Quantification of mitral valve regurgitation in dogs with degenerative mitral valve disease by use of the proximal isovelocity surface area method

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Objective—To determine the within-day and between-day variability of regurgitant fraction (RF) assessed by use of the proximal isovelocity surface area (PISA) method in awake dogs with degenerative mitral valve disease (MVD), measure RF in dogs with MVD, and assess the correlation between RF and several clinical and Doppler echocardiographic variables.

Design—Prospective study.

Animals—6 MVD-affected dogs with no clinical signs and 67 dogs with MVD of differing severity (International Small Animal Cardiac Health Council [ISACHC] classification).

Procedures—The 6 dogs were used to determine the repeatability and reproducibility of the PISA method, and RF was then assessed in 67 dogs of various ISACHC classes. Mitral valve regurgitation was also assessed from the maximum area of regurgitant jet signal-to-left atrium area (ARJ/LAA) ratio determined via color Doppler echocardiographic mapping.

Results—Within- and between-day coefficients of variation of RF were 8% and 11%, respectively. Regurgitation fraction was significantly correlated with ISACHC classification and heart murmur grade and was higher in ISACHC class III dogs (mean ± SD, 72.8 ± 9.5%) than class II (57.9 ± 20.1%) or I (40.7 ± 19.2%) dogs. Regurgitation fraction and left atrium-to-aorta ratio, fractional shortening, systolic pulmonary arterial pressure, and ARJ/LAA ratio were significantly correlated.

Conclusions and Clinical Relevance—Results suggested that RF is a repeatable and reproducible variable for noninvasive quantitative evaluation of mitral valve regurgitation in awake dogs. Regurgitation fraction also correlated well with disease severity. It appears that this Doppler echocardiographic index may be useful in longitudinal studies of MVD in dogs. (*J Am Vet Med Assoc* 2007;231:399–406)

Degenerative MVD is characterized by valvular degeneration and is the most common heart disease in small-breed dogs.[1,2] It results in poor apposition of the mitral valve leaflets during systole and valvular regurgitation, which is detected as a left apical systolic heart murmur. The severity of mitral valve regurgitation is a major determinant of natural progression of the disease; worsening of the regurgitation leads to several complications such as chamber dilation and left-sided congestive heart failure. As in humans with valvular regurgitation,[3,4] accurate noninvasive quantification of mitral regurgitation is therefore important to assess MVD severity, monitor its progression, and evaluate the potential beneficial effects of treatments on valvular dysfunction in dogs.

A combination of 2-D and Doppler echocardiography is considered the method of choice for noninvasive detection and evaluation of valvular regurgitation by both human[4] and veterinary cardiologists.[5] Combination of 2-D and M-mode echocardiography permits the evaluation of valvular structure and the impact of volume overload on cardiac chambers[4] and provides indirect information regarding valvular dysfunction. A direct evaluation of valvular incompetence

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Abbreviations

MVD	Mitral valve disease
2-D	Two-dimensional
ARJ/LAA	Area of the regurgitant jet area signal to left atrium area
PISA	Proximal isovelocity surface area
EROA	Effective regurgitant orifice area
RF	Regurgitant fraction
ISACHC	International Small Animal Cardiac Health Council
Ao	Aortic diameter
LA	Left atrial dimension
PAH	Pulmonary arterial hypertension
DDE-PAH	Doppler echocardiography–derived evidence of pulmonary arterial hypertension
CV	Coefficient of variation

may be obtained via Doppler echocardiography. The color Doppler mode allows direct visualization of the regurgitation jet (origin, width, spatial orientation, and extension in the receiving chamber), and the maximum ARJ/LAA ratio provides an evaluation of mitral valve regurgitation severity.[4] The PISA method (also called the flow convergence method) is another Doppler technique routinely used in human medicine to quantify valvular regurgitation.[4] The main advantage of the PISA method is that it may allow more reliable discrimination of mitral valve regurgitation severity, providing quite accurate measurement of the EROA, the flow rate through the regurgitant orifice, and finally, the RF (the percentage of stroke volume ejected into the left atrium during systole).[4] The PISA method is based on the hydrodynamic continuity principle, which states that as blood approaches a flat regurgitant orifice, its velocity increases to form concentric, hemispheric shells of increasing velocity and decreasing surface area.[4] The PISA method has been validated in vitro[6–8] and also in humans.[9,10] However, to our knowledge, no studies have been performed to ascertain the repeatability and reproducibility of the PISA technique for the noninvasive assessment of RF in dogs with naturally occurring MVD, although 1 study[11] involving a small number of dogs was performed to assess how this Doppler index varies with disease severity.

The purpose of the study reported here was to determine the within-day and between-day intra-observer variability of RF assessed by the PISA method in awake dogs with naturally occurring mitral valve regurgitation attributable to MVD, measure RF in a large population of dogs affected with MVD of differing severity (ie, heart failure), and assess the correlation between RF and several clinical and Doppler echocardiographic variables including ARJ/LAA ratio (assessed via color Doppler mapping).

Materials and Methods

Animals—Client-owned dogs with MVD were prospectively recruited at the Cardiology Unit of Alfort. Owner's consent was obtained before enrollment. The diagnosis of MVD was made on the basis of several criteria: left apical systolic heart murmur that developed when the dog was > 1 year old; no history of infectious disease; and echocardiographic and Doppler signs of MVD, including evidence of irregular and thickened mitral valve leaflets in the right parasternal 4-chamber view and a color-flow jet of mitral valve insufficiency in the left atrium throughout systole in the left parasternal 4-chamber view. The degree of heart failure was classified according to ISACHC recommendations.[12] Thoracic radiography was performed for all dogs with clinical signs (ISACHC classes II and III), and dogs were excluded from the study if a concomitant respiratory disease was detected.

Phase 1—Within-day and between-day variabilities of the Doppler echocardiographic variables were determined by performing 36 Doppler echocardiographic examinations on 6 dogs with class I MVD that were not receiving treatment. The mean ± SD age of the dogs was 11.5 ± 2.4 years (range, 9 to 15 years), and mean weight was 7.6 ± 4.0 kg (16.72 ± 8.8 lb; range, 3.1 to 14.4 kg [6.82 to 31.68 lb]). For each dog, the Doppler echocardiographic examinations were performed on 4 days over a 2-week period. The group included 3 Poodles (2 sexually intact males and 1 neutered female), 1 Beagle (a sexually intact female), 1 Yorkshire Terrier (a neutered female), and 1 Shih Tzu (a sexually intact female). On each study day, 3 dogs were examined on 3 nonconsecutive occasions. Each variable was measured 3 times during 3 consecutive cardiac cycles, and the mean values were used to determine within- and between-day variabilities. This protocol involved a single trained observer (VC).

Phase 2—Dogs with MVD that were categorized as ISACHC classes I, II, or III were prospectively recruited over a 2-year period by the same observer involved in phase 1 (VC) and by 3 other observers (VG, APN, and FS). The latter 3 observers had been trained by the first observer in the use of the PISA method for at least 6 consecutive months before performing the Doppler echocardiographic examinations.

Two-dimensional and Doppler echocardiographic examinations with continuous ECG monitoring were carried out in standing awake dogs by use of ultrasound units[a,b] equipped with 7.5- to 10-MHz, 5- to 7.5-MHz, and 2- to 5-MHz phased-array transducers, as previously described and validated by the authors.[13]

2-D and M-mode echocardiography—Left ventricular chamber diameters were measured from the right parasternal location by use of the 2-D–guided M-mode[14] (according to the recommendations of the American Society of Echocardiography[15]), and the fractional shortening was then calculated. Measurements of the Ao and LA were obtained by use of a 2-D method as previously described,[16] and the LA/Ao ratio was calculated.

Doppler evaluation of PAH—All ultrasonographic examinations included a color Doppler analysis of tricuspid and pulmonary valve flows to detect any tricuspid or pulmonary valve regurgitant jets. When such a regurgitant jet was identified, the maximal regurgitant flow velocity was assessed by use of the continuous Doppler mode, and high velocity values (ie, ≥ 2.5 m/s and ≥ 2 m/s for tricuspid and pulmonary valve regurgitant jets, respectively) were recorded. A peak end-diastolic pulmonary valve regurgitant flow velocity ≥ 2 m/s was considered indicative of diastolic DDE-PAH. A peak tricuspid valve regurgitant flow velocity ≥ 2.5 m/s was considered indicative of systolic DDE-PAH. These 2 velocity thresholds correspond to high pulmonary arterial pressure values (reference ranges,[17] 15 to 25 mm Hg and 5 to 10 mm Hg in systole and diastole, respectively). The modified Bernoulli equation (pressure difference [ΔP] = $4 \times \text{velocity}^2$) was applied to the maximal velocity of telediastolic pulmonary and systolic tricuspid valve insufficiencies to calculate the diastolic pulmonary artery-to-right ventricle pressure gradient and the systolic right ventricle-to-right atrium pressure gradient across the tricuspid valve, respectively.[18] Systolic pulmonary arterial pressure was then calculated by addition of the estimated right atrial pressure to the systolic right ventricle-to-right atrium pressure gradient. The estimated right atrial pressure was 5 mm Hg in dogs with an apparently normal right atrium, 10 mm Hg in dogs with a large right atrium but no right-sided heart failure, and 15 mm Hg in dogs with right-sided heart failure.[17]

Quantification of mitral valve regurgitation via color Doppler mapping technique and PISA method—Color Doppler echocardiography was used to examine mitral valve regurgitation, and the ARJ/LAA ratio was calculated as previously described.[19] On the basis of this Doppler method, mitral valve regurgitation was classified as mild (ARJ/LAA ratio < 30%), moderate (ARJ/LAA ratio ≥ 30% but ≤ 70%), or severe (ARJ/LAA ratio > 70%). The PISA method was performed as previously described.[4,11] The color flow Doppler jet of mitral valve regurgitation was first identified in the left apical 4-chamber view with optimal gain setting, which was defined as the maximal gain level possible without background noise.[3] The view was then focused on the mitral valve region and magnified to identify the flow convergence region proximal to the regurgitant orifice. The baseline of the color flow scale was then shifted so that the Nyquist limit (or aliasing velocity) was decreased to a value of 18 to 39 cm/s in the direction of flow. The baseline shift was adjusted to obtain the most hemispheric shape of the proximal isovelocity region (ie, a hemicircle of aliasing flow pattern on the left ventricular side of the mitral valve; **Figure 1**).

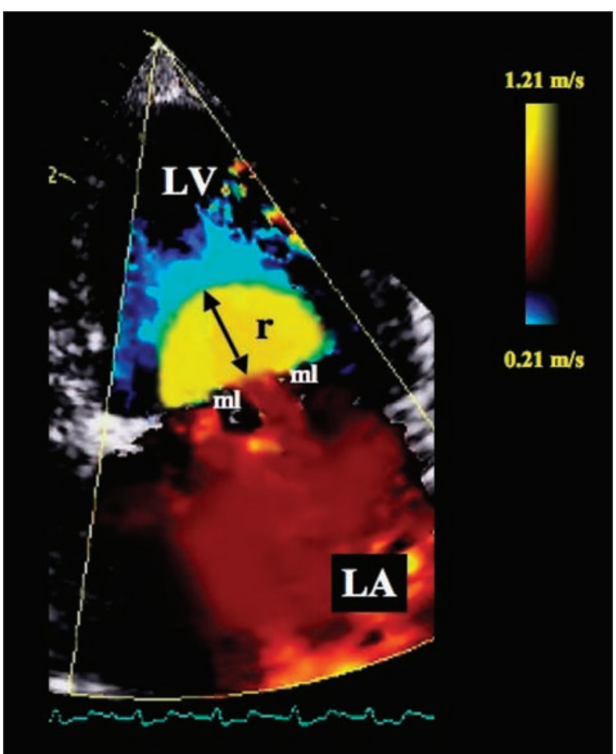

Figure 1—Color flow Doppler image (with continuous ECG tracing) from the left apical 4-chamber ultrasonographic view illustrating the hemicircle of the flow convergence region proximal to the mitral valve in a dog with MVD. The color flow baseline was shifted down and adjusted to obtain a well-defined hemicircle. The first aliasing limit for flow toward the mitral valve defines the PISA with a flow velocity (or aliasing velocity) of 0.21 m/s. The radius (r) of the proximal isovelocity hemicircle was measured from the regurgitant orifice to the blue-yellow aliasing border. LV = Left ventricle. LA = Left atrium. ml = Mitral valve leaflets.

Dogs for which a hemicircle could not be observed because of low-quality images, eccentric regurgitation, or a small or absent proximal isovelocity area as a result of mild regurgitation were not included in the study. All measurements were performed in midsystole for 3 consecutive cardiac cycles by use of the cineloop mode. The radius of each hemicircle (which corresponds to the distance between the aliasing blue-yellow border and the regurgitant orifice) was measured, and the regurgitant flow rate through the mitral valve orifice was calculated by use of a formula as follows:

$$\text{Flow rate (mL/s)} = (2\pi r^2) \times V_{al}$$

where r is the radius of the isovelocity hemicircle (cm) and V_{al} is the aliasing velocity (cm/s). A continuous-wave Doppler trace of the mitral valve regurgitation jet was then recorded, and peak velocity (V) and the velocity time integral (VTI) were measured. The EROA was calculated by use of a formula as follows:

$$\text{EROA (cm}^2\text{)} = \text{flow rate (mL/s)/V (cm/s)}$$

The regurgitant volume (RSV) was then calculated by use of a formula as follows:

$$\text{RSV (mL)} = \text{EROA (cm}^2\text{)} \times \text{VTI (cm)}$$

Finally, the variable of interest, RF, was calculated by use of a formula as follows:

$$\text{RF (\%)} = \text{RSV (mL)/ RSV (mL)} + \text{ASV (mL)}$$

where ASV is the aortic stroke volume calculated as previously described by Kittleson and Brown[11] by use of the aortic diameter and the mean of 3 consecutive velocity time integrals obtained from pulsed wave Doppler traces of systolic aortic flow velocity on the left apical 5-chamber view.

Statistical analysis—For the validation protocol (phase 1), a linear model was used for each echocardiographic Doppler and TDI variable in the within-day and between-day variability analysis as follows:

$$Y_{ijk} = \mu + \text{day}_i + \text{dog}_j + (\text{day} \times \text{dog})_{ij} + \varepsilon_{ijk}$$

where Y_{ijk} is the kth value measured for dog j on day i, μ is the general mean, day_i is the differential effect of day i, dog_j is the differential effect of dog j, $(\text{day} \times \text{dog})_{ij}$ is the interaction term between day and dog, and ε_{ijk} is the model error. The SD of repeatability was estimated as the residual SD of the model and the SD of reproducibility as the SD of the differential effect of day. The corresponding CVs were determined by dividing each SD by the mean.

For phase 2, the data were expressed either as mean ± SD values or as percentages. The nonparametric Spearman correlation coefficient was calculated between RF and ISACHC class or murmur grade. The Pearson product moment correlation was used to study correlations between RF and LA/Ao ratio, RF and ARJ/LAA ratio, and RF and pulmonary arterial pressure. A 1-way ANOVA, followed if necessary by a Student *t* test with Bonferroni correction, was used to compare Doppler echocardiographic variables among the 3 ISACHC classes. Values of $P < 0.05$ were considered significant.

Results

Phase 1—The within-day and between-day intraobserver variabilities of Doppler echocardiographic variables were assessed. The within- and between-day CV values for the ARJ/LAA ratio were 7% and 8%, corresponding to SD values of 4% and 5%, respectively. The within- and between-day CV values for RF were 8% and 11%, corresponding to SD values of 4% and 6%, respectively. No significant interaction was detected between day and dog for the 2 Doppler echocardiographic variables tested.

Phase 2—Regurgitant fraction was assessed in 73 dogs with MVD via the PISA method. Six (8.2%) dogs were excluded from the study because of an eccentric jet or inadequate images of a hemispheric proximal isovelocity region. Therefore, 67 dogs were enrolled in the study **(Table 1)**. As expected, the study population was mostly composed of male adult dogs (mean age, 10.5 ± 3.0 years; range, 4 to 16 years) of small breeds weighing < 10 kg (< 22 lb). The most frequently represented breeds were Poodle (miniature and toy) and Cavalier King Charles Spaniel.

The treatment at the time of diagnosis was known for all 67 dogs included in phase 2. Twenty-nine (43.3%) dogs were receiving ≥ 1 treatment for heart failure, including angiotensin converting enzyme inhibitors such as benazepril, enalapril, imidapril, or ramipril (9 [31%] dogs); furosemide (20 [69%] dogs); and spironolactone (8 [27.6%] dogs).

In all dogs, cardiac auscultation revealed a left apical systolic heart murmur (grades 1 to 5/6). The murmur was classified as grade 1/6 and 2/6 in 1 (1.5%) dog each, grade 3/6 in 9 (13%) dogs, grade 4/6 in 36 (54%) dogs, and grade 5/6 in 20 (30%). Forty-six of the 67 (68.7%) dogs had no clinical signs and therefore were categorized as ISACHC class I **(Table 2)**. In 32 of the 46 (69.6%) dogs in class I, the LA/Ao ratio (range, 0.66 to 1.10) was within reference limits[16]; those dogs were therefore categorized as class Ia. The other 14 (30.4%) dogs had a dilated left atrium (LA/Ao ratio, 1.14 to 2.20) and were categorized as class Ib. The remaining dogs had clinical signs and were categorized as ISACHC class II (n = 6 [9.0%]) or ISACHC class III (15 [22.4%]).

Assessment of mitral regurgitation via color Doppler mapping and PISA method—Echocardiographic and Doppler data were obtained from all dogs included in phase 2 (Table 2). The mean RF and ARJ/LAA ratio values for the study population of 67 dogs were 49.4 ± 22.0% (range, 0.6% to 84.4%) and 82.1 ± 22.6% (range, 23.9% to 100%), respectively. The maximum RF value was < 85%. The ARJ/LAA ratio attained the maximum value of 100% in 32 (47.8%) dogs; these dogs included 14 of 46 (30.4%) dogs in ISACHC class I, 4 of 6 (66.7%) dogs in class II, and 14 of 15 (93.3%) dogs in class III. Among those 32 dogs, RF ranged from 22.3% to 84.4%.

Table 1—Characteristics of 67 dogs with MVD of differing severity in which RF was assessed for correlation with several clinical and Doppler echocardiographic variables.

Characteristic		No. of dogs (%)
Sex	Male	42 (62.7)
	Female	25 (37.3)
Age (y)	< 1–5	7 (10.5)
	> 5–10	26 (38.8)
	>10	34 (50.7)
Breed	Poodle (14 Miniature and 2 Toy)	16 (23.9)
	Cavalier King Charles Spaniel	16 (23.9)
	Yorkshire Terrier	8 (11.9)
	Mixed	6 (9.0)
	Bichon	5 (7.5)
	Pyrenean Shepherd	3 (4.5)
	Shih Tzu	3 (4.5)
	Golden Retriever	2 (3.0)
	Brittany	2 (3.0)
	Other breed (1 dog/breed; Doberman Pincher, Teckel, Pekinese, Beagle, Jack Russell Terrier, Schnauzer)	6 (9.0)
Body weight (kg [lb])	< 10 (22)	42 (62.7)
	10–20 (22–44)	23 (34.3)
	> 20 (44)	2 (3.0)

Table 2—Main echocardiographic and Doppler variables (mean ± SD and range) in 67 dogs with MVD categorized according to ISACHC heart failure class.

	ISACHC heart failure class		
Variable	I (n = 46 [68.7%])	II (n = 6 [9.0%])	III (n = 15 [22.4%])
LA/Ao ratio	1.07 ± 0.33 (0.65–2.20)	1.63 ± 0.32† (1.19–2.15)	2.20 ± 0.85† (1.15–4.63)
Fractional shortening (%)	43.1 ± 7.3 (27.8–59.0)	46.3 ± 10.7 (34.6–63.0)	51.9 ± 7.6† (34.8–61.0)
Systolic pulmonary arterial pressure (mm Hg)*	49 ± 21 (28–95) (n = 18)	85 ± 31‡ (50–121) (n = 4)	88 ± 20† (62–116) (n = 8)
ARJ/LAA ratio (%)	75.6 ± 23.7 (23.9–100.0)	88.4 ± 18.0 (61.9–100.0)	99.5 ± 2.1†,§ (91.8–100.0)
RF (%)	40.7 ± 19.2 (0.6–77.6)	57.9 ± 20.1‖ (28.0–80.6)	72.8 ± 9.5†,§ (51.1–84.4)

*Only assessed in dogs with systolic DDE-PAH. †For this variable, value was significantly ($P < 0.001$) different from that in class I. ‡For this variable, value was significantly ($P < 0.01$) different from that in class I. §For this variable, value was significantly ($P < 0.05$) different from that in class II. ‖For this variable, value was significantly ($P < 0.05$) different from that in class I.

The RF was significantly ($P < 0.001$) correlated with the ARJ/LAA ratio ($r = 0.58$). Mean RF in dogs with mild mitral valve regurgitation as assessed by use of the color Doppler mapping method (ARJ/LAA ratio < 30%) was 10.6 ± 11.2%; this value was significantly lower than that determined in dogs with moderate (ARJ/LAA ratio ≥ 30% but ≤ 70%) or severe (ARJ/LAA ratio > 70%) regurgitation (37.0 ± 17.3% [$P < 0.05$] and 54.9 ± 20.0% [$P < 0.001$], respectively).

Correlations of ARJ/LAA ratio and RF with clinical variables—A significant ($P < 0.001$) correlation was identified between heart murmur grade and RF ($r = 0.67$) and heart murmur grade and ARJ/LAA ratio ($r = 0.62$). A significant ($P < 0.001$) correlation was also detected between ISACHC class and RF ($r = 0.66$). The RF was significantly different between ISACHC classes I and II ($P < 0.05$), between classes I and III ($P < 0.001$), and also between classes II and III ($P < 0.05$). Interestingly, a wide range of ARJ/LAA ratios was apparent among the 46 ISACHC class I dogs; on the basis of the ARJ/LAA ratio, mitral valve regurgitation was classified as mild, moderate, and severe in 3 (6.5%), 11 (23.9%), and 32 (69.6%) dogs, respectively. Similarly, a wide range of RF was detected among the 46 ISACHC class I dogs; values were < 30%, 30% to 50%, and > 50% in 15 (32.6%), 16 (34.8%), and 15 (32.6%) dogs, respectively.

Correlations of ARJ/LAA ratio and RF with other Doppler echocardiographic variables—A significant correlation was detected between RF and LA/Ao ratio ($r = 0.59$; $P < 0.001$; **Figure 2**) and also between RF and fractional shortening ($r = 0.38$; $P < 0.01$). There was a significant ($P = 0.002$) correlation between ARJ/LAA and LA/Ao ratios ($r = 0.43$).

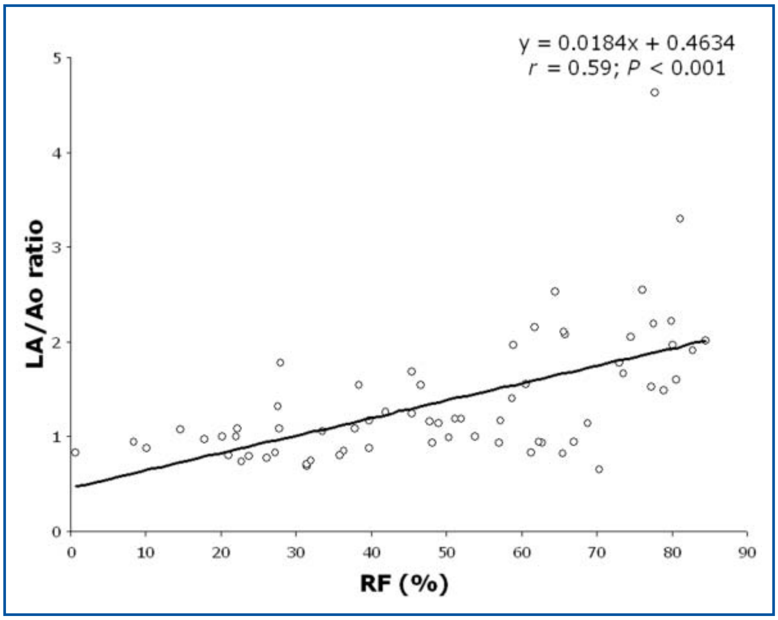

Figure 2—Correlation between the LA/Ao ratio and the RF (assessed via 2-D echocardiography and the PISA method, respectively) in 67 dogs with MVD of differing severity. The line represents the linear regression between the 2 variables.

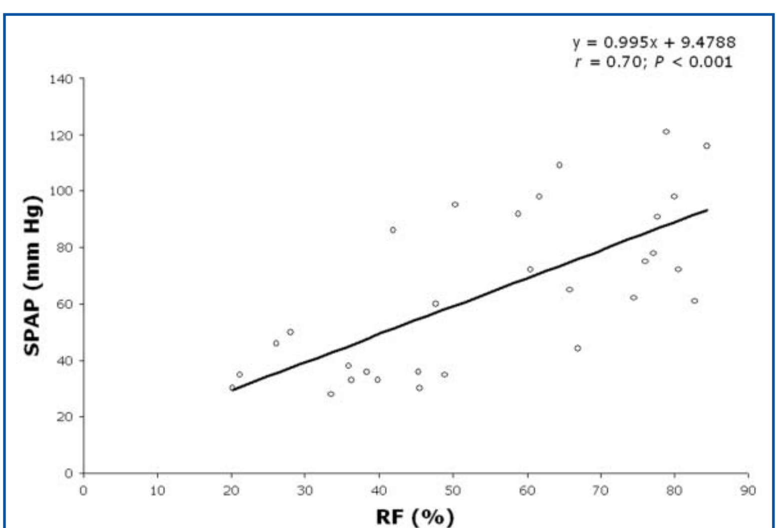

Figure 3—Correlation between the systolic pulmonary pressure (SPAP) value and RF in a subset of the 67 dogs in Figure 1 composed of 30 dogs with DDE-PAH. Of those dogs, 3 had DDE-PAH during both diastole and systole, and 27 had DDE-PAH during systole only. The line represents the linear regression between the 2 variables.

Twenty-seven of the 67 (40.3%) dogs included in phase 2 had echocardiographic signs of ruptured chordae tendineae (ie, evidence of a mitral valve flail with the leaflet tip pointing back into the left atrium during systole), which were confirmed in several 2-D imaging planes by use of the left and right parasternal 4-chamber views. The 27 dogs with ruptured chordae tendineae had a significantly higher LA/Ao ratio (1.80 ± 0.82; $P < 0.001$), ARJ/LAA ratio (93.4 ± 12.4%; $P < 0.001$), and RF (66.2 ± 15.9%; $P < 0.001$) than the 40 dogs without ruptured chordae tendineae (1.09 ± 0.36, 74.5 ± 24.7%, and 38.1 ± 18.0%, respectively).

Of the 67 dogs with MVD, 30 had DDE-PAH. Of those 30 dogs, 3 had DDE-PAH during both diastole and systole and 27 had DDE-PAH during systole only. The diastolic pulmonary artery-to-right ventricle pressure gradient could not be assessed in 4 of the dogs with DDE-PAH during systole only because of a lack of diastolic pulmonary valve regurgitant flow. In the other 23 dogs, a diastolic pulmonary valve regurgitant flow of low velocity (< 0.6 m/s) was detected, thereby excluding diastolic DDE-PAH. Mean systolic pulmonary arterial pressure in the 30 dogs with DDE-PAH was 64.2 ± 28.8 mm Hg (range, 28 to 121 mm Hg). Mean diastolic pulmonary pressure in the 3 dogs with DDE-PAH during both diastole and systole was 28.0 ± 8.5 mm Hg (16 to 35 mm Hg). In the 30 dogs with systolic DDE-PAH, systolic pulmonary arterial pressure was significantly ($P < 0.001$) correlated with RF ($r = 0.70$; **Figure 3**).

Discussion

Few studies[20,21] have focused on the use of the PISA method in dogs, except for investigations in dogs with experimentally induced valvular regurgitation and in a small population of dogs with naturally occurring MVD.[11,22] To our knowledge, the present study is the first in which variability of RF calculated by the PISA method in dogs has been assessed. It is also the first in which RF in dogs has been prospectively analyzed with regard to heart failure severity, several Doppler echocardiographic variables (ARJ/LAA ratio, fractional shortening, and pulmonary arterial pressure), and the presence of ruptured chordae tendineae in a large population of dogs with naturally occurring MVD.

One of the methods commonly used to assess mitral valve regurgitation severity noninvasively in veterinary medicine is to calculate the ARJ/LAA ratio by use of color Doppler mapping. A major advantage of this method is the rapidity and ease of data acquisition. The ARJ/LAA ratio is a semiquantitative index, which may be influenced by several factors, including arterial blood pressure, left atrial pressure, hemodynamic factors (eccentric wall-impinging jets can appear considerably smaller than centrally directed jets of similar hemodynamic severity), pulse repetition frequency, and gain settings.[4,23] Another limitation of the ARJ/LAA ratio, as highlighted by the data obtained in the present study, is that the maximum value of 100% is attained in a large proportion of dogs in each heart failure category (in the present study, 100% was attained by 30.4%, 66.7%, and 93.3% of dogs in ISACHC classes I, II, and III, respectively), which precludes accurate discrimination among dogs with severe mitral valve regurgitation. In contrast, RF determined via flow convergence or the PISA method cannot attain a maximum value of 100% in any dog and should therefore be better suited to such discrimination. The flow convergence or PISA method is commonly used to quantify mitral valve regurgitation in humans. Studies[24,25] in humans have revealed that color flow Doppler imaging of the flow convergence region is relatively independent of technical factors and provides a reliable method for estimating the severity of mitral regurgitation, compared with invasive techniques such as selective angiography. Although the PISA method is more time-consuming than color Doppler mapping and many precautions need to be taken to ensure optimal acquisition of the flow convergence images,[4] the results of the present study have indicated that RF repeatability and reproducibility in awake dogs is good and comparable to that of the ARJ/LAA ratio—the within- and between-day CV values for both Doppler echocardiographic indices were < 12% without any interaction between dog and day. These results are in agreement with those obtained in humans.[26] Choi et al[21] determined that intra- and interobserver variability for mitral regurgitant stroke volume assessments in dogs were much higher (21.7% and 18.4%, respectively). However, the variability of the EROA (another PISA-derived index) in the latter report[21] was quite good (< 15%). The EROA is a commonly used variable that is generated via the PISA method to assess the severity of valvular disease in humans.[4] In the present study, we chose to focus on a single variable, RF, which is a ratio that may be compared among dogs of various sizes. Compared with EROA, one could argue that assessment of the RF is associated with more variability because it is calculated from the EROA value and also from the peak velocity and velocity time integral of the mitral valve regurgitation jet and aortic stroke volume. Nevertheless, the results of the present study indicated that RF is a repeatable and reproducible variable with within- and between-day CV values of 8% and 11%, respectively.

Another objective of our study was to assess the correlation between RF and several clinical and imaging markers of MVD severity. The data obtained indicated that RF was significantly correlated not only with heart murmur grade and heart failure category but also with the LA/Ao ratio and systolic pulmonary arterial pressure. In a recent study[27] conducted by our group, DDE-PAH was not an uncommon finding in dogs with MVD (total prevalence of 14%), and the prevalence and degree of DDE-PAH were closely related to the severity of the disease. In the present study, RF differed significantly between dogs with or without rupture of the chordae tendineae, which is a potentially severe complication of MVD. These data have thus confirmed that, as determined in human studies,[28,29] RF adequately reflects the clinical severity of the valvular disease as well as its hemodynamic and physiopathologic consequences in dogs.

The first consequence of mitral valve regurgitation on heart morphology is left atrial dilation that may be noninvasively estimated from the LA/Ao ratio obtained via 2-D echocardiography. In the present study, RF was significantly correlated with the LA/Ao ratio, although the left atrial size in a large number of dogs (32/67 [47.8%]) was considered normal. A similar correlation was previously identified by Kittleson et al[11] in a smaller population of dogs (n = 17), all of which had left atrial dilation.

Interestingly, the dogs without clinical signs (ISACHC class I) in the present study had a wide range of RF (0.6% to 77.6%). Because most of the dogs included in the present study were small-sized dogs living in towns (Paris or suburbs of Paris), 1 hypothesis to explain the absence of clinical signs despite a high RF might be the very limited daily exercise of the dogs. A sedentary life would decrease the risk of cardiac decompensation. This dispersion of RF values in the asymptomatic stage in humans with mitral valve regurgitation is well known, and use of the PISA method is now routinely recommended at this stage for the quantitative grading of mitral valve incompetence and improved definition of high-risk patients that might benefit from early medical or surgical treatment.[4,30] It has recently been reported[4,30] that the clinical outcome of asymptomatic mitral valve regurgitation in humans (eg, death from cardiac causes, cardiac events, and the 5-year survival rate) is highly dependent on the quantitative grading of mitral regurgitation. Humans without clinical signs who have severe regurgitation assessed by flow convergence technique (EROA > 40 mm^2 or RF > 50%) should even be considered for cardiac surgery. The clinical outcome of MVD-affected dogs without clinical signs is still poorly defined, and criteria for identification of dogs in heart failure class I that are at a higher risk of early decompensation have still not been determined. In the present study, approximately a third of the dogs without clinical signs had an RF > 50%. Whether or not this subgroup of dogs had a higher risk of early decompensation, and whether those dogs would benefit from early medical treatment, more so than dogs without clinical signs but with lower RF, needs to be investigated in further studies.

Muzzi et al[19] detected a significant correlation between ARJ/LAA ratio and RF in dogs with MVD, although a different method than that applied in the present study was used to calculate RF; those investigators calculated the percentage difference between mitral valve and aortic stroke volume as assessed via pulsed-wave Doppler mode, which has several limitations.[31] In the present study, the ARJ/LAA ratio assessed via color Doppler mapping was also significantly correlated with RF. Furthermore, that method of assessment of ARJ/LAA ratio had good repeatability and reproducibility. Therefore, it appears that this index can be used to assess mitral valve regurgitation severity and can also be recommended for long-term follow-up of dogs with MVD despite its limitations. The severity of MVD may thus be better assessed by combining the 2 Doppler echocardiographic indices (ARJ/LAA ratio and RF) because they have different advantages and drawbacks. Area of the regurgitant jet area signal is still one of the variables used in humans to determine the management of mitral valve regurgitation[4] because measurements obtained from Doppler color flow images correlate well with those obtained via angiography[32] and ARJ/LAA ratio compensates for several PISA method limitations. The shape of the regurgitant orifice, for example, changes the shape of the hemicircle of aliasing flow pattern on the left ventricular side of the mitral valve that has to be established for use of the PISA method and thus may reduce the method's accuracy.[4,33,34] The PISA method is more accurate for central jets than for eccentric jets and for regurgitations associated with a circular orifice rather than for those associated with a noncircular orifice.[4,33,34] Moreover, in some instances, it may be difficult to judge the precise location of the orifice and the flow convergence shape. Any error introduced is then squared, which can markedly affect the resulting flow rate and EROA. In addition, the presence of multiple regurgitant jets, which can occur in dogs with severe disease, precludes use of the PISA method.[4,33,34] Lastly, if the valvular regurgitation is mild, no flow convergence can be detected.[4]

The study of this report has several limitations. Despite the fact that most of the PISA examinations were performed by the same investigator (VC), for whom the variability among assessments was known, some examinations were also performed by well-trained residents, for whom the variability among assessments was not assessed. Moreover, > 40% of the dogs had received medical treatment for heart failure including angiotensin converting enzyme inhibitors, furosemide, and spironolactone, which might have interfered with the study results and modified both their RF and ARJ/LAA ratio as well as other echocardiographic variables to an unknown extent. In addition, RF was not compared with invasive indices such as angiographic grading to determine its accuracy in quantifying the severity of mitral valve regurgitation. Nevertheless, the results of the present study have suggested that the RF assessed by the flow convergence method is a repeatable and reproducible variable for the noninvasive evaluation of mitral valve regurgitation in awake dogs with MVD. It also correlated well with disease severity. We believe that this Doppler index is reliable, and its assessment can therefore be recommended for use, in combination with evaluation of other Doppler echocardiographic variables, in longitudinal studies of MVD in dogs.

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a. Vingmed system 5, Vivid 5, General Electric Medical System, Waukesha, Wis.
b. Vivid 7, General Electric Medical System, Dimension BT04 digital ultrasound system, GE-Vingmed Ultrasound, Horten, Norway.

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