Evaluation of diastolic blood flow dynamic of the left ventricle in dogs with mitral valve regurgitation using vector flow mapping

Shimizu, M.[1]; Tanaka, R.[2*]; Fukushima, R.[2]; Hamabe, L.[3] and Sasaki, N.[2]

[1]Department of Veterinary Diagnostic Imaging, Faculty of Veterinary Medicine, Tokyo University of Agriculture and Technology, 3-5-8 Saiwai-Cho, Fuchu-Shi, Tokyo, 183-8509, Japan; [2]Department of Clinical Sciences, Faculty of Veterinary Medicine, Tokyo University of Agriculture and Technology, 3-5-8 Saiwai-Cho, Fuchu-Shi, Tokyo, 183-8509, Japan; [3]Graduated from Faculty of Veterinary Medicine, Tokyo University of Agriculture and Technology, 3-5-8 Saiwai-Cho, Fuchu-Shi, Tokyo, 183-8509, Japan

[*]***Correspondence:*** *R. Tanaka, Department of Clinical Sciences, Faculty of Veterinary Medicine, Tokyo University of Agriculture and Technology, 3-5-8 Saiwai-Cho, Fuchu-Shi, Tokyo, 183-8509, Japan. E-mail: ryo@vet.ne.jp*

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Summary

Mitral valve regurgitation (MVR) is a common valvular disease in dogs. Hydrokinetic evaluation of the blood flow within the ventricles has become possible by vector flow mapping (VFM), which shows the blood flow within the ventricles in vector and vortex flows. Blood flow within the left ventricle of MVR dogs was compared at different stages of MVR and to that of normal dogs. 14 normal dogs and 40 clinical cases of MVR were used. Echocardiographic videos were collected and vectors and vortexes were analysed by VFM analysis using software. In diastole, reversal of vectors which formed vortexes was observed around the anterior leaflet of the mitral valve in the control group. In the MVR dogs, in addition to that, reversed vectors were also observed at the left ventricular free-wall which formed Vortexes along the Posterior Wall (PWv). As MVR became more severe, PWv occupied a wider range; however, it was not observed at the outflow tract, suggesting that it occurs to lower transfer effectiveness. Controlling transfer effectiveness may be considered to alleviate the exacerbation of the heart failure caused by MVR.

Key words: Echocardiography, Heart disease, Small animal, Cardiology

Introduction

Evaluating cardiac functions by echocardiography is becoming an important topic in current cardiovascular medicine. Although cardiac catheterization enables the evaluation of cardiac congestion by measuring the left ventricular end-diastolic pressure, noninvasive echo-cardiography is becoming the main technique for the evaluation of clinical conditions of cardiac diseases (Ouellet *et al*., 2009). Various ultrasonographical measurements including the tissue Doppler technique and 2-dimentional tissue tracking have been developed as substitutes for cardiac catheterization (Chetboul *et al*., 2004; Chetboul *et al*., 2007; Ishikawa *et al*., 2011).

The evaluation of cardiac blood flow has been carried out so far by measuring flow velocity or the presence or absence of a mosaic pattern. However, vector flow mapping (VFM), which visualizes vortices in the left ventricle (LV) as a vector by calculating horizontal velocity components using information obtained from color Doppler, has been recently developed as an innovative technique (Uejima *et al*., 2010). In veterinary medicine, due to the lack of applicability in clinical cases, the clinical implications of this method are yet to be fully understood; nevertheless, the technology seems promising as a new parameter for the evaluation of cardiac functions. In human medicine, in research focusing on LV blood flow, the evaluation of blood flow within the cardiac chambers has been attempted by high speed mapping techniques using MRI (Kilner *et al*., 1993; Bogren *et al*., 1995; Kim *et al*., 1995; Kilner *et al*., 2000). However, understanding flow dynamic by MRI is limited and impractical for veterinary medicine.

Mitral valve regurgitation (MVR) is the most common cardiac valvular disease in dogs. Compensatory cardiac hyperfunction is seen in early stages of MVR, after which heart failure gradually develops. Judging whether this hyperfunction is a necessary or excessive compensatory reaction is very difficult and can be a problem when considering the appropriate use of drugs that suppress compensatory reactions such as the beta-blocker. By conducting hydrodynamic evaluations of the blood flow within the ventricle, new light is shed on another perspective of this clinical condition which could not have been evaluated with the currently used parameters.

Vector flow mapping, developed by Otsuki and Tanaka in 1998, is a revolutionary technique enabling the display of blood flow vector by calculating the horizontal velocity component from blood flow information obtained from the color Doppler (Okada *et al*., 2009). The direction and velocity of blood flow is shown as the direction and length of the vector. In addition, it is possible to visualize the vortex by deriving a line of

equal quantity of flow using the velocity vector.

In human medicine, studies have been conducted on blood flow structure within the left ventricle (LV), the mechanism of ejection, and quantitative evaluations of aortic regurgitation (Zhang *et al*., 2004), and VFM has been reported to be a sensitive method to depict flow structures derived from color Doppler velocities with reasonable accuracy (Uejima *et al*., 2010, Nogami *et al*., 2012).

In the present study, to evaluate hydrodynamic changes in the interventricular blood flow by cardiac function changes, hydrodynamic evaluation of the left ventricle was performed on clinical MVR cases in dogs using VFM. By comparing MVR cases with normal cases and those with clinical conditions, differences between interventricular blood flow were evaluated for the control and the MVR groups as well as various disease stages of the MVR group.

Materials and Methods

Animals

Dogs which had undergone echocardiographic examinations performed at Tokyo University of Agriculture and Technology from July 2009 to July 2010 were used. Those that did not show signs of cardiac disease on echocardiography were used as the control group (4 males and 10 females, 5 beagles, 2 dachshunds, and 1 specimen from each of the following breeds: Maltese, Pomeranian, Yorkshire terrier, Cavalier King Charles Spaniel, golden retriever, Whippet, and a mixed-breed dog). Body weight ranged from 1.9 to 24.0 kg, and age ranged from 10 months to 15 years. Dogs diagnosed with MVR on echocardiography were used as the MVR group (16 males and 24 females. 12 Cavalier King Charles Spaniels, 8 Chihuahua, 7 Shih Tzus, 3 mixed-breed dogs, 2 Yorkshire terrier, 2 Miniature Schnauzers, and one from each of the following breeds: Maltese, Beagle, Pomeranian, English Springer Spaniel, Toy Manchester Terrier, Shiba Inu). Their body weight ranged from 1.8 to 13.6 kg, and their age from 5 to 19 years. The dogs were operated in accordance to the guidelines for the Institutional Animal Care and Use Committee of the University of Agriculture and Technology.

Some MVR dogs did not receive any medication, while others were prescribed cardiac medications either by the researchers or by other veterinarians. Medicines included angiotensin converting enzyme inhibitors (ACE-I), diuretics, and positive inotropes. The number of dogs with International Small Animal Cardiac Health Council (ISACHC) functional classification of heart failure class (Atkins *et al*., 2009) Ia, Ib, II and III of MVR were 23, 11, 4, and 2, respectively. Mitral valve regurgitation cases that had concurrent shunt diseases such as ventricular septal defect were excluded from the study.

Data were acquired from both control and MVR groups, and comparative evaluations of the diastolic LV inflow were performed using VFM analysis.

Acquisition of data

Echocardiographical examinations were performed on control and MVR groups, and the acquired data was recorded. Each dog was positioned in left recumbency, and the region of interest (ROI) was adjusted to contain all the LVs in the long axis four-chamber view of the left parasternal position. Three or more consecutive heart beats were videotaped. The information obtained from the color Doppler was transferred to the analysis software. An ultrasonic diagnostic imaging unit (Prosound α10, Hitachi Aloka Medical, Ltd., Mitaka, Tokyo, Japan) and an analysis software (DAS-RS1, Hitachi Aloka Medical, Ltd., Mitaka, Tokyo, Japan) were used for the acquisition and analysis of the data.

Analysis of data

Within the transferred data, videos with adequate color information quality were selected, and three continuous heart beats were analyzed. Any aliasing effect was corrected using DAS-RS1. First, the velocity vector of the blood flow was displayed (the length of the yellow vector representing velocity, and the red point representing the apex of the vector) from the velocity component of the ultrasonic beam direction and velocity component, which bisects with the beam. The vortex in the LV is visualized using a uniform flow curve obtained from the velocity vector display (vortex mode). The vortex scale from the vortex mode is standardized; however, in cases where the vortex in the LV could not be seen with the standardized scale, they were observed with a smaller scale. The vortex in the LV was observed on a flame during early-diastole (during E wave) and during atrial systole (during A wave). If a vortex was confirmed in one of three heart cycles, it was considered positive for vortex.

Results

VFM analysis of the control group

The E-velocity of the blood flow vector within the LV was observed as a velocity component in the direction of the left atrium towards the apex of LV (flow A), and rather than moving towards the apex, the velocity component then reversed around the anterior leaflet of the mitral valve towards the LVOT (flow B) (Fig. 1). After flow A was ejected out into the LV, it moved along the LVFW towards the apex of LV where it reversed towards the outflow direction. In flow B, vortex formation was confirmed by the vortex mode. Similar flow vector was also observed with the A wave. Vortex around the anterior leaflet of the mitral valve was observed from early diastolic to systolic phases. Formation of vortex was observed around the posterior leaflet of the mitral valve in 2 of the 14 control group cases (flow C). Turbulence, such as vortex, was not observed except for flow B and the two cases of flow C.

VFM analysis of the MVR group

Flow A and B, as seen in the control group, and flow C were observed in some cases. However, in addition to

these blood flows, a flow which reversed from the LV apex towards the LV posterior wall was also observed. Vector occurred in either E or A waves, or both, and the formation of vortex by the vortex mode were seen in almost all cases (PW vortex (PWv), Table 1). In addition, differences in the morphology and distribution of PWv were observed depending on MVR severity.

1. Cases classified as ISACHC Ia

The vector that turned over towards the LV posterior wall was observed towards the LV apex at the papillary muscle level (Fig. 2a). By observing the vortex mode it is understood that PWv did not cover a large proportion of the LV. Among the 23 cases of ISACHC Ia, 13 cases had PWv during the E wave, 5 cases during the A wave, 4 cases had during both E and A waves, and 1 case did not have a PWV during either waves.

2. Cases classified as ISACHC Ib

The vector turning over towards the posterior wall and its area of distribution were larger compared to the vector in the ISACHC 1a cases (Fig. 2b). A broader area of PWv was also observed using the vortex mode compared to that of the ISACHC 1a cases. Among the 11 ISACHC Ib cases, 7 had PWv during E wave, 2 during A wave, and 2 at both waves. PWv was observed during either E or A waves or both in all of the ISACHC 1b cases.

3. Cases of ISACHC II

In some cases of ISACHC II, PWv reached towards the apex at the posterior leaflet of the mitral valve (Fig. 2c). All 4 cases confirmed the presence of vortex at both E and A waves.

4. Cases of ISACHC III

The vector reflecting over towards the posterior wall was similar to the ventricular septum or the larger ones (Fig. 2d). For the vortex mode too, comparable vortex or broader areas of PVw were formed at the ventricular septum. In ISACHC III cases, PWv was observed at both E and A waves in 2 ISACHC III cases.

Discussion

Concepts regarding heart blood flow acquired by VFM analysis have been reported in the past (Phillips *et al*., 1995; Li *et al*., 2009). Flow within the ventricle is classified into laminar and disturbed flows. Similar to vortex, disturbed flow is produced when the laminar flow is conveyed from a narrow to a wide space. This phenomenon, known as "flow separation", is ruled by Reynold's number to generate a disturbed flow by flow separation.

$N_R = 2rv\rho/\eta$

where,
N_R: Reynolds number
r: Radius of the blood vessel
v: Flow velocity
ρ: Density of liquid
η: Viscosity

The incidence of turbulent flow increases with Reynold's number, which is increased with either the elevation of blood flow velocity, the increased density of liquid, or the reduction of its viscosity If such flow occurs, energy is expended on its production, resulting in greater energy loss compared to a laminar flow.

The significance of the vortex, which evolves within

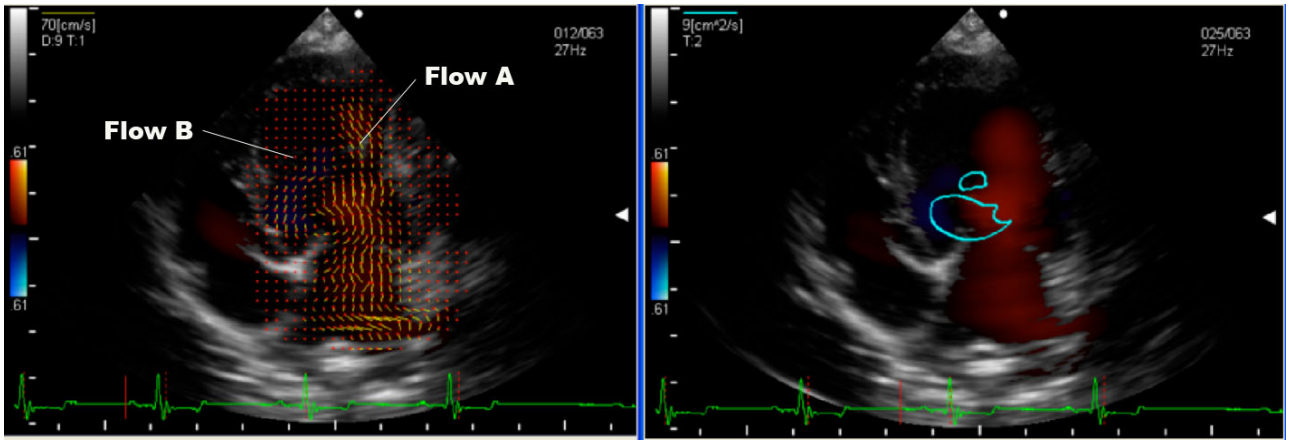

Fig. 1: VFM analysis of the control group. E-velocity of the blood flow vector within the LV was observed as a velocity component in the direction of the left atrium towards the apex of LV (flow A), and rather than going towards the apex, the velocity component then reversed around the anterior leaflet of the mitral valve towards the LVOT (flow B)

Table 1: Abnormal PW vortex observed in the MVR group

	ISACHC Ia	ISACHC Ib	ISACHC II	ISACHC III	Total
PWv	E 13 (56.5%)	E 7 (63.6%)	E 0	E 0	20 (50%)
Positive	A 5 (21.7%)	A 2 (18.2%)	A 0	A 0	7 (17.5%)
	E&A 4 (17.4%)	E&A 2 (18.2%)	E&A 4 (100%)	E&A 2 (00%)	12 (30%)
Negative	1 (4.3%)	0	0	0	1 (2.5%)
Total	23	11	4	2	40

If a vortex was confirmed in one of the three heart cycles on the vortex mode, it was considered positive for vortex

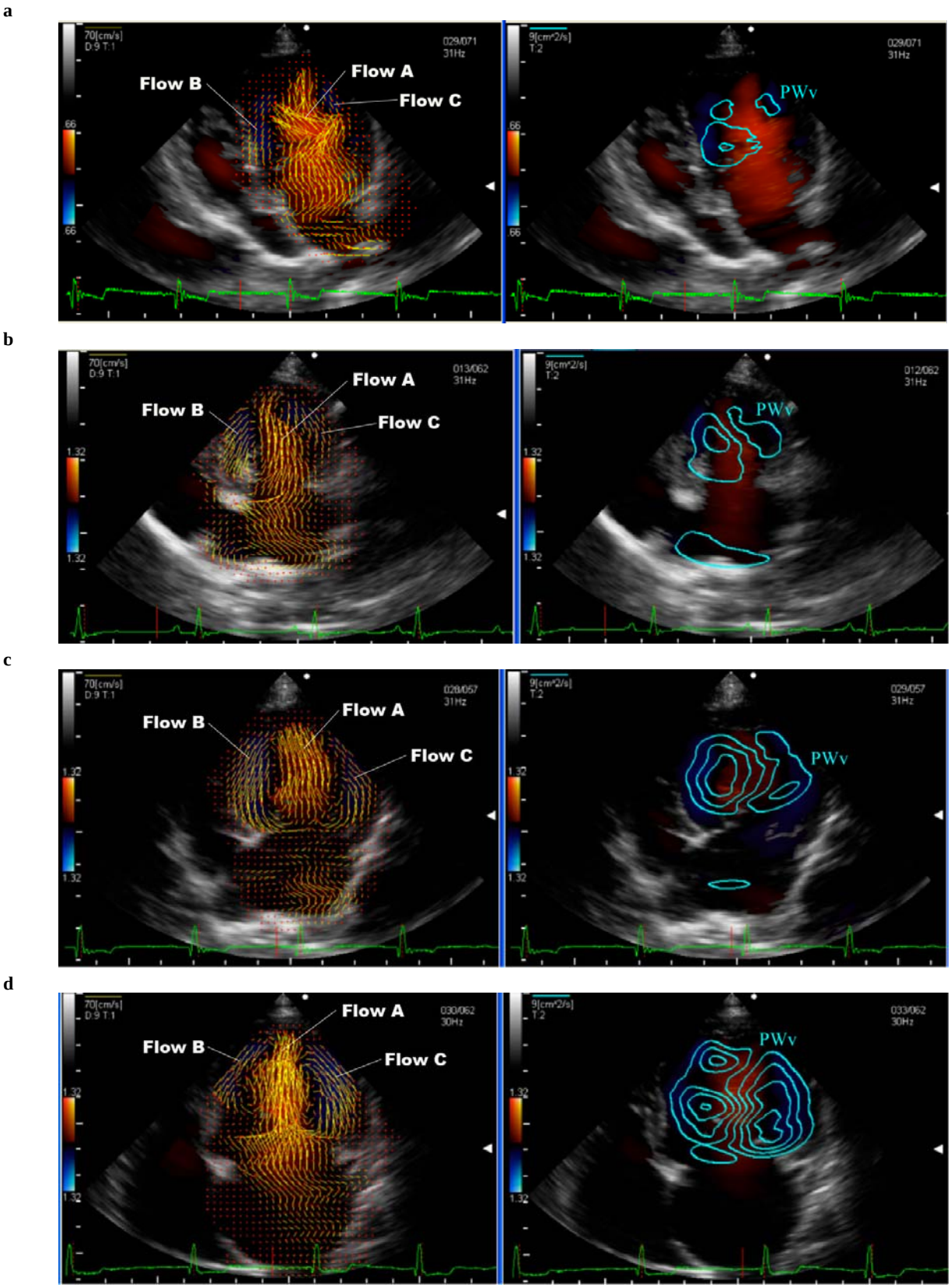

Fig. 2: VFM analysis in MVR group. a: Cases classified as ISACHC Ia. Vector turned over towards LV posterior wall (flow C) was observed towards apex of LV at papillary muscle level. This flow creates a vortex (PWv) on vortex mode, shown as blue circle along the LV posterior wall. b: Cases classified as ISACHC Ib. Vector turned over towards posterior wall (flow C) became larger, and PWv area became more distinct. c: Cases classified as ISACHC II. PWv became larger, reaching almost towards apex at posterior leaflet of mitral valve. d: Cases classified as ISACHC III. Vector reflected over posterior wall (flow C) was similar to those at ventricular septum (flow B). PWv became much larger, constituting more than half of left ventricle

the heart, has been previously discussed for the normal human heart. The vortex near the anterior leaflet of the mitral valve is believed to help close it. In the present study, vector flow mapping analysis of the control group's LV blood flow was similar to that of the normal human heart, and for the studied dogs, the vortex near the anterior leaflet of the mitral valve, observed from early diastole to systole, seems to have helped the valve's closure and energy storage by rotation as well.

In this study, the presence of abnormal PWv, which was not observed in the control group, was confirmed in the MVR group. For the control group, PWv occasionally differed in location from the vortex observed near the posterior leaflet of the mitral valve, which suggests that the MVR group had some reason to produce PWv. The first possibility is the expansion of the left atrium by the elevated left arterial pressure. At systole, the amount of energy increases with the volume of blood stored in the left atrium due to regurgitation, leading to the increased velocity of the blood inflow to the LV at diastole and a higher Reynold's number, resulting finally, in the generation of a disturbed flow. Secondly, the left ventricular volume overload is progressed by MVR, and is supposed to increase the area where blood is ejected from the left atrium. As shown by the Reynold's number formula, the movement of a liquid from narrow to wide areas can generate a disturbed flow. The left ventricular end-diastolic diameter of a normal dog without any cardiac condition is kept at a balance to prevent the generation of any disturbed flow. However, when LV is expanded by MVR, it disturbs the balance and PWv is generated.

When the vortex near the anterior leaflet of the mitral valve is used to close the valve and eject blood, PWv neither heads toward the outflow tract nor helps close the mitral valve. According to vector indications, PWv flows from the inside to the outside of the ventricle. On the other hand, cardiac enlargement might exacerbate by the blood that flows outside. For these reasons, it is concluded that the disadvantages of PWv, which is the loss of energy caused by the creation of the vortex, are more than the advantages of creating it. In addition, as the vortex enlarges, energy loss and reduction of ejection efficiency occur, worsening cardiac failure. In this study, ISACHC III cases formed a PWv equal to or larger than the "main flow", which is the vortex seen near the septum. PWv generation is also likely to have negative effects on heart motions, suggesting that its control can be an effective treatment for heart failure.

There are limitations that need to be acknowledged and addressed regarding this study. When VFM analysis is conducted, identical sections must be used to analyze various breeds and sizes of dogs as well as the position of their hearts. Verifications performed at our institute confirmed different appearances of the vortex on 4- and 2-chamber views from the left parasternal region. For this reason, a wealth of highly accurate images is necessary to conduct VFM analyses of large numbers of clinical cases. Vortex evaluation by VFM analysis also allows for qualitative evaluations; nevertheless, quantitative evaluation still remains a challenge. By decreasing the size of the vortex indication scale, assessments regarding vortex formation become possible. However, unless the scale is standardized, quantitative evaluations will not be possible. Currently, Aloka Medical, Ltd. is working to enable the quantitative evaluation of the vortex using vorticity by expressing rotatory circulation. If such evaluation becomes possible, classification of cardiac failure based on severity grade and classification of clinical conditions will be feasible.

Another point regarding the present study is that the dogs were all clinical cases treated with various medications depending on their conditions. In the future, it is necessary to evaluate the influence of these medications on the analysis of VFM. If drug therapies affect PWv, new options for therapeutic strategies considering energy efficiency will be available.

VFM analysis allows for the conformation of vortex which could not have been evaluated by color Doppler evaluation alone. Evaluating flow dynamics within the ventricle using VFM is suggested since it not only allows for hydrodynamic evaluation but also introduces the concept of "energy efficiency" which has not been given ample attention so far.

Additional investigations on the pathologic significance of the vortex are needed in the future. However, VFM evaluation of blood flow within the heart can lead to the establishment of a classification of clinical conditions and treatment planning, with special focuse on the new concept of the energy efficiency evaluation.

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Conflict of interest statement

There are no sources of funding, financial conflicts of interest or disclaimers regarding this study.

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