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Measurement of pulmonary transit time in healthy cats by use of ultrasound contrast media "Sonovue®": Feasibility, reproducibility, and values in 42 cats

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Abstract *Objective:* To evaluate the feasibility of measuring pulmonary transit time (PTT) in healthy cats by transthoracic echocardiography using the ultrasound contrast agent Sonovue®. To determine normalized PTT (nPTT) values in 42 healthy cats and to estimate the interobserver variability and the within-day repeatability of nPTT measurements.
Animals: Forty-two privately owned healthy cats of different breeds, gender and age presented for cardiac examination.
Methods: A bolus injection of contrast agent (Sonovue®) was administered intravenously. The right parasternal short axis echocardiographic view was used to record the contrast agent's transit time from the pulmonary artery to the left atrium. Pulmonary transit time and nPTT were determined independently by three examiners with different levels of experience.
Results: Normalized PTT was 4.12 ± 1.0 (mean ± SD) in our population. The median interobserver variability across our population was 6.8%, the median within-day variability for the three observers were 13.1%, 12.7% and 13%. No effect of the observer's experience on nPTT measurement was identified. Age, sex and body weight did not significantly influence nPTT.
Conclusions: This study demonstrates that nPTT measurement is feasible in cats using ultrasound and the blood pool contrast media Sonovue®. Measurements of

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nPTT can be performed in a clinical setting. Normalized PTT values in healthy cats are comparable with those reported in healthy dogs.

Abbreviations

CHF	congestive heart failure
CO	cardiac output
ECG	electrocardiogram
MMVD	myxomatous mitral valve disease
FPRNA	first-pass radionuclide angiocardiography
HCM	hypertrophic cardiomyopathy
mRR	mean R—R interval
nPTT	normalized pulmonary transit time
PBV	pulmonary blood volume
PTT	pulmonary transit time
TA	displayed time at which the contrast agent is first visible within the left atrium
TP	displayed time at which the contrast agent is passing the pulmonic valve

Introduction

Pulmonary transit time (PTT) is the time for a sample of blood to pass through the pulmonary circulation. It depends on pulmonary blood volume (PBV) and cardiac output (CO) according to the formula PTT = PBV/CO. Usually it is normalized to the heart rate (nPTT = PTT/mRR; nPTT = normalized PTT, mRR = mean R—R interval). Thus, nPTT represents the number of stroke volumes that are necessary to drive a sample of blood from the pulmonic valve to the left atrium.[1,2]

Most studies on nPTT in humans and animals have used first-pass radionuclide angiography (FPRNA).[1,3,4] It has been shown in humans that nPTT is independent of body size and loading conditions,[5—7] and that it changes only minimally with exercise.[3,8,9]

In dogs, significantly elevated nPTT was observed with compensated myxomatous mitral valve disease (MMVD), and substantial lengthening of nPTT was found in congestive heart failure. These increases in nPTT were due to increased pulmonary blood volume rather than decreased forward cardiac output.[1,10,11]

Recently, nPTT was measured in dogs using second-generation ultrasound contrast media.[12 a,b] Two of these studies used Sonovue® as the contrast agent.[a,b,c] The interobserver and within-day variability of PTT and nPTT measurements were within reasonable limits for clinical use, and nPTT was not influenced by age, body weight, gender or heart rate.[c,d]

The contrast agent Sonovue® is based on stabilized sulfur hexafluoride (SF_6) microbubbles surrounded by a phospholipid shell. Sulfur hexafluoride is an inorganic, colorless and odorless gas with a low solubility in blood. The agent is supplied as a lyophilisate, which is mixed with saline to form a white suspension. Because 90% of the bubbles are smaller than 8 μm, they are able to access the entire pulmonary blood volume, which makes Sonovue® highly suitable for measuring PTT. In human medicine, Sonovue® has been shown to be safe in both abdominal and cardiac applications. In a study with a sample size of 23,188 procedures, the severe adverse event rate was 0.0086%.[13]

Diagnosis and staging of feline cardiomyopathies, as well as risk assessment in affected cats, are currently based on thoracic radiographs, echocardiography and biomarkers. Echocardiographic diagnosis and evaluation of left ventricular systolic and diastolic function are mainly estimated by measuring anatomic dimensions and performing Doppler recordings, which are usually sensitive to changes in loading conditions. Even though left atrial enlargement is easy to recognize on ultrasound and is associated with reduced survival time,[14,15] a considerable overlap of left atrial size between cats with CHF and asymptomatic cats has

[a] Kresken JG, Wendt RT, Häggström J. Echocardiographical estimate of pulmonary transit time (PTT, nPTT) in dogs using the echocardiographic contrast media Sonovue®. Proceedings, 19th ECVIM-CA Congress, 2009, Porto, Portugal.

[b] Wendt RT, Kresken JG, Häggström J. Repeatability and interobserver variability of pulmonary transit time (PTT, nPTT) in dogs using the echocardiographic contrast media Sonovue®. Proceedings, 20th ECVIM-CA Congress, 2010, Toulouse, Frankreich.

[c] Sonovue®, Bracco Diagnostics, Milano, Italy.

[d] Esaote MyLab 70, Milano, Italy.