Use of tissue Doppler imaging to confirm the diagnosis of dilated cardiomyopathy in a dog with equivocal echocardiographic findings

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- ➤ At present, diagnosis of the preclinical phase of dilated cardiomyopathy in dogs remains a challenge for veterinarians.
- ➤ Tissue Doppler imaging is a recently developed ultrasonographic technique that allows quantification of regional myocardial function in real time by measurement of myocardial velocities.
- ➤ In dogs with equivocal conventional echocardiographic findings of dilated cardiomyopathy, severe myocardial alterations may be detected via tissue Doppler imaging.

A 1-year-old 42-kg (92.4-lb) sexually intact female Great Dane was referred to the Cardiology Unit of Alfort for echocardiographic examination prior to anesthesia for surgical correction of prolapse of the right third eyelid gland. The dog had no history of clinical signs related to disease of the respiratory or cardiovascular system. Findings of a physical examination were within normal limits.

By use of an ultrasound machine[a] equipped with a 2.5- to 3.5-MHz phased-array transducer, **2-dimensional (2D)** and M-mode echocardiography, color-flow imaging, spectral Doppler examination, and **tissue Doppler imaging (TDI)** were performed by the same trained observer (VC) with continuous ECG monitoring. For all ultrasonographic examinations, the dog was awake and gently restrained in a standing position; this method has already been proven by our group to have good repeatability and reproducibility for conventional echocardiography[1] as well as TDI examination.[2,b,c]

For 2D color TDI examination, real-time color Doppler was superimposed on the gray scale with a frame rate ≥ 100 frames/s. The Doppler gain was adjusted to maintain optimal coloring of the myocardium, and Doppler velocity range was set as low as possible to avoid aliasing. **Left ventricular free wall (LVFW)** velocities resulting from the radial left ventricular motion were measured in the right parasternal ventricular short-axis view between the 2 papillary muscles, as previously described.[2,c] The angle of the beam was carefully aligned to be perpendicular to the LVFW. Measurements were made on an endocardial and an epicardial segment (2 × 2 mm) of the LVFW. Simultaneous endocardial and epicardial velocity profiles were obtained by use of a stand-alone, off-line measuring system.[d]

During this initial evaluation of the dog (day 0), conventional M-mode and 2D echocardiographic parameters[3-5] were assessed (**Table 1**). No left ventricular or left atrial dilatation was observed on the initial echocardiogram. The left ventricular and septal systolic thickenings were normal in appearance. The ratio of the pre-ejection period (40 milliseconds) to left ventricle ejection time (160 milliseconds) was not greater than that expected for a clinically normal dog. The E point-to-septal separation distance and the shortening fraction were at the upper and lower reference limits, respectively. The index of sphericity (ratio of the left ventricle diastolic length to the M-mode left ventricle diastolic dimension[6]) was also considered equivocal, although the sensitivity and specificity of this parameter are still unknown; in the dog of this report, the index of sphericity was 1.43, and index values < 1.65 are considered to represent increased sphericity. Spectral Doppler imaging of the mitral inflow confirmed that the **ratio of the diastolic E wave to the diastolic A wave (E:A ratio)** was within the normal range (E:A ratio, 1.5; reference range, 1.04 to 2.42[7]), and that the E wave deceleration time was not decreased (90 milliseconds; normal lower limit, 80 milliseconds[6]), compared with that expected in clinically normal dogs. Very rarely, isolated unifocal left ventricular premature beats (0 to 2 beats/min) with a normal heart rate (112 beats/min; reference range, 100 to 130 beats/min[3]) were observed on ECG monitoring. At this point of the evaluation on day 0, the shortening fraction, sphericity index, E point-to-septal separation distance, and presence of ventricular premature beats were all considered to be evidence of possible **dilated cardiomyopathy (DCM)**. However, according to the proposed ultrasound criteria for the diagnosis of canine DCM,[6] the total score for this dog was 4 (3 points for the slight decrease in the index of sphericity and 1 for the rare ventricular premature beats), whereas a total minimum score of 6 is needed to confirm DCM.

During the evaluation of the dog on day 0, a TDI examination was also performed. As previously described,[2,c] the radial velocity profiles included 1 positive systolic wave and 2 negative diastolic waves (E and A, in early diastole and late diastole, respectively; **Figure 1**). However, compared with reference values, systolic and early diastolic endocardial velocities were lower than normal, leading to a marked decrease in the 2 corresponding

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Table 1—Conventional M-mode and 2-dimensional echocardiographic parameters measured in a Great Dane during the initial evaluation (day 0) and at reevaluation 4 months later.

Echocardiographic parameters	Day 0 (weight, 42 kg [92.4 lb])	Normal ranges for day-0 values*	Reevaluation (weight, 47 kg [103.4 lb])	Normal ranges for reevaluation values*
Left ventricular end-diastolic diameter (mm)	43.5	46.2–51.2[4]	62.3	48.7–54.4[4]
Left ventricular end-systolic diameter (mm)	32.0	29.0–32.6[4]	46.8	30.7–34.8[4]
Interventricular septal systolic thickening (%)	38.5	34–73.2[5]	35.6	34–73.2[5]
LVFW systolic thickening (%)	56.1	45.7–75.9[5]	40.8	45.7–75.9[5]
Shortening fraction (%)	28.5	18–36[3]	24.6	18–36[3]
Left atrium size (mm)	22.8	27–30[4]	41.3	28.4–32.0[4]
Aorta diameter (mm)	27.8	28.8–31.2[4]	32.1	30.6–33.4[4]
Left atrium size-to-aorta diameter ratio	0.82	0.83–1.13[5]	1.28	0.83–1.13[5]
E point-to-septal separation (mm)	10.6	5.0–12.0[3]	9.9	5.0–12.0[3]
Pre-ejection period-to-left ventricular ejection time ratio	0.20	0.10–0.54[5]	0.32	0.10–0.54[5]

*Normal ranges for Great Danes that weigh 52 to 75 kg (114.4 to 165.0 lb) have been described.[3] However, no specific reference ranges are available for young Great Danes < 52 kg. Therefore, the normal ranges of left ventricular and atrial diameters, aortic diameters, and myocardial wall thicknesses indicated are those described in adult dogs of 42 kg (day 0) and 47 kg (at reevaluation).[4] Reference ranges for derived echocardiographic parameters are those reported by Koch et al[3] or by Boon et al[5] if data were not available for Great Danes.

LVFW = Left ventricular free wall.

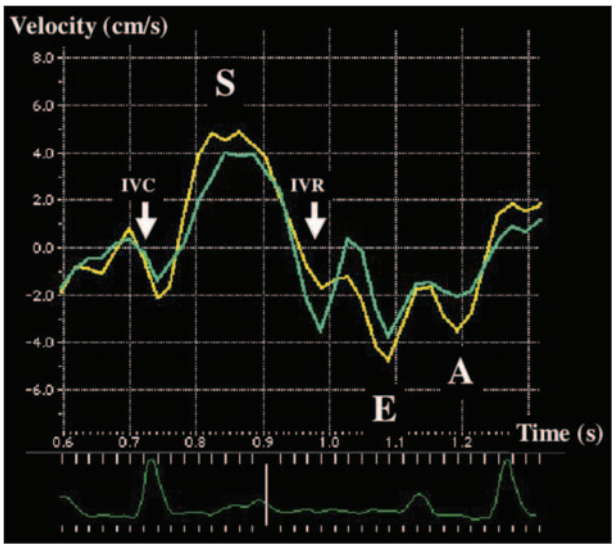

Figure 1—Analysis of left ventricular free wall (LVFW) radial motion during the initial echocardiographic evaluation (day 0) of a Great Dane by use of 2-dimensional color tissue Doppler imaging in the right parasternal short-axis view. The yellow and green curves (endocardial and epicardial velocity profiles, respectively) are nearly superimposed during the whole cardiac cycle, indicating the lack of systolic and diastolic myocardial velocity gradients. The trace at the bottom of the image represents the corresponding ECG. IVC = Isovolumic contraction phase. S = Peak velocity of the LVFW during systole. IVR = Isovolumic relaxation phase. E = Peak velocity of the LVFW during early diastole. A = Peak velocity of the LVFW during late diastole.

Table 2—Radial tissue Doppler imaging (TDI) parameters measured in the endocardial and epicardial layers of the LVFW of a Great Dane at initial evaluation (day 0).

TDI parameters (cm/s)	Day 0	Reference ranges (cm/s)[c]
S wave (endocardial)	4.4	6.0 ± 1.01
S wave (epicardial)	3.9	3.4 ± 0.77
Systolic velocity gradient ($S_{endocardial} - S_{epicardial}$)	0.5	2.5 ± 0.97
E wave (endocardial)	5.4	8.1 ± 1.82
E wave (epicardial)	5.3	3.5 ± 0.78
Early diastolic velocity gradient ($E_{endocardial} - E_{epicardial}$)	0.1	4.5 ± 1.78
A wave (endocardial)	5.3	3.7 ± 0.99
A wave (epicardial)	2.8	1.7 ± 0.65
Late diastolic velocitygradient ($A_{endocardial} - A_{epicardial}$)	2.5	1.9 ± 0.70

S wave = Peak velocity of the LVFW during systole. E wave = Peak velocity of the LVFW during early diastole. A wave = Peak velocity of the LVFW during late diastole.

myocardial velocity gradients (**Table 2**). Moreover, the E:A ratio was decreased particularly in the endocardial segment. Late diastolic endocardial and epicardial velocities were not decreased, and the corresponding velocity gradient was within the normal range. On the basis of these TDI data, it was concluded that the dog had a severe systolic and early diastolic myocardial alteration, which was highly suggestive of DCM.[c] Because of this, the dog did not undergo surgical repair of the prolapsed third eyelid and the owner was advised to return the dog within the next 4 to 6 months for reevaluation of both conventional and TDI echocardiographic parameters.

Four months later, the dog was reevaluated as planned. The owner noticed progressive exercise intolerance since the last examination. On physical examination, capillary filling time and the color of the mucous membranes were considered normal. However, the dog was tachypneic (≥ 50 breaths/min). Auscultation revealed the presence of paroxysmal tachycardia that was associated with a weak arterial pulse. Thoracic radiography revealed left-sided cardiomegaly without pulmonary edema. Several episodes of unifocal ventricular tachycardia (heart rate > 220 beats/min) were observed on an ECG and also during the ultrasonographic examination. While echocardiographic measurements were made, the evaluator (VC) ensured that ventricular tachycardia was not present (Table 1). Conventional echocardiography confirmed a marked systolic and diastolic left ventricular dilatation associated with a left atrial dilatation (41.3 vs 22.8 mm at day 0; reference range, 28.4 to 32.0 mm[4]; **Figure 2**). The index of sphericity had decreased dramatically, indicating a marked rounding of the left ventricle (0.98 vs 1.42 at day 0). By use of the proposed criteria for diagnosis of DCM in dogs,[6] the total score for the dog was 8 (3 points for the decrease in the index of sphericity, 3 for the left ventricular dilatation, 1 for the ventricular arrhythmias, and 1 for the left atrial dilatation); thus, the diagnosis of DCM was confirmed.

Results of previous studies in humans and various animal models of human heart diseases have indicated that TDI is a sensitive technique for the diagnosis of subtle regional myocardial dysfunction, such as

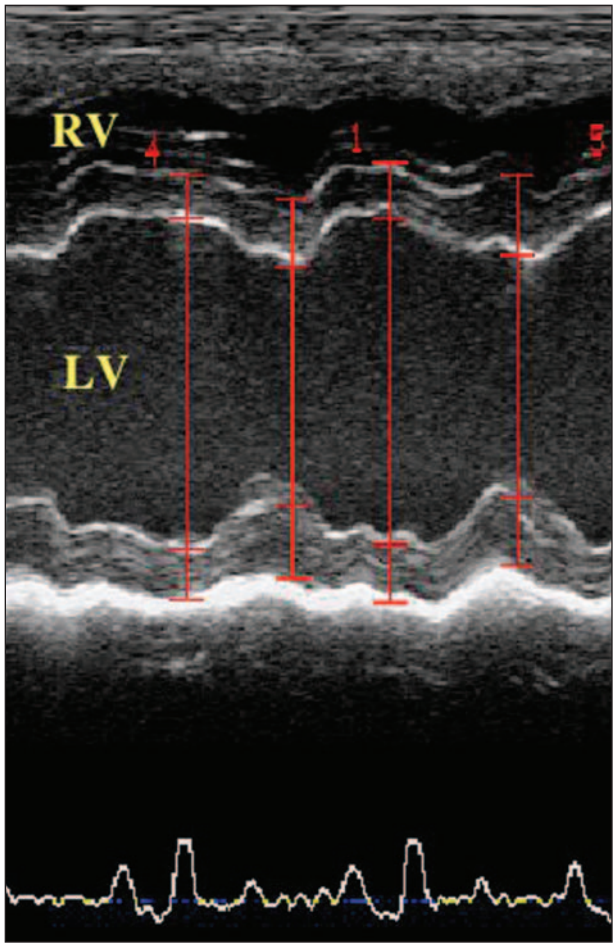

Figure 2—Left ventricular M-mode echocardiographic image obtained from the dog in Figure 1 four months after the day-0 evaluation. Notice the systolic and diastolic left ventricular dilatation. The trace at the bottom of the image represents the corresponding ECG. LV = Left ventricle. RV = Right ventricle.

ischemia,[8,9] heart transplant disorders,[10] and cardiomyopathies. The myocardial disorders that have been studied most via TDI are primary or secondary **hypertrophic cardiomyopathies (HCM)** in human patients[11,12] and also in animal models of HCM involving rats and rabbits.[13,14] In a study involving a transgenic rabbit model of human HCM, Nagueh et al[14] reported that TDI accurately identified the mutant transgenic rabbits irrespective of the extent of cardiac hypertrophy; via TDI, all mutant rabbits (even those without left ventricular hypertrophy) had significantly reduced systolic and diastolic myocardial velocities, which indicated that TDI was more sensitive for detection of moderate myocardial alterations than were conventional echocardiographic methods. Similar findings have been reported for humans with familial HCM; myocardial contraction and relaxation velocities detected via TDI were reduced in patients with familial HCM, including those without left ventricular hypertrophy.[12] The detection of reduced myocardial contraction and relaxation velocities via TDI had a sensitivity of 100% and a specificity of 93% for identifying human patients with mutations in the absence of left ventricular hypertrophy.[12]

At present, conventional echocardiography is used to screen for DCM in humans and animals, and the diagnosis is made on the basis of detection of reduced inotropism, dilatation of cardiac chambers, and increased sphericity.[6] However, these ultrasonographically detectable functional and morphologic changes are sometimes absent depending on the stage of the disease,[6] and diagnosis of the preclinical phase of DCM in dogs (occult DCM[15]) still remains a challenge. In another study[e] by our group, the accuracy of TDI for detection of early myocardial dysfunction associated with DCM in Golden Retrievers with muscular dystrophy was demonstrated. Because of a decrease in the endocardial-epicardial gradient,[16] the dogs with the dystrophin mutation were detected via TDI before development of congestive heart failure and myocardial dysfunction, as determined by conventional echocardiographic parameters (ie, left ventricular dimensions and shortening).[e] However, to our knowledge, the accuracy of TDI for early detection of naturally occurring DCM in dogs in a clinical setting has not been reported. In the dog of this report, the systolic and diastolic radial myocardial motion was markedly altered 4 months before development of unequivocal signs of DCM. This finding, which needs to be confirmed in other dog breeds and in a larger number of animals, provides new insight into the pathogenesis of DCM; it also suggests that TDI may be a sensitive technique of screening for DCM during the preclinical phase in dogs, which is not detectable via currently used conventional echocardiographic techniques. At present, dobutamine stress echocardiography is a method of determining the presence of preclinical systolic and diastolic myocardial dysfunction.[17] This technique has been evaluated in healthy Doberman Pinschers to determine which parameters were associated with the development of occult DCM.[18] Further studies are required to compare the sensitivities of TDI and dobutamine stress echocardiography for identification of occult cardiomyopathies in dogs. The preclinical diagnosis of cardiomyopathies in dogs could enable veterinary practitioners to institute medical treatment early and thereby prevent the development of heart failure; it could also help to identify dogs carrying a mutation for DCM, enabling exclusion of those individuals from breeding programs.

[a]Vingmed system 5, General Electric Medical System, Waukesha, Wis.
[b]Chetboul V, Athanassiadis N, Carlos C, et al. Quantification of longitudinal left ventricular motion using tissue Doppler imaging: new indices of myocardial function in dogs (abstr). *J Vet Intern Med* 2003;17:399.
[c]Chetboul V, Athanassiadis N, Carlos C, et al. Quantification of radial left ventricular motion in healthy dogs using tissue Doppler imaging: intraday and interday variability (abstr). *J Vet Intern Med* 2003;17:440.
[d]Echo Pac 5.4 software for system 5, GE-Vingmed Ultrasound, Waukesha, Wis.
[e]Chetboul V, Escriou C, Blot S, et al. Early detection of regional myocardial function alterations in a dog model of dilated cardiomyopathy by tissue Doppler imaging study (abstr). *Circulation* 2001;104(suppl 17):351.

References

1. Chetboul V, Athanassiadis N, Concordet D, et al. Observer-dependent variability of quantitative clinical endpoints: the example of canine echocardiography. *J Vet Pharmacol Ther* 2004;27:49–56.

2. Chetboul V, Athanassiadis N, Carlos C, et al. Assessment of repeatability, reproducibility, and effect of anesthesia on determination of radial and longitudinal left ventricular velocities via tissue Doppler imaging in dogs. *Am J Vet Res* 2004;65:909–915.

3. Koch J, Pedersen HD, Jensen AL, et al. M-mode echocardiographic diagnosis of dilated cardiomyopathy in giant breed dogs. *Zentralbl Veterinarmed [A]* 1996;43:297–304.

4. Boon JA. *Veterinary echocardiography, two-dimensional and M-mode imaging (handy reference)*. Jackson, Wyo: Teton NewMedia, 2003.

5. Boon JA, Wingfield WE, Miller CW. Echocardiographic indices in the normal dog. *Vet Radiol Ultrasound* 1983;24:214–221.

6. Dukes-McEwan J, Borgarelli M, Tidholm A, et al. Proposed guidelines for the diagnosis of canine idiopathic dilated cardiomyopathy (The ESVC Taskforce for Canine Dilated Cardiomyopathy). *J Vet Cardiol* 2003;2:7–19.

7. Boon JA. Echocardiographic reference values. In: *Manual of veterinary echocardiography*. Baltimore: Lippincott Williams & Wilkins, 1998;453–473.

8. Derumeaux G, Ovize M, Loufoua J, et al. Assessment of nonuniformity of transmural myocardial velocities by color-coded tissue Doppler imaging: characterization of normal, ischemic, and stunned myocardium. *Circulation* 2000;101:1390–1395.

9. Derumeaux G, Loufoua J, Pontier G, et al. Tissue Doppler imaging differentiates transmural from nontransmural acute myocardial infarction after reperfusion therapy. *Circulation* 2001;103:589–596.

10. Puleo JA, Aranda JM, Weston MW, et al. Noninvasive detection of allograft rejection in heart transplant recipients by use of Doppler tissue imaging. *J Heart Lung Transplant* 1998;17:176–184.

11. Palka P, Lange A, Fleming AD, et al. Differences in myocardial velocity gradient measured throughout the cardiac cycle in patients with hypertrophic cardiomyopathy, athletes and patients with left ventricular hypertrophy due to hypertension. *J Am Coll Cardiol* 1997;30:760–768.

12. Nagueh SF, Bachinski LL, Meyer D, et al. Tissue Doppler imaging consistently detects myocardial abnormalities in patients with hypertrophic cardiomyopathy and provides a novel means for an early diagnosis before and independently of hypertrophy. *Circulation* 2001;104:128–130.

13. Derumeaux G, Mulder P, Richard V, et al. Tissue Doppler imaging differentiates physiological from pathological pressure-overload left ventricular hypertrophy in rats. *Circulation* 2002;105:1602–1608.

14. Nagueh SF, Kopelen HA, Lim DS, et al. Tissue Doppler imaging consistently detects myocardial contraction and relaxation abnormalities, irrespective of cardiac hypertrophy, in a transgenic rabbit model of human hypertrophic cardiomyopathy. *Circulation* 2000;102:1346–1350.

15. Calvert CA, Jacobs GJ, Pickus CW. Unfavourable influence of anaesthesia and surgery on Doberman Pinschers with occult cardiomyopathy. *J Am Anim Hosp Assoc* 1996;32:57–62.

16. Uematsu M, Miyatake K, Tanaka N, et al. Myocardial velocity gradient as a new indicator of regional left ventricular contraction: detection by a two-dimensional tissue Doppler imaging technique. *J Am Coll Cardiol* 1995;26:217–223.

17. McEntee K, Amory H, Clercx C, et al. Physiologic response to dobutamine infusion during cardiac stress testing of dogs. *Am J Vet Res* 1998;59:1160–1165.

18. Minors SL, O'Grady MR. Resting and dobutamine stress echocardiographic factors associated with the development of occult dilated cardiomyopathy in healthy Doberman Pinscher dogs. *J Vet Intern Med* 1998;12:369–380.