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Ultrasonographic measurement of flow-mediated vasodilation in dogs with chronic valvular disease

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Abstract *Objectives:* To measure flow-mediated vasodilation (FMD) in healthy dogs and in client-owned dogs with chronic valvular disease (CVD) and to investigate possible correlations between markers of CVD severity and FMD.
Animals: Twelve dogs with CVD and 11 healthy weight-matched dogs.
Methods: Brachial artery FMD following 5 min inflation of a cuff around the antebrachium was measured in 12 dogs with CVD and 11 healthy weight-matched dogs. Measurements were also obtained in the healthy dogs 5 min after cuff placement but without inflation ('sham cuff placement'). Dogs with CVD underwent echocardiography to confirm and characterize their disease.
Results: In healthy dogs (median age 4 [2—6] years), median FMD was 7.7% versus 3.4% with sham cuff placement ($P = 0.003$). In dogs with CVD (median age 8 [4—16] years) median FMD was 5.5% versus 7.7% in healthy dogs ($P = 0.131$). FMD showed an inverse correlation with left ventricular end-diastolic diameter normalized for body weight ($r = -0.76$, $P = 0.0043$).
Conclusions: Brachial FMD in dogs with early CVD inversely correlates with severity of left ventricular remodelling.

Introduction

Systemic vascular homeostasis is dependent on a functional endothelium.[1,2] Normal endothelial

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Abbreviations

Ao	aorta
CVD	chronic valvular disease
FMD	flow-mediated vasodilation
FVI	flow velocity integral
LA	left atrium
LVEDD	left ventricular end-diastolic diameter
LVEDDN	normalized left ventricular end-diastolic diameter
LVESD	left ventricular end-systolic diameter
NO	nitric oxide
%Diam	percentage change in vessel diameter

function has an important role in the regulation of vascular tone.[3,4] Abnormal vascular endothelial function has been implicated in the pathogenesis of cardiovascular disease and has been documented in human patients with both ischemic and non-ischemic heart disease.[5–12] Abnormal vascular endothelial function has also been documented in dogs with rapid ventricular pacing-induced heart failure.[13]

Non-invasive assessment of endothelial function by measurement of nitric oxide metabolites has been reported in dogs with naturally occurring heart disease.[14,15] Alternative techniques have recently been reported for measuring endothelial function that are suitable for use in dogs, including the measurement of brachial artery flow-mediated dilation (FMD).[16–19,a,b]

Flow-mediated dilation is the phenomenon whereby conduit arteries dilate in response to an increase in flow. A flow stimulus in the brachial artery may be created by inducing reactive hyperemia in the distal limb. A blood pressure cuff is placed between the elbow and the carpus and inflated to a pressure at least 50 mmHg greater than arterial systolic pressure for 5 min. The resulting transient vascular occlusion induces tissue ischemia distal to the cuff. Distal resistance arteries dilate in response to the induced tissue ischemia such that when the cuff is deflated there is a transient increase in flow to the distal tissues (reactive hyperemia). This produces a simultaneous upstream increase in blood flow, which increases endothelial shear stress resulting in endothelial nitric oxide (NO) release. Nitric oxide acts locally on arterial smooth muscle to cause vasodilation. This brachial artery dilation may be recorded non-invasively using 2D ultrasonography. FMD is typically quantified as maximal percentage change in luminal diameter. Measurement of FMD is the most widely-used technique in the assessment of human endothelial function.[20,21]

Chronic valvular disease (CVD) is the most commonly diagnosed heart disease in dogs.[22] Several echocardiographic variables are recognised as prognostic markers in dogs, including left atrium to aortic root ratio (LA/Ao) and normalized left ventricular end-diastolic diameter (LVEDDN).[23,24] Correlations between FMD and echocardiographic variables have not been reported in dogs. We hypothesized that FMD measurement would be possible in client-owned dogs with CVD and that the magnitude of the recorded response would be reduced in dogs with advanced disease.

The purpose of this study was to measure FMD in a group of healthy dogs and a group of client-owned dogs with naturally occurring CVD and to investigate any possible correlations between known markers of disease severity and FMD.

Animals, materials and methods

Animals

All studies conformed to the ethical standards of the WALTHAM Ethical Review Committee and the RVC Ethics and Welfare Committee.

Eleven healthy dogs and 20 dogs with CVD were recruited to the study. Healthy dogs were studied at the WALTHAM Centre for Pet Nutrition (WCPN).[c] Dogs with CVD were recruited as part of an ongoing prospective study of CVD at the Royal Veterinary College (RVC), Beaumont Animals' Hospital.[d]

All healthy dogs were screened by a board-certified cardiologist to exclude heart disease based on physical examination and echocardiography. All healthy dogs were housed together ensuring equivalent diurnal lighting patterns and all received a consistent diet (Pedigree Complete).[c] All healthy dogs were habituated to the FMD procedure prior to the study, so that they remained relaxed and still throughout FMD recording. Food was withheld from healthy dogs for a minimum of 6 h and exercise was avoided for a minimum of 4 h prior to measurement.

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