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Real-Time 3-Dimensional Echocardiographic Assessment of Effective Regurgitant Orifice Area in Dogs With Myxomatous Mitral Valve Disease

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Background: Effective regurgitant orifice area (EROA), calculated from the vena contracta width (VCW) as the narrowest portion of the proximal regurgitant jet, might be used to estimate severity of mitral regurgitation. However, this simplified assumption only holds when the EROA is circular, which might not be true in dogs with myxomatous mitral valve disease (MMVD).

Hypothesis: Effective regurgitant orifice area in dogs with MMVD is noncircular, and using color Doppler real-time 3-dimensional (RT3D) echocardiography, measured EROA in the en face view will be significantly different from calculated EROA.

Animals: Hundred and fifty-eight privately owned dogs with naturally occurring MMVD.

Materials and Methods: Prospective observational study comparing en face view of EROA with calculated EROA using VCW in 4-chamber (4Ch) and 2-chamber (2Ch) view only or combined 4Ch and 2Ch views using RT3D echocardiography.

Results: The calculated EROA using the 2Ch view showed a systematic underestimation of 17% compared with the measured en face EROA corrected for body surface area. The calculated EROA using 4Ch and 4Ch + 2Ch views showed less agreement with the en face EROA, and the difference between methods increased with increasing EROA. The difference between calculated and measured EROA showed a systematic underestimation of the calculated EROA by 36% (4Ch) and 33% (4Ch + 2Ch), respectively, compared to measured en face EROA.

Conclusion and Clinical Importance: When replacing measured EROA with calculated EROA using VCW measurements, the 2Ch view is preferred in dogs with MMVD.

Key words: Color flow Doppler; Mitral regurgitation; Regurgitant jet area; Vena contracta.

Myxomatous mitral valve disease (MMVD) is the most common type of heart disease in dogs, and assessment of disease severity is essential for appropriate clinical management and prognostication. Various qualitative and quantitative 2-dimensional (2D) echocardiographic methods have been used for this purpose. Cardiac chamber remodeling, in particular the size of the left atrium (LA),[1–3] as well as quantification of mitral regurgitation (MR)[4–6] remains the 2 most commonly used methods to assess severity of MMVD. Color flow Doppler echocardiography provides information regarding the size of the regurgitant jet, its width and spatial orientation, as well as flow

Abbreviations:

2Ch	2-chamber
2D	2-dimensional
3D	3-dimensional
4Ch	4-chamber
Ao	aorta
AUC	area under the curve
CHF	congestive heart failure
CV	coefficient of variation
EROA	effective regurgitant orifice area
HR	heart rate
IQR	interquartile range
LA/Ao	left atrial short-axis to aortic short-axis diameter ratio
LAA	left atrial area
LAlax/Ao	left atrial long-axis to aortic short-axis diameter ratio
LA	left atrium
LVIDDn	left ventricular end-diastolic internal diameter corrected for body weight
LVIDSn	left ventricular end-systolic internal diameter corrected for body weight
LV	left ventricle
MMVD	myxomatous mitral valve disease
MR	mitral regurgitation
MV	mitral valve
RJA	regurgitant jet area
ROC	receiver operating characteristics
RT3D	real-time 3-dimensional
SD	standard deviation
TR	tricuspid regurgitation
VC	vena contracta
VCW	vena contracta width

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The examinations were performed at Anicura Albano Animal Hospital. Part of the study was presented as an abstract at the 24th ECVIM-CA Congress, September 2014, Mainz, Germany.

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convergence into the regurgitant orifice.[7] The ratio of regurgitant jet area (RJA) to LA area (RJA/LAA) is commonly used as a qualitative or semiquantitative method to assess the severity of mitral valve (MV) disease in people and dogs.[5,8] Although this method is easily performed, it is influenced by several factors such as systemic blood pressure (ie, the driving pressure), left ventricular (LV) contractility, loading conditions, LA compliance, spatial orientation of the jet, pulse repetition frequency, and color gain settings.[9] Using the proximal isovelocity surface area (PISA) method to assess severity of MR is also largely dependent on gain settings and includes multiple computational steps based on the assumption of a hemispheric shape of the proximal flow, which only holds for a circular regurgitant orifice.[10] The vena contracta (VC) is measured as the narrowest portion of the proximal regurgitant jet visualized by the use of color flow Doppler and is characterized by high velocity laminar flow. The width of the vena contracta (VCW) is considerably less sensitive to technical factors compared to RJA, and is independent of flow rate and driving pressure for a fixed orifice, but might change with hemodynamics or during the cardiac cycle if the regurgitant orifice is dynamic.[9] The VCW, reflecting the regurgitant orifice area, has been shown to correlate with the severity of the MR lesion in people.[11,12] A recent study of 10 dogs with MMVD showed good correlation between cardiac magnetic resonance imaging-derived MR fraction and VCW to aortic diameter ratio and E wave velocity measured by 2D echocardiography.[7] A retrospective study of a large number of dogs with MMVD, classified with 5 levels of MR severity, showed median VCW of 0.29–0.46 cm in the 4-chamber (4Ch) view.[13]

Effective regurgitant orifice area (EROA) corresponds hemodynamically to the cross-sectional area of the VC.[14] However, this simplified assumption only holds when the EROA is circular, which might not be true in dogs with MMVD. The VCW might differ between the 4Ch view and the 2-chamber (2Ch) apical view of the cardiac chambers, because the 2Ch view is oriented parallel to the MV leaflet coaptation line and generally shows a wider VC compared to the 4Ch view.[15] Thus, the regurgitant orifice in MR commonly is not circular and should therefore not be measured in only the 4Ch view.[16] However, the exact shape and size of EROA cannot be accurately assessed by color Doppler 2-dimensional echocardiography alone. Real-time 3-dimensional (RT3D) echocardiography allows visualization of a regurgitant jet from any plane, and EROA can be directly measured without the use of a predefined geometric model. Hence, the most important advantage of RT3D echocardiography is independence of geometric modeling and image plane positioning.[17] Studies in human patients with MR showed excellent correlation between measurements of EROA using RT3D echocardiography and magnetic resonance imaging.[16] In vitro studies have shown that VC area measured by RT3D Doppler echocardiography strongly correlates with a known orifice area.[18,19]

The aim of our study was to compare measured EROA in the en face view using color Doppler RT3D echocardiography with calculated EROA estimated in 4Ch and 2Ch apical views of the LV in the same RT3D acquisition in dogs with MMVD.

Materials and Methods

Dogs

Privately owned dogs with MMVD presented to Albano Animal Hospital, Stockholm, Sweden, were included in the study. All dogs were examined clinically and by use of the same equipment and the same protocol. Diagnostic criteria for MMVD included MV leaflets that were thickened or prolapsing or both, and MR detected on color-coded Doppler echocardiogram.[20] Dogs with multiple jets were excluded from the study, as were dogs in which an arrhythmia was detected. Dogs were classified with and without CHF according to the American College of Veterinary Internal Medicine (ACVIM) classification of MMVD.[21,22] All examinations were performed and later evaluated by 1 veterinary specialist in cardiology (AT). The study was approved by the Ethical Committee for Animal welfare in Stockholm, Sweden.

Two-Dimensional Echocardiography

Two-dimensional and RT3D echocardiographic examinations were performed with an ultrasound unit[a] using 5.0–8.5 MHz phased-array transducers (for 2D) and 5- or 7-MHz matrix transducers (for RT3D) in all dogs. Dogs were unsedated and gently restrained in right and then left lateral recumbency during the examination. Measurements of LV diameters were made using 2D-guided M-mode obtained from parasternal right-sided short-axis views according to the American Society of Echocardiography.[23] Ventricular end-diastole was defined as the first frame after MV closure, and ventricular end-systole was defined as the frame before MV opening. Left ventricular internal diameter was normalized for body weight at end-diastole (LVIDDn) and at systole (LVIDSn) using the formulas: LVIDD/(body weight [kg])$^{0.294}$ and LVIDS/(body weight [kg])$^{0.294}$, respectively.[24] Measurements of aorta (Ao) and LA in early ventricular diastole were made on the 2D right parasternal short-axis view obtained at the level of the aortic valve at the first frame after aortic valve closure.[20] Dogs were classified as having mild, moderate, or severe MMVD based on LA/Ao $\leq$1.5, >1.5 and <1.8, and $\geq$1.8, respectively.[25] Measurements of LA also were made in right parasternal long-axis view (LAlax), and both short-axis and long-axis LA dimensions were indexed to Ao diameter measured in short-axis view.[26] Measurements on M-mode images of LV and 2D images of Ao and LA were made directly on the monitor freeze-frame image. For color flow investigation of MR and tricuspid valve regurgitation (TR) flow, the Nyquist velocity limit was set at 0.6–0.7 m/s.[27] The RJA/LAA ratio was subjectively assessed as <30% (mild), 30–50% (moderate), or >50% (severe).[25] Continuous-wave Doppler was used to measure MR and TR velocities, and pulsed-wave Doppler was used to measure aortic, pulmonic, and E and A wave velocities.

Three-Dimensional Echocardiography

The RT3D images of the LA and LV were obtained using the ×5 or ×7 matrix transducer (depending on the size of the dog) to obtain a pyramidal volume in real time. Transducer position was optimized to obtain apical 4Ch and 2Ch views of LA and LV. Four smaller real-time volumes, acquired from 4 consecutive cardiac cycles, were combined to produce a larger pyramidal volume, providing a full-volume dataset. For RT3D color flow Doppler examinations, Nyquist limits were set between 0.6 and 0.7 m/s.[27] Frame rates of 17–20 frames/s were used for RT3D color Doppler investigations.[28]

Off-line analyses of color Doppler RT3D images were made using a software program[b]. Jets were categorized as being concentric or eccentric in the 4Ch apical view. For eccentric jets, deviation from midline in the 4Ch view was estimated as ±30°, 45°, or 60° from midline. The mid-systolic frame representing the largest orifice size where the jet was best defined was selected for measurements of the VCW and EROA. The image plane then was manually adjusted to be perpendicular to the jet direction, and the cropping plane was moved along the jet direction until the smallest jet cross-sectional area at the level of the VC just proximal to the MV orifice was visualized. The VCW then was measured in 4Ch and 2Ch views, and direct measurement of the EROA was made in the en face view (Fig 1). All measurements were made in the same acquisition with exact same timing. Effective regurgitant orifice area was calculated from the VCW in the 4Ch view and in the 2Ch view only (assuming a circular regurgitant orifice) and from measurements of VCW in both 4Ch and 2Ch views (assuming an elliptical regurgitant orifice) using the common formula.[16] An asymmetry index of the calculated EROA was expressed as the ratio of 2Ch diameter/4Ch diameter of VCW.[15] Measured and calculated EROA were indexed to body surface area (BSA) using the following formula: $(BW^{0.67}/100) \times 10.1$.[29]

Variability

Within-day intra- and interobserver variation was evaluated by 2 observers (AT and ABW) in 5 additional dogs with MMVD Class B2 (3 dogs) or C2 (2 dogs) not included in the study. Each observer performed 5 examinations on each dog on a given day. Effective regurgitant orifice area was measured in the en face view off-line by each observer separately.

Beat-to-beat variation was assessed in all dogs in the study where 3 consecutive measurements of EROA were made from the en face view.

Statistical Analysis

A computer program[c] was used for all statistical analyses, and data are presented as medians and interquartile ranges (IQR). Echocardiographic and Doppler variables in dogs with and without CHF were compared (Table 1). The nonparametric Kruskal–Wallis test was used for testing equality of medians. The probability of a noncircular EROA was calculated using Wilcoxon signed-rank test. Bland-Altman plots were used to evaluate agreement between BSA-indexed values of measured EROA in the en face view and calculated values of EROA in 4Ch view, 2Ch view, and 4Ch + 2Ch view.[30] The agreement between the compared methods was further evaluated by fitting a linear curve to the

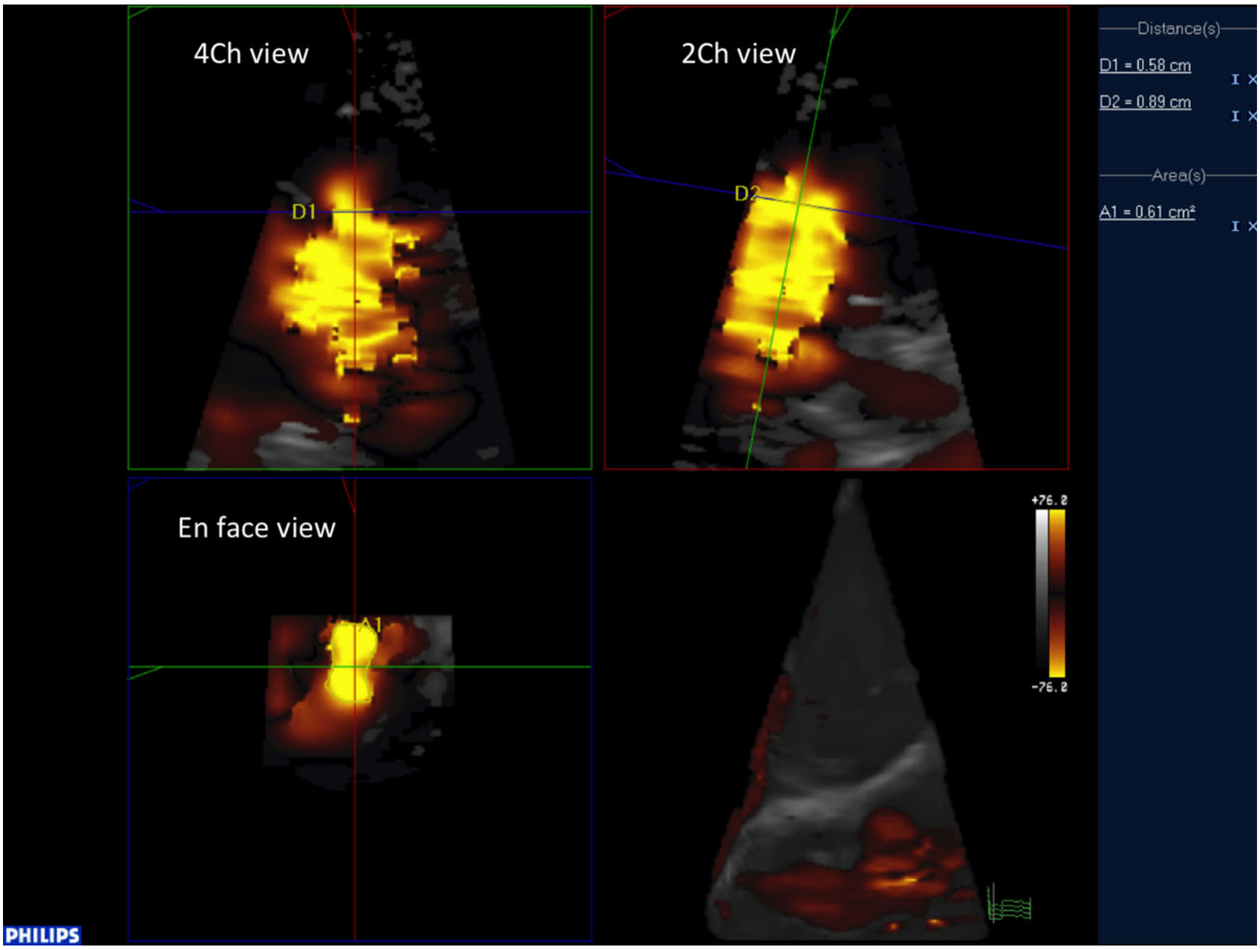

Fig 1. Measurements in the same real-time 3-dimensional color Doppler dataset of vena contracta in the 4-chamber (4Ch), 2-chamber (2Ch), and the en face view in a dog with myxomatous mitral valve disease. The area in the en face view measured 0.61 cm^2, whereas the calculated areas using 4Ch view only, 2Ch view only, or a combination of 4Ch and 2Ch views equaled 0.26, 0.62, and 0.41 cm^2, respectively.

Table 1. Echocardiographic variables in 158 dogs with myxomatous mitral valve disease with (Class C) and without (Class B) congestive heart failure. Continuous data are presented as median and IQR.

Variable	Class B Dogs (n = 126)	Class C Dogs (n = 32)	P-Value
LA/Ao	1.13 (1–1.24)	1.83 (1.55–2.18)	<.0001
LAlax/Ao	1.97 (1.71–2.21)	2.9 (2.46–3.42)	<.0001
LVIDDn	1.75 (1.57–1.96)	2.27 (2.07–2.40)	<.0001
LVIDSn	1.05 (0.92–1.19)	1.27 (1.07–1.43)	<.0001
Mitral E wave (cm)	0.68 (0.57–0.84)	1.04 (0.8–1.19)	<.0001
Mitral A wave (cm)	0.65 (0.57–0.82)	0.74 (0.65–0.9)	.053
Mitral E/A	1 (0.9–1.2)	1.25 (1–1.83)	.0021
RJA/LAA <30%	58/126 (46%)	1/32 (3%)	<.0001
RJA/LAA 30–50%	40/126 (32%)	8/32 (25%)	<.0001
RJA/LAA >50%	28/126 (22%)	23/32 (72%)	<.0001
Asymmetry index: VCW (2Ch/VCW (4Ch)	1.08 (0.86–1.45)	1.39 (1.1–1.83)	.0013
VCW (4Ch) (cm)	0.47 (0.35–0.58)	0.56 (0.48–0.65)	.0019
VCW (2Ch) (cm)	0.5 (0.38–0.68)	0.85 (0.61–1.0)	<.0001
EROA/BSA (cm^2/m^2) calculated from 4Ch	0.33 (0.2–0.58)	0.58 (0.39–0.82)	.0001
EROA/BSA (cm^2/m^2) calculated from 2Ch	0.4 (0.24–0.72)	1.3 (0.83–1.76)	<.0001
EROA/BSA (cm^2/m^2) calculated from 4Ch + 2Ch	0.38 (0.23–0.63)	0.83 (0.61–1.3)	<.0001
EROA (cm^2) measured in the en face view	0.28 (0.18-0.42)	0.52 (0.37–0.87)	<.0001
EROA/BSA (cm^2/m^2) measured in the en face view	0.56 (0.38–0.91)	1.3 (0.90–2.05)	<.0001

LA, left atrium (short-axis view); Ao, aorta; LAlax, left atrium (long-axis view); LVIDDn, left ventricular end-diastolic internal diameter corrected for body weight; LVIDSn, left ventricular systolic internal diameter corrected for body weight; RJA, regurgitant jet area; LAA, left atrial area; VCW, vena contracta width; 2Ch, 2-chamber view; 4Ch, 4-chamber view; EROA, effective regurgitant orifice area; BSA, body surface area; IQR, interquartile range.

observed points. Estimates of slope of the curve and intercept of the y-axis and their P-values were used to evaluate the presence of systematic differences between the methods. The diagnostic efficacy in predicting presence or absence of CHF was evaluated by use of receiver operating characteristic (ROC) curve for EROA/BSA measured in the en face view. Area under the curve (AUC), operating point, sensitivity, and specificity were determined. Mean values and standard deviations (SD) were used to determine the coefficient of variation (CV), where SD is expressed as percentage of the mean value. The impact of dog, observer, and acquisition on variability was further evaluated by variance component analysis. Level of significance was set at $P < .05$.

Results

Dogs

A total of 158 privately owned dogs of 41 breeds were included in the study: Cavalier King Charles spaniel (34), Miniature Schnauzer (18), Dachshund (15), mixed breed (11), Chinese Crested (9), Chihuahua (6), and <5 dogs of 35 other breeds. There were 94 (59%) males and 64 (41%) females. Age at presentation ranged from 3.8 to 15.3 years, median 10.3 years (IQR, 8.4–11.8 years). Body weight ranged from 2 to 36.7 kg, median 9.8 kg (IQR, 6.9–12.7 kg). According to the ACVIM classification of MMVD, 32 (20%) dogs were classified with congestive heart failure (CHF) (2 in Class C1 and 30 in Class C2) and 126 (80%) dogs did not have CHF (115 dogs in Class B1 and 11 dogs in Class B2). Heart rate ranged from 80 to 222 beats/min, median 130 (IQR, 117–144 beats/min). Sinus rhythm was present in all dogs. At the time of examination, 41 (26%) dogs underwent medical treatment, in which 38 dogs received pimobendan, 32 dogs furosemide, 31 dogs benazepril, 3 dogs spironolactone, 2 dogs digoxin, and 1 dog sildenafil.

Two- and 3-Dimensional Echocardiography

Baseline echocardiographic variables are presented in Table 1 with dogs dichotomized according to presence of CHF. Three consecutive measurements of EROA in the enface view were obtained in 83 dogs. At least 2 consecutive measurements of EROA in the en face view were obtained in 140 dogs, whereas only 1 measurement was obtained in 18 dogs. Based on ROC analysis, the optimal cut-off for EROA/BSA in the en face view between dogs with MR and CHF vs those with MR but without CHF was found to be 0.8 cm^2/m^2 (AUC = 0.853 [CI, 0.788–0.904]). Dogs were dichotomized at this operating point for EROA/BSA in Table 2. The RJA/LAA ratio was subjectively estimated as <30% (mild) in 59 (37%) dogs, 30–50% (moderate) in 48 (30%) dogs, and >50% (severe) in 51 (33%) dogs. Dogs were classified as having mild, moderate, or severe MMVD based on LA/Ao ≤1.5 in 123 (78%) dogs, >1.5 and <1.8 in 15 (9%) dogs, and ≥1.8 in 20 (13%) dogs, respectively.[25] Classification of MMVD severity based on RJA/LAA differed in 84 (53%) dogs from the classification based on LA/Ao. Tricuspid regurgitation pressure gradient was measured in 66 dogs and ranged from 12 to 71 mmHg, median 34 mmHg (IQR, 20.3–43 mmHg). Concentric MR jets were found in 104 (66%) dogs. For eccentric jets, deviation from midline in the 4Ch view was estimated as ±30° in 41 (26%) dogs, and ±45° or 60° in 13 (8%) dogs. Asymmetry index of the calculated EROA as the ratio of 2Ch diameter/4Ch diameter of VCW was equal to 1 in 2 (1%)

Table 2. Echocardiographic variables in 158 dogs with myxomatous mitral valve disease dichotomized at effective regurgitant orifice measured by real-time 3-dimensional echocardiography in the en face view and normalized for BSA (EROA/BSA) = 0.8 cm^2/m^2. Continuous data are presented as median and IQR.

Variable	EROA/BSA <0.8 cm^2/m^2 (n = 93)	EROA/BSA ≥0.8 cm^2/m^2 (n = 65)	P-Value
LA/Ao	1.12 (1–1.21)	1.52 (1.18–1.85)	<.0001
LAlax/Ao	1.91 (1.71–2.20)	2.55 (2.06–3.10)	<.0001
LVIDDn	1.66 (1.5–1.91)	2.09 (1.91–2.33)	<.0001
LVIDSn	1.01 (0.88–1.16)	1.17 (0.99–1.34)	<.0001
Mitral E wave (cm)	0.67 (0.56–0.79)	0.94 (0.70–1.11)	<.0001
Mitral A wave (cm)	0.64 (0.56–0.78)	0.75 (0.62–0.88)	.0020
Mitral E/A	1 (0.9–1.2)	1.1 (1–1.6)	.0101
RJA/LAA <30%	50/93 (54%)	9/65 (14%)	<.0001
RJA/LAA 30–50%	27/93 (29%)	21/65 (32%)	<.0001
RJA/LAA >50%	16/93 (17%)	35/65 (54%)	<.0001
CHF Class B	89/93 (96%)	37/65 (57%)	<.0001
CHF Class C	4/93 (4%)	28/65 (43%)	<.0001
Asymmetry index	1.09 (0.87–1.44)	1.22 (0.96–1.63)	.1000
VCW 4Ch (cm)	0.44 (0.32–0.51)	0.58 (0.49–0.73)	<.001
VCW 2Ch (cm)	0.43 (0.37–0.57)	0.74 (0.60–0.90)	<.0001
EROA/BSA (cm^2/m^2) calculated from 4Ch	0.28 (0.17–0.36)	0.72 (0.45–1.05)	<.0001
EROA/BSA (cm^2/m^2) calculated from 2Ch	0.32 (0.22–0.53)	1.07 (0.67–1.57)	<.0001
EROA/BSA (cm^2/m^2) calculated from 4Ch + 2Ch	0.32 (0.22–0.42)	0.79 (0.65–1.18)	<.0001

LA, left atrium (short-axis view); Ao, aorta; LAlax, left atrium (long-axis view); LVIDDn, left ventricular end-diastolic internal diameter corrected for body weight; LVIDSn, left ventricular systolic internal diameter corrected for body weight; RJA, regurgitant jet area; LAA, left atrial area; VCW, vena contracta width; 2Ch, 2-chamber view; 4Ch, 4-chamber view; EROA, effective regurgitant orifice area; BSA, body surface area; CHF, congestive heart failure; IQR, interquartile range.

dogs, was >1 in 100 (64%) dogs, and was <1 in 56 (35%) dogs. Median asymmetry index was 1.1 (IQR, 0.89–1.54) for all dogs, and 1.08 and 1.39 for class B and C dogs, respectively. The probability of a noncircular EROA was $P < .001$. Asymmetry index was significantly higher for class C dogs compared with Class B dogs, whereas no significant difference was found between groups dichotomized at EROA/BSA = 0.8 cm^2/m^2 (P = .013 and P = .1, respectively).

Comparisons Among 4 Different Methods to Estimate EROA

Bland-Altman plots comparing measured EROA in the en face view with calculated EROA using the 4Ch or 2Ch view alone or a combination of 4Ch and 2Ch views corrected for BSA are shown in Figures 2–4. The calculated EROA using 2Ch view showed best agreement with the measured en face EROA with a systematic underestimation of 13 mm^2, which corresponds to 17% (Fig 2). Calculated EROA, using either the 4Ch view alone or a combination of the 4Ch and 2Ch view, did not show good agreement with the measured EROA in the en face view, and the difference between methods increased with increasing size of EROA (Figs 3 and 4). The difference, expressed as a percentage between the en face view and calculated EROA based on the 4Ch view alone or the combination of 4Ch and 2Ch views divided by en face EROA measurement, did not increase with increasing EROA, but showed a systematic underestimation of EROA by 36% when using the 4Ch view only, and by 33% when using both 4Ch and 2Ch views, compared to RT3D (Table 3).

Variability

Intra- and interobserver CV ranged from 8.5–26% and 2.5–42%, respectively. Variance component analysis showed that the patient had a major impact on variability accounting for 88% of total variability, whereas observer and acquisition only accounted for 0.20 and 0.18%, respectively.

The beat-to-beat variation of EROA assessed in the en face view, in which 3 consecutive measurements were obtained (n = 83), had a median CV of 30% (IQR, 14–44%) for all dogs. The beat-to-beat variation was greatest for dogs with RJA/LAA <30% (median, 38; IQR, 23–48%) in which 12 dogs had CV >50%. The median CV for dogs with RJA/LAA 30–50% was 30 (IQR, 11–42%) and smallest for dogs with RJA/LAA >50% (median, 22%, IQR; 13–38%).

Discussion

The major finding of our study is that calculated estimations of EROA using the 2Ch view showed the best agreement with the EROA measured in the en face view corrected for BSA in dogs with MMVD. This finding suggests that, in the absence of RT3D echocardiography, VCW is preferably measured in the 2Ch view only rather than in the 4Ch view or by use of a combination of 4Ch and 2Ch views. However, additional studies are needed to assess agreement between VCW measured in the 2Ch view obtained by RT3D and 2D echocardiography.

Calculated estimations of EROA normalized to BSA using the 4Ch view alone or a combination of the 4Ch and 2Ch views not did show good agreement with the

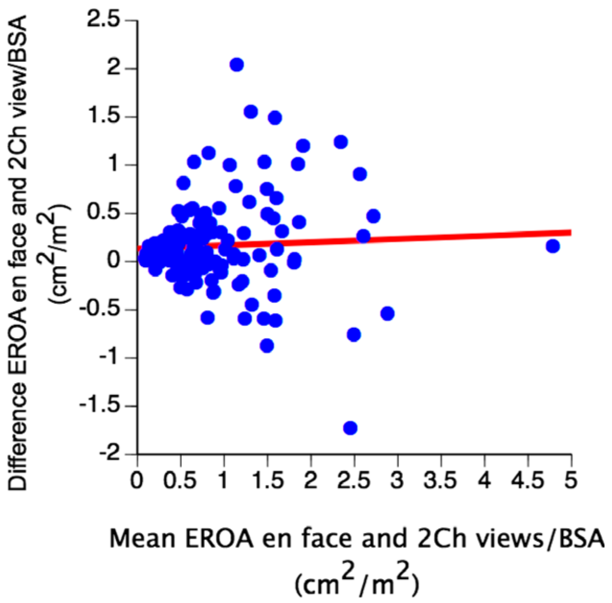

Fig 2. Bland-Altman plot comparing measured effective regurgitant orifice area (EROA) in the en face view and calculated EROA using the vena contracta width in the 2-chamber view only in 158 dogs with myxomatous mitral valve disease. All measurements were obtained in the same real-time 3-dimensional color Doppler dataset.

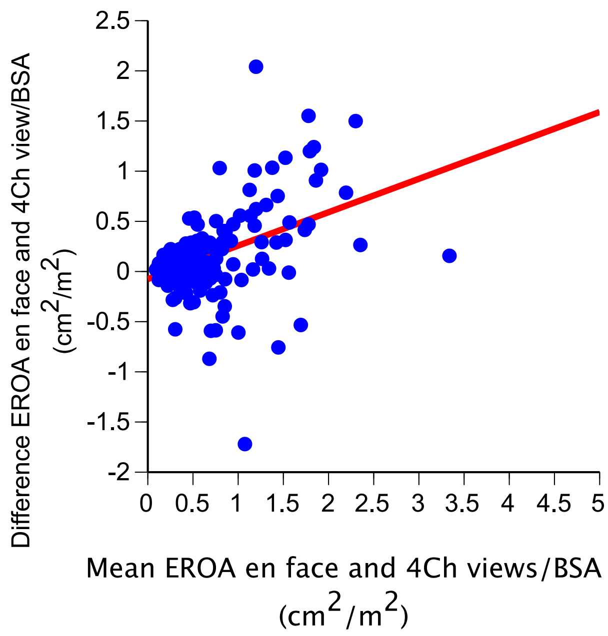

Fig 3. Bland-Altman plot comparing measured effective regurgitant orifice area (EROA) in the en face view and calculated EROA using the vena contracta width in the 4-chamber view only in 158 dogs with myxomatous mitral valve disease. All measurements were obtained in the same real-time 3-dimensional color Doppler dataset.

measured EROA using the en face view. The difference between methods increased with increasing size of EROA. Interestingly, the distribution of residuals to the

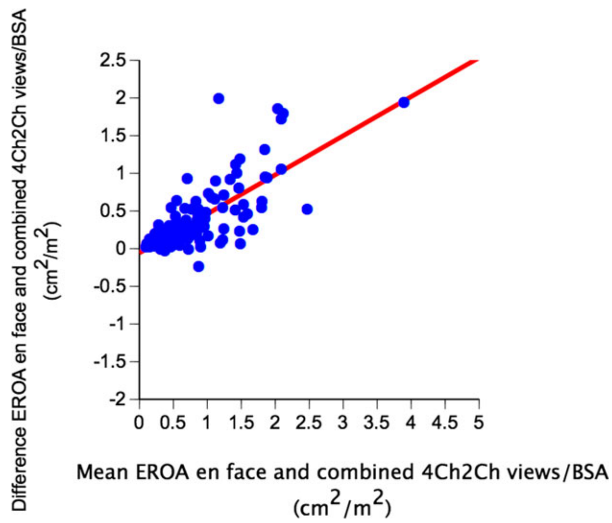

Fig 4. Bland-Altman plot comparing measured effective regurgitant orifice area (EROA) in the en face view and calculated EROA using the vena contracta width in the 4- and 2-chamber view in 158 dogs with myxomatous mitral valve disease. All measurements were obtained in the same real-time 3-dimensional color Doppler dataset.

Table 3. Results from linear curve fitting in the Bland-Altman plots comparing 4 methods, that is, real-time 3-dimensional (RT3D) en face view and 4-chamber (4Ch), 2-chamber (2Ch) and a combination of 4Ch and 2Ch views, to estimate effective regurgitant orifice area (EROA) in 158 dogs with myxomatous mitral valve disease. All measurements were indexed to body surface area (BSA).

Compared Methods	Intercept	*P*-Value	Slope	*P*-Value
En face—4Ch	−0.004	.95	0.53	<.0001
En face—2Ch	0.13	.015	0.033	.52
En face—4Ch + 2Ch	−0.06	.09	0.52	<.0001
En face—4Ch/en face	0.39	<.0001	−0.05	.34
En face—2Ch/en face	0.28	<.0001	−0.13	.004
En face—4Ch + 2Ch/en face	0.31	<.0001	0.04	.47

fitted line in the Bland-Altman plots showed least mean value and SDs for the combined 2Ch/4Ch, and the EROA was not overestimated in any dog compared to the en face view. When the difference was expressed as a percentage of EROA measured in the en face view, a systematic underestimation of EROA by 33% (2Ch/4Ch) or 36% (4Ch alone), regardless of EROA size, was found. These findings are similar to findings in studies of humans[16] and indicate that VCW might not be a good estimate of EROA when measured in 4Ch or a combination of 4Ch and 2Ch views. The fact that calculated EROA using 2Ch measurement only did not overestimate measured EROA in the en face view suggests that measurement of the maximal diameter was not achieved in the 2Ch view.

The asymmetric geometry of MR flow in dogs with MMVD is evidenced by RT3D images (Fig 1) and the fact that the asymmetry index, calculated as the ratio of 2Ch diameter/4Ch diameter of VCW, differed from 1 in 99% of dogs in our study. This finding is in agreement with studies in human patients with MR or TR.[15,31] The asymmetry index of the estimated EROA was >1 in 64% of dogs, indicating that the MR jet was wider in 2Ch view compared with 4Ch view in the majority of dogs with MMVD. This finding is in agreement with studies of human patients with MR.[15,28] The asymmetry index was significantly higher for Class C dogs compared to Class B dogs, indicating that the asymmetry of EROA increases with increasing severity of MMVD. Awareness of EROA asymmetry is thus important when assessing disease severity in dogs with MMVD using VCW as an estimate, especially in dogs with more advanced disease. Awareness of EROA asymmetry, as visualized by the en face view using RT3D echocardiography, is also relevant for PISA estimations, which are based on the assumption of a circular regurgitant orifice.

Visualization of the RJA in the receiving chamber provides information of its presence and spatial orientation and often is used as a semiquantitative assessment of disease severity.[9] However, numerous physiologic and technical factors affect the size of the RJA, such as systemic blood pressure, loading conditions, LA compliance, LA-LV pressure gradient, spatial orientation of the jet, pulse repetition frequency, and color gain settings. The RJA/LAA ratio is determined mainly by jet momentum, which is determined by LV contractility.[32] In our study, classification of MMVD severity based on RJA/LAA did not correlate with the classification based on LA/Ao in 53% of dogs. Thus, estimations of RJA/LAA might be less appropriate to assess MR severity.

Comparisons of EROA by each of the 4 methods in this study relate to instantaneous measurements. Dynamic variations of EROA over the cardiac cycle and between cycles might be expected to occur in dogs with MMVD. The beat-to-beat variation of EROA was large for individual dogs with small regurgitant jets in this study, and variance component analysis showed that the patient had a major impact on variability. A median CV value of 30% indicates that EROA varies with loading conditions as described in human patients,[33] and individual measurements of EROA might be misleading in some dogs with MMVD, especially in those with mild MR. This is an obvious limitation of our study regarding the use of the size of the EROA as an estimate of MR severity, as discussed below.

Limitations

For a fixed orifice, the VCW is independent of flow rate and driving pressure.[9] However, for a dynamic regurgitant orifice, as evidenced in our study by the beat-to-beat variation of EROA, changes are to be expected during the cardiac cycle and with changing hemodynamics. Although effort was made to make 3 consecutive measurements in the same phase of systole, timing might differ slightly between measurements. Also, the relatively low frame rate in 3D mode might have influenced results by inappropriate determination of EROA.[28] Based on the fact that systemic blood pressure was not consistently measured in the dogs of our study, different driving pressures might have influenced results. Treatment, instituted in 26% of the dogs in our study at the time of examination, might have affected EROA measurements.[33] In our study, all measurements were made in the exact same acquisition in each dog, which is considered an advantage in a comparative study. However, results of our study might not be applicable to other dogs, where measurements are made in 2D images, because comparisons then are made between images obtained at different times and possibly different localizations. Also, a true cross-sectional plane of VCW using 2D imaging might be difficult to obtain, especially with eccentric jets.

In conclusion, when replacing measured EROA with calculated EROA using VCW measurements, the 2Ch view is preferred in dogs with MMVD. However, whether or not RT3D measurements of EROA are superior to calculated EROA using measurements of VCW to predict clinical outcome in dogs with MMVD remains to be investigated. The high beat-to-beat variation and patient-induced variability might compromise the ability to accurately assess the severity of MR in dogs with MMVD.

Footnotes

[a] iE33; Philips Ultrasound, Bothell, WA

[b] QLAB advanced quantification, version 9.0, Philips Ultrasound, Bothell, WA

[c] JMP, v. 11.0, SAS Institute Inc, Cary, NC

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Conflict of Interest Declaration: Authors declare no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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