of NT-proBNP measurement to differentiate cardiac from non-cardiac causes of respiratory distress or pleural effusion; in this scenario, it was assumed that dyspnoea and/or tachypnoea would be recorded in the CN. In the present study, only 8.1% of dogs in which NT-proBNP was measured were dyspnoeic, and 5.9% were tachypnoeic. This suggests that NT-proBNP measurement was infrequently used to differentiate cardiac from non-cardiac causes of respiratory distress in dogs presenting to the primary veterinary practices surveyed here. This may be because no point-of-care ELISA is available for use with canine samples. With typical turn-around times for NT-proBNP measurements by reference laboratories of approximately 3–4 days, measurement provides little clinical benefit in emergency and acute settings. However, only 10.1% of cats in which NT-proBNP was measured were dyspnoeic, and 14.0% were tachypnoeic. This suggests that NT-proBNP measurement was also infrequently used to differentiate cardiac from non-cardiac causes of respiratory distress and pleural effusion in cats presenting to the primary veterinary practices surveyed here. This cannot be explained by the practical constraints imposed by the need to send samples to a reference laboratory, as a point-of-care ELISA is available for use with feline samples. Possible explanations for this finding include lack of awareness among veterinary surgeons of the evidence supporting the use of NT-proBNP measurement in cats with respiratory distress/pleural effusion or a preference for the use of diagnostic alternatives in the emergency setting (e.g., thoracic ultrasound and focussed echocardiography).[26] Nevertheless, increasing practitioner awareness of the usefulness of the point-of-care ELISA to distinguish cardiac from non-cardiac causes of respiratory distress/pleural effusion in cats has the potential to facilitate early initiation of appropriate treatment and therefore potentially improve outcomes.

The second indication for NT-proBNP measurement considered was the screening of cats for occult cardiomyopathies. The clinical findings that would be expected to prompt NT-proBNP measurement in this scenario include the detection of a heart murmur, gallop sound or arrhythmia and health screening before general anaesthesia. In the present study, a murmur was recorded in the CN of 55.6% of cats, a gallop sound in 5.1%, an arrhythmia in 4.7%, and pre-anaesthetic screening was mentioned in 12.8%. It seems likely, therefore, that NT-proBNP measurement may have frequently been used to screen cats in this population for cardiomyopathies.

The third indication for NT-proBNP measurement considered was for the prediction of CHF and/ or mortality in dogs with MMVD. Echocardiographically confirmed MMVD was recorded in five dogs; echocardiography was performed subsequent to NT-proBNP measurement in one of these dogs. Additionally, MMVD was suspected, but not confirmed, in two CKCS. Measurement of NT-proBNP for risk stratification in MMVD, therefore, appears to be an infrequent indication in this population. Nevertheless, a murmur was the most common clinical finding recorded in dogs (41.2% of dogs), and breeds known to be predisposed to MMVD were frequently represented in the study population, including CKCS, Jack Russell terriers, Yorkshire terriers, chihuahuas and King Charles spaniels. Although it is not possible to determine the clinician's motivation for measurement of NT-proBNP from the information available in the CN with any certainty, it seems likely that the test was performed for risk stratification of dogs with known or presumed MMVD in at least some of these cases.

The fourth indication for NT-proBNP measurement considered was the serial measurement for monitoring of disease progression in dogs with MMVD.[6,22] Serial measurements of NT-proBNP were only recorded in eight dogs (one of which had echocardiographically confirmed MMVD) suggesting that longitudinal disease monitoring was an infrequent indication in this population, either for MMVD or any other cardiac disease.

The final indication for NT-proBNP measurement considered was for the screening of the dobermann for occult DCM. Only eight dobermanns were included in the present study population, two of which had echocardiographically confirmed DCM, suggesting that either NT-proBNP measurement was infrequently used for this indication or that dobermanns were infrequently presented to the practices included in the study. Of the non-dobermann dogs in which DCM was mentioned in the CN, two cocker spaniels, one crossbreed, one poodle and one dog, in which the breed was not recorded, had suspected DCM, and one cocker spaniel, one springer spaniel and one Irish wolfhound had echocardiographically confirmed DCM. However, other breeds predisposed to myocardial disease, such as boxers and great danes, were represented with similar frequency to dobermanns; it is possible that the test was used to screen these dogs for myocardial disease and/or risk-stratify dogs with previously diagnosed disease, although a confirmed or suspected diagnosis of DCM was not recorded in the CN for any of these dogs.

The findings of the present study suggest some additional clinical scenarios in which primary veterinarians measured NT-proBNP that are not directly supported by previously published studies. First, the presence of cough was the second most common clinical finding associated with NT-proBNP measurement in dogs. Coughing is a common finding in dogs with heart disease, especially those with left atrial enlargement secondary to MMVD causing mainstem bronchial compression,[27] and 62.7% of coughing dogs also had a heart murmur. Although not a published indication for NT-proBNP measurement in MMVD,[28] this suggests that this test is being used in practice to differentiate cardiac from non-cardiac causes of coughing in dogs. However, cardiac causes of coughing in diseases other than MMVD are uncommon in dogs, and as MMVD severity is positively correlated with heart murmur intensity,[29] it is unlikely that clinically significant structural heart disease would be present in a coughing dog in the absence of a heart murmur. In the 12% of dogs in which a cough was the only clinical finding recorded, measurement of NT-proBNP was therefore likely to be associated with a low pre-test probability of cardiac disease, which in turn reduces the positive predictive value of the test.[28] Nevertheless, it is also possible that the test was being used to confirm the clinicians' suspicion that significant cardiac disease was unlikely in these cases; in the setting of low pre-test probability, diagnostic accuracy to effectively rule out a disease is likely to be high.

In cats, the presence of cough was recorded in 9.7% of cats. Coughing is a relatively infrequent finding in cats with cardiac disease and is more likely to be associated with primary respiratory disease.[30,31] This might reflect a lack of awareness of species differences in the presenting signs of cardiac disease or the clinicians may consider cardiac disease unlikely and therefore perform this test to effectively rule it out. As discussed above, in the setting of a low pre-test probability, this might increase the likelihood of false positive results, but false negative results are unlikely.

Second, a wide variety of other clinical findings, which were potentially referrable to the cardiovascular system (e.g., exercise intolerance, lethargy, etc.), were recorded in the CNs of many of the dogs and cats in which neither a murmur nor tachypnoea nor dyspnoea were reported. Although these indications are not supported by evidence from published studies, it seems most likely that NT-proBNP measurement represented an attempt to determine whether the clinical signs were related to cardiac or non-cardiac disease in these cases.

The third clinical scenario not supported by the results of published studies is suspected thromboembolic disease in cats. The reported prevalence of arterial thromboembolism (ATE) in cats with HCM is 12%–21%,[32,33] with the risk increasing with the severity of HCM, although not all cats presenting with ATE have underlying cardiac disease. Prognosis is influenced by the severity of any underlying cardiac disease, with both CHF at the time of presentation and decreased left atrial function being negative prognostic indicators.[34,35] The use of NT-proBNP measurement to screen for underlying cardiomyopathies in cats with suspected ATE, therefore, appears logical, especially as this test is likely to be more affordable than a focussed echocardiogram and does not require any specialist equipment or skills. Nevertheless, the diagnostic accuracy of the test has not been reported in this clinical setting and might be negatively affected by concurrent systemic effects associated with ATE (e.g., decreased glomerular filtration rate in cats with renal involvement).

The fourth clinical scenario not supported by the results of published studies is the serial measurement of NT-proBNP in cats, which was performed in 11 cats in the present study. It appears likely that serial measurements are being used to monitor cardiac disease in this species, possibly as a more affordable alternative to serial echocardiography. This appears logical, although data are required to determine the magnitude of change in measurement that should trigger further investigation or intervention.

Future research to investigate the diagnostic accuracy and utility of NT-proBNP measurement in each of these four clinical scenarios would provide valuable information for veterinarians who are already using the test for these indications without data to support accurate interpretation.

This study has a number of limitations. First, the level of detail recorded in the CN for each appointment was variable. In some cases, a clear and detailed record of the presenting signs and physical examination findings was available; in others, no information at all was recorded. This highlights a challenge in using CNs for research unless the data are collected prospectively. For example, echocardiography was only specifically mentioned in the CNs of five cats in which NT-proBNP was measured; however, specific cardiac diagnoses and echocardiographic findings were reported in 11 cats, suggesting that echocardiography might have been performed, but not recorded, in an additional six cats. Nevertheless, one of the purposes of a clinical record is to allow a clinician who is naïve to the case to understand the animal's clinical status; it is noteworthy that this was not always possible.

Second, the choice of clinical findings to explore in the present study was limited to those believed to be most relevant, according to the judgement of the authors; other factors that might have been relevant in individual cases may therefore not have been considered. Additionally, it is likely that more than one factor was taken into consideration when deciding whether to measure NT-proBNP; this could not be interpreted from this retrospective dataset.

Finally, the data analysed represent a retrospective convenience sample, with associated inherent limitations. These include misclassification bias, confounding (e.g., important risk factors may be present but not measured) and selection bias. However, the large initial sample size and geographical distribution suggest that the findings are generalizable to UK primary practice.

In conclusion, the most common clinical finding associated with NT-proBNP measurement in both dogs and cats is a heart murmur. Screening of cats for cardiomyopathies appeared to be the most common indication for testing that relates to the results of previously published studies. Additional indications not based on previous published studies included differentiation of cardiac from non-cardiac causes of coughing and other clinical signs potentially referrable to the cardiovascular system, screening cats with suspected ATE for underlying cardiac disease and monitoring of feline cardiac disease via serial NT-proBNP measurements. A prospective investigation of clinical reasoning underpinning NT-proBNP measurement in primary veterinary practice is warranted and may be used to direct future continuing professional development training.

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CONFLICT OF INTEREST

Dr. Hezzell has previously received research and travel funding from IDEXX Laboratories Inc.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The present study was approved by the University of Liverpool Institutional Research Ethics Committee (ethical approval reference RETH000964). SAVSNET collects EHRs in real time from veterinary practices that volunteer to take part and that are using a compatible version of practice management software (currently Premvet, Robovet and Teleos). Owners attending these SAVSNET practices are given the option to opt out at the time of their consultation, thereby excluding their data. For those that participate, data are collected on a consultation-by-consultation basis, and include animal signalment (species, breed, sex, neutering status, age, vaccination and treatment history, weight, insurance and microchipping status), clinical notes written by the attending veterinary practitioner or nurse, and owner's postcode.

AUTHOR CONTRIBUTIONS

Sarah O'Shaughnessy analysed and interpreted data, drafted the article and approved the final version. India Crawford analysed and interpreted data, revised the article and approved the final version. David Hughes analysed data and approved the final version on the article. Elena Arsevska, David Singleton and PJ Noble acquired data, revised the article and approved the final version. Melanie Hezzell designed the study, analysed data, drafted the article, approved the final version and is responsible for the integrity of the data and the accuracy of the data analysis.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available upon reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES

1. Chetboul V, Tissier R, Villaret F, Nicolle A, Déan E, Benalloul T, et al. Epidemiological, clinical, echo-doppler characteristics of mitral valve endocardiosis in Cavalier King Charles in France: a retrospective study of 451 cases (1995 to 2003). Can Vet J. 2004;45(12):1012–5.
2. Wess G, Schulze A, Butz V, Simak J, Killich M, Keller LJM, et al. Prevalence of dilated cardiomyopathy in Doberman

Pinschers in various age groups. J Vet Intern Med. 2010; 24(3):533–8.
3. Payne JR, Brodbelt DC, Luis Fuentes V. Cardiomyopathy prevalence in 780 apparently healthy cats in rehoming centres (the CatScan study). J Vet Cardiol. 2015;17(Suppl 1):S244–57.
4. de Lemos JA, McGuire DK, Drazner MH. B-type natriuretic peptide in cardiovascular disease. Lancet. 2003;362(9380):316–22.
5. Oyama MA. Using cardiac biomarkers in veterinary practice. Clin Lab Med. 2015;35(3):555–66.
6. Hezzell MJ, Boswood A, Chang YM, Moonarmart W, Souttar K, Elliott J. The combined prognostic potential of serum high-sensitivity cardiac troponin I and N-terminal pro-B-type natriuretic peptide concentrations in dogs with degenerative mitral valve disease. J Vet Intern Med. 2012;26(2):302–11.
7. Wess G, Butz V, Mahling M, Hartmann K. Evaluation of N-terminal pro-B-type natriuretic peptide as a diagnostic marker of various stages of cardiomyopathy in Doberman Pinschers. Am J Vet Res. 2011;72(5):642–9.
8. Connolly DJ, Soares Magalhaes RJ, Fuentes VL, Boswood A, Cole G, Boag A, et al. Assessment of the diagnostic accuracy of circulating natriuretic peptide concentrations to distinguish between cats with cardiac and non-cardiac causes of respiratory distress. J Vet Cardiol. 2009;11(Suppl 1):S41–50.
9. Fox PR, Rush JE, Reynolds CA, Defrancesco TC, Keene BW, Atkins CE, et al. Multicenter evaluation of plasma N-terminal probrain natriuretic peptide (NT-pro BNP) as a biochemical screening test for asymptomatic (occult) cardiomyopathy in cats. J Vet Intern Med. 2011;25(5):1010–6.
10. Fox PR, Oyama MA, Reynolds C, Rush JE, DeFrancesco TC, Keene BW, et al. Utility of plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) to distinguish between congestive heart failure and non-cardiac causes of acute dyspnea in cats. J Vet Cardiol. 2009;11 (Suppl 1):S51–61.
11. Takemura N, Toda N, Miyagawa Y, Asano K, Tejima K, Kanno N, et al. Evaluation of plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) concentrations in dogs with mitral valve insufficiency. J Vet Med Sci. 2009;71(7):925–9.
12. Chetboul V, Serres F, Tissier R, Lefebvre HP, Sampedrano CC, Gouni V, et al. Association of plasma N-terminal pro-B-type natriuretic peptide concentration with mitral regurgitation severity and outcome in dogs with asymptomatic degenerative mitral valve disease. J Vet Intern Med. 2009;23(5):984–94.
13. Oyama MA, Fox PR, Rush JE, Rozanski EA, Lesser M. Clinical utility of serum N-terminal pro-B-type natriuretic peptide concentration for identifying cardiac disease in dogs and assessing disease severity. J Am Vet Med Assoc. 2008;232(10):1496–503.
14. Fine DM, Declue AE, Reinero CR. Evaluation of circulating amino terminal-pro-B-type natriuretic peptide concentration in dogs with respiratory distress attributable to congestive heart failure or primary pulmonary disease. J Am Vet Med Assoc. 2008;232(11):1674–9.
15. Oyama MA, Rush JE, Rozanski EA, Fox PR, Reynolds CA, Gordon SG, et al. Assessment of serum N-terminal pro-B-type natriuretic peptide concentration for differentiation of congestive heart failure from primary respiratory tract disease as the cause of respiratory signs in dogs. J Am Vet Med Assoc. 2009;235(11):1319–25.
16. Humm K, Hezzell M, Sargent J, Connolly DJ, Boswood A. Differentiating between feline pleural effusions of cardiac and non-cardiac origin using pleural fluid NT-proBNP concentrations. J Small Anim Pract. 2013;54(12):656–61.
17. Hezzell MJ, Rush JE, Humm K, Rozanski EA, Sargent J, Connolly DJ, et al. Differentiation of cardiac from noncardiac pleural effusions in cats using second-generation quantitative and point-of-care NT-proBNP measurements. J Vet Intern Med. 2016;30(2):536–42.
18. Boswood A, Dukes-McEwan J, Loureiro J, James RA, Martin M, Stafford-Johnson M, et al. The diagnostic accuracy of different natriuretic peptides in the investigation of canine cardiac disease. J Small Anim Pract. 2008;49(1):26–32.
19. Fox PR, Oyama MA, Hezzell MJ, Rush JE, Nguyenba TP, DeFrancesco TC, et al. Relationship of plasma N-terminal pro-brain natriuretic peptide concentrations to heart failure classification and cause of respiratory distress in dogs using a 2nd generation ELISA assay. J Vet Intern Med. 2015;29(1):171–9.
20. Hassdenteufel E, Henrich E, Stosic A. Assessment of circulating N-terminal pro B-type natriuretic peptide concentration to differentiate between cardiac from noncardiac causes of pleural effusion in cats. J Vet Emerg Crit Care. 2013;23(4):416–22.
21. Machen MC, Oyama MA, Gordon SG, Rush JE, Achen SE, Stepien RL, et al. Multi-centered investigation of a point-of-care NT-proBNP ELISA assay to detect moderate to severe occult (pre-clinical) feline heart disease in cats referred for cardiac evaluation. J Vet Cardiol. 2014;16(4):245–55.
22. Reynolds CA, Brown DC, Rush JE, Fox PR, Nguyenba TP, Lehmkuhl LB, et al. Prediction of first onset of congestive heart failure in dogs with degenerative mitral valve disease: the PREDICT cohort study. J Vet Cardiol. 2012;14(1):193–202.
23. Singletary GE, Morris NA, Lynne O'Sullivan M, Gordon SG, Oyama MA. Prospective evaluation of NT-proBNP assay to detect occult dilated cardiomyopathy and predict survival in Doberman Pinschers. J Vet Intern Med. 2012;26(6):1330–6.
24. Sanchez-Vizcaino F, Jones PH, Menacere T, Heayns B, Wardeh M, Newman J, et al. Small animal disease surveillance. Vet Rec. 2015;177(23):591–4.
25. Haggstrom J, Kvart C, Hansson K. Heart sounds and murmurs: changes related to severity of chronic valvular disease in the Cavalier King Charles spaniel. J Vet Intern Med. 1995;9(2):75–85.
26. Ward JL, Lisciandro GR, Ware WA, Viall AK, Aona BD, Kurtz KA, et al. Evaluation of point-of-care thoracic ultrasound and NT-proBNP for the diagnosis of congestive heart failure in cats with respiratory distress. J Vet Intern Med. 2018;32(5):1530–40.
27. Ferasin L, Crews L, Biller DS, Lamb KE, Borgarelli M. Risk factors for coughing in dogs with naturally acquired myxomatous mitral valve disease. J Vet Intern Med. 2013;27(2):286–92.
28. Oyama MA, Boswood A, Connolly DJ, Ettinger SJ, Fox PR, Gordon SG, et al. Clinical usefulness of an assay for measurement of circulating N-terminal pro-B-type natriuretic peptide concentration in dogs and cats with heart disease. J Am Vet Med Assoc. 2013;243(1):71–82.
29. Ljungvall I, Rishniw M, Porciello F, Ferasin L, Ohad DG. Murmur intensity in small-breed dogs with myxomatous mitral valve disease reflects disease severity. J Small Anim Pract. 2014;55(11):545–50.
30. Smith S, Dukes-McEwan J. Clinical signs and left atrial size in cats with cardiovascular disease in general practice. J Small Anim Pract. 2012;53(1):27–33.
31. Dickson D, Little CJL, Harris J, Rishniw M. Rapid assessment with physical examination in dyspnoeic cats: the RAPID CAT study. J Small Anim Pract. 2018;59(2):75–84.
32. Payne J, Luis Fuentes V, Boswood A, Connolly D, Koffas H, Brodbelt D. Population characteristics and survival in 127 referred cats with hypertrophic cardiomyopathy (1997 to 2005). J Small Anim Pract. 2010;51(10):540–7.
33. Fox PR, Liu SK, Maron BJ. Echocardiographic assessment of spontaneously occurring feline hypertrophic cardiomyopathy. An animal model of human disease. Circulation. 1995;92(9):2645–51.
34. Smith SA, Tobias AH, Jacob KA, Fine DM, Grumbles PL. Arterial thromboembolism in cats: acute crisis in 127 cases (1992-2001) and long-term management with low-dose aspirin in 24 cases. J Vet Intern Med. 2003;17(1):73–83.
35. Payne JR, Borgeat K, Brodbelt DC, Connolly DJ, Luis Fuentes V. Risk factors associated with sudden death vs. congestive heart failure or arterial thromboembolism in cats with hypertrophic cardiomyopathy. J Vet Cardiol. 2015;17(Suppl 1):S318–28.

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