NOTE *Internal Medicine*

Examination of Quantitative Analysis and Measurement of the Regurgitation Rate in Mitral Valve Regurgitation by the "Proximal Isovelocity Surface Area" Method

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ABSTRACT. In 33 dogs with mitral valve insufficiency (MR), assessed as severe by semi-quantitative color flow Doppler echocardiography, regurgitation volumes were measured by the "Proximal Isovelocity Surface Area" (PISA) method. Good correlation ($p<0.01$, $r=0.97$) between the regurgitation volumes determined by the "PISA" and pulsed Doppler methods was confirmed. As evaluated by the "PISA" method, regurgitation rates in the 32 dogs with measurable regurgitation volumes ranged from 23 to 73%, with a mean of 51.6 ± 11.8%. Regurgitation volumes ranged from 3.3 to 32 m*l*, with a mean of 8.4 ± 6.4 m*l*.—KEY WORDS: canine, mitral valve regurgitation, Proximal Isovelocity Surface Area (PISA).

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Semi-quantitative analyses of regurgitation volume by angiocardiography or color flow Doppler echocardiography are commonly used to evaluate the severity of heart valve insufficiency in medicine [5, 7, 12]. The Sellers classification (I-IV) has been reported as a useful semi-quantitative evaluation method of severity for angiocardiography [7], while several semi-quantitative classifications, which divide severity into three grades (mild, moderate and severe) by assessing the area and maximum size of the terminus of the regurgitation jet signal into the left atrium, can be used for color flow Doppler echocardiography [5, 12]. Recently, however, the "Proximal Isovelocity Surface Area" (PISA) method, which estimates regurgitation volume quantitatively, has been utilized for evaluating heart valve diseases. This method differs from the semi-quantitative methods based on measuring the distal jet area using color flow Doppler echocardiography. When a hemisphere centering on the orifice of a regurgitating valve is visualized, the flow velocity within the hemisphere is constant. Therefore, the volume of blood passing through this hemisphere is equal to that leaving the orifice of the regurgitating valve, and can be calculated by multiplying velocity by surface area. Regurgitation volumes calculated by this method have been reported to correlate well with the severity of mitral and aortic valve regurgitation [4, 6, 8, 10, 13, 14]. We hypothesized that if the "PISA" method could be utilized to assess mitral valve insufficiency (MR) in dogs, and if the regurgitation volume, regurgitation rate and area of the regurgitating valve orifice could be measured quantitatively, a more accurate diagnosis could be made and the interpretation of disease severity could be improved.

In this study, we therefore used the "PISA" method on dogs which had been diagnosed as having severe MR by semi-quantitative color flow Doppler echocardiography, in order to examine its usefulness. Moreover, the regurgitation rate (regurgitation volume compared against inflow volume) was calculated from measurements obtained using both the "PISA" and pulsed Doppler methods , and the correlation was examined.

"PISA" method was utilized on 33 dogs semi-quantitatively assessed as having severe MR by regurgitation jet measurements, and with a large, clearly defined acceleration flow, on color flow Doppler echocardiography. The dogs (21 males and 12 females) used were 19 Malteses, five poodles, four pomeranians, two Yorkshire terriers and three mongrels. Their ages ranged from 6 to 16 years (mean: 10.8 years) and their body weights from 1.6 to 17 kg (mean: 3.8 kg). The causes of mitral valve regurgitation were prolapse of the anterior mitral leaflet in 32 dogs and prolapse of the posterior mitral leaflet in one, as assessed by echocardiography. Moreover, observations of the regurgitation regions on short-axis views of the ventricle revealed five anterolateral commissures, ten posteromedial commissures, eleven middle regions, four complications and three unclear cases. General evaluations by echocardiography confirmed the presence of several characteristics of MR, such as reinforcement of the luminance and myxomatous degeneration of the mitral valve, dilation of the left atrium and left ventricle, and an increase in fractional shortening. Enlargement of the left atrium and left ventricle was confirmed in every animal by radiography, and vertebral heart sizes ranged from 9.5 to 12.7 vertebrae (mean: 11) [1]. Increases in the height of the R-wave in lead II were observed on electrocardiography. Clinical observations revealed that all dogs had a normal appetite and normal vigor. Twelve had a mild cough, while 14 had a severe cough and intolerance to exercise. However, the other seven had no noticeable clinical symptoms. All of the dogs fell in to New York Heart Association functional classes II to IV [3] and into categories III to VI in the Levine classification of cardiac murmurs [2].

Evaluations were performed using a commercially available ultrasound system (Hewlett Packard SONOS-500) and a 5.0-MHz transducer. When using the pulse Doppler

method, the ultrasonic beam angle was set at less than 20°. The ultrasound equipment was set at transmit power or dynamic range and the filter at medium to high. Time-gain-compensation was approximately set in every case.

Calculation of the regurgitation volume by the "PISA" method was carried out by calculating the acceleration flow toward the mitral valve regurgitation orifice on a left or right parasternal long-axis view using color flow Doppler echocardiography. The regurgitation volume (Qpisa) was calculated using the equation $V \times t \times 2 \pi r^2$ (V: aliasing velocity, t: regurgitation time, r: radius of the isovelocity area). Aliasing velocities (V) were set at 27, 41, 49, 50 and 63 cm/s, depending on the maximum size of the isovelocity area and its most distinct formation at the semicircle. The radius of each isovelocity area (r) was measured a mean of four times (Fig. 1). Regurgitation times were measured by the M-mode color Doppler method (Fig. 2).

Calculation of the regurgitation volume by the pulsed Doppler method (Qpw) was carried out using the equation Qpw=LVIF–LVOF. Left ventricular inflow (LVIF) was calculated using the equation $\pi r^2 \times$ TVI , where πr^2 (r: radius of mitral valve annulus) was the cross-sectional area of the mitral valve annulus on a left or right parasternal long-axis view and TVI, the time-velocity integral of left ventricular inflow through the mitral valve annulus. Similarly, left ventricular outflow (LVOF) was calculated using the equation $\pi r^2 \times$ TVI, where πr^2 (r: radius of aortic valve annulus) was the cross-sectional area of the aortic valve annulus and TVI, the time-velocity integral of left ventricular outflow through the aortic valve annulus.

All analyses were conducted using the Statistical Analysis System program (Stat View, version 4.5, Abacus Concepts Inc., Berkeley, CA, 1996), and the significance level was set at less than 5%.

The optimum setting for the aliasing velocity on the 5.0-MHz transducer when using the "PISA" method was determined to be 41 cm/s in this group of dogs and very high correlation [correlation coefficient (r)=0.97 $p<0.01$] between Qpisa and Qpw was confirmed (Fig. 3). Regurgitation volumes measured by the "PISA" method ranged from 3.3 to 32 m*l* with a mean of 8.4 ± 6.4 m*l*. In 32 dogs (excluding one with unmeasurable values) that had been semi-quantitatively assessed as having severe MR by color flow Doppler echocardiography, regurgitation rates ranged from 23 to 73%, with a mean of 51.6 ± 11.8% (Fig. 4). Eighteen of the 32 dogs (56%) had a regurgitation fraction of more than 50%.

In this study we attempted to evaluate the usefulness of the "PISA" method in assessing MR, a common heart disease in dogs. We initially did not think "PISA" method could be applied to dogs clinically, partly because their heart rates are more than those of humans and partly because of the formation of leaking orifices due to mitral valve degeneration. Despite these concerns, most cases, the flow volume in which the acceleration flow forms produced a clearly defined semicircle, enabling measurement. However, the aliasing velocity of the acceleration flow formed a near-circle in dogs with severe mitral valve degeneration and prolapse. Accordingly, the "PISA" measurements overestimated regurgitation when compared with the pulsed Doppler. On the contrary, the "PISA" measurements underestimated regurgitation when compared with the pulsed Doppler when the aliasing velocities of the acceleration flow forms were not clearly represented. Therefore, the "PISA"

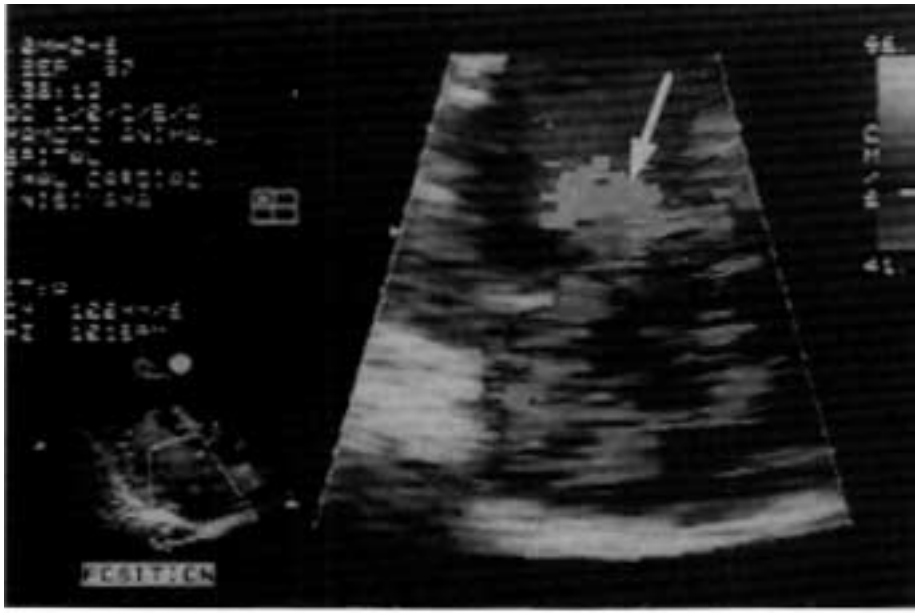

Fig. 1. Color flow Doppler echocardiogram in the left parasternal long-axis view; At acceleration flow through leaking orifice set at aliasing velocity of 41 cm/s. It is indicated by arrow.

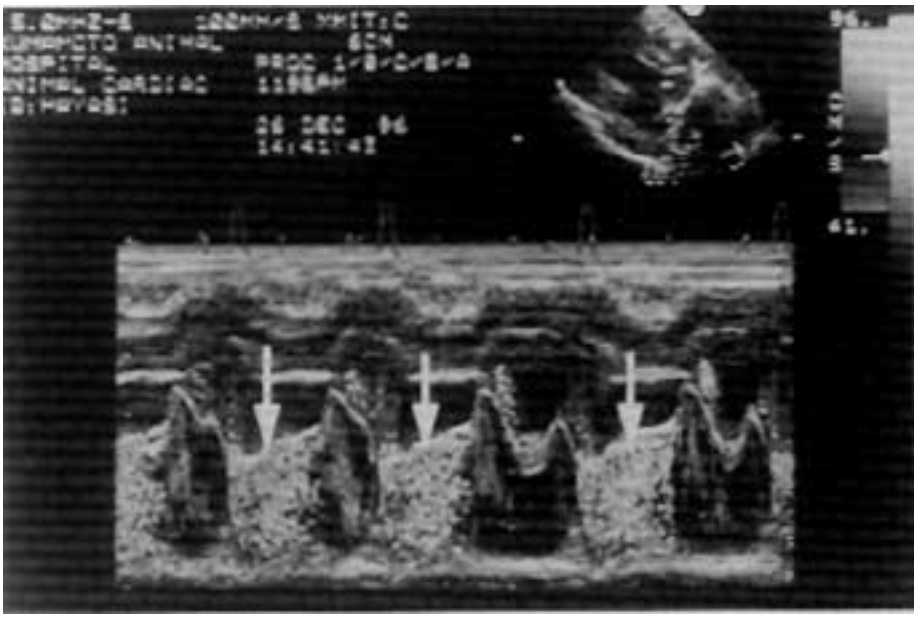

Fig. 2. M-mode color Doppler echocardiogram in the right parasternal long-axis view; With M-mode method set at aliasing velocity of 41 cm/s, regurgitation time of one heart rate was obtained. It is indicated by arrow.

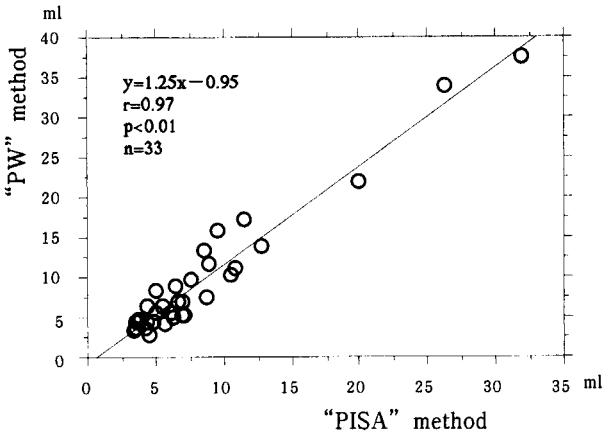

Fig. 3. Correlation of regurgitation volumes obtained with the "PISA" method and the pulse Doppler method; The values of regurgitation volume with both methods showed significantly high.

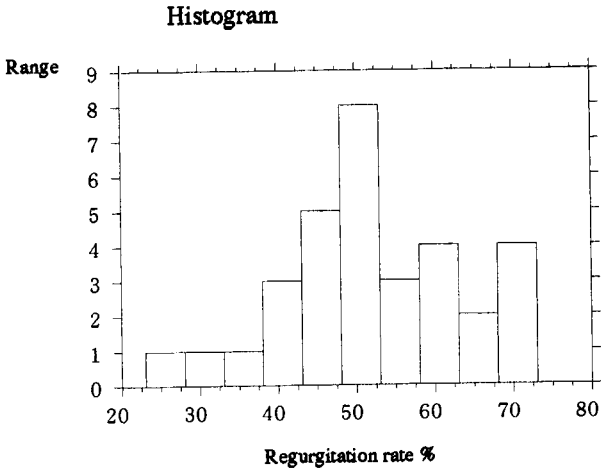

Fig. 4. Histogram of regurgitation rate; Regurgitation rate of 32 dogs ranged from 23 to 73% with a mean of 51.6 ± 11.8%. Moreover, 21 dogs showed regurgitation rate of more than 50%.

method should only be used when the acceleration flow forms a clear semicircle. Calculating the regurgitation volume by the pulsed Doppler method had several disadvantages compared with the "PISA" method.

Firstly, measurements took a lot of time because of the complicated procedure. Secondly, large errors in measurements could easily occur because of the direction of blood flow and the angle of the ultrasonic beam. Thirdly, errors in measuring the cross-sectional area of the mitral and aortic valve annulus cause great differences in the volume flow rate. Finally, this method cannot be used in dogs with aortic valve regurgitation or shunt disease. Consequently, the "PISA" method is easier to use as it exhibits less of these stated shortcomings than pulsed Doppler method. Moreover, the advantage of the "PISA" method is that, though pulsed Doppler method exhibits a difference in the measuring times of LVIF and LVOF, the "PISA" method obtains the instantaneous regurgitation. In humans, regurgitation fraction 20 to 30% is considered as a mild, 30 to 50% as a moderate, and more than 50% as a severe [8, 9, 11]. Fourteen dogs were semi-quantitatively

evaluated as having severe regurgitation. However, they were classified as having moderate or mild regurgitation when the regurgitation fraction was calculated. The reason for this is that the annular area was presumed as circular when obtaining the LVIF. Moreover, it is conceivable that another cause could be, despite the blood flow forms being obtained as the average of four measurements, the slight differences in regurgitation with respect to the heart rate. In addition, it has been reported that the formation of experimental regurgitation orifices can change the regurgitation volume value measured by the "PISA" method [10]. However, if a regurgitation fraction of more than 50% is regarded as a severe case according to the criteria in human [8, 9, 11], then 44% of our semi-quantitatively evaluated dogs had their disease severity overestimated. Thus, semi-quantitative evaluations by color Doppler echocardiography can create substantial errors. One possible reason for these errors is the use of visual estimations to detect the reach and size of the regurgitant jet. Others include technical problems, such as difficulties in adjusting the direction of the regurgitant jet and variability in setting the color gain. Therefore, the "PISA" method, which is based on measurements of the acceleration flow from the leaking orifice and is not affected by the above problems, appears to be more accurate in evaluating the severity of regurgitation. Most of the dogs with a regurgitation fraction of more than 50% in this study were diagnosed as being equivalent to New York Heart Association functional class IV [3]. Therefore, the "PISA" method is sufficiently useful for clinical practice, because it allows easy determination of regurgitation volume and, moreover, is non-invasivel. We feel that this method shoud be studied further, and that it will be come an important tool in evaluating the severity of regurgitation, especially combined with expected future developments in surgery.

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