



Swedish University of
Agricultural Sciences

**Effects of mitral valve regurgitation in the dog
on the right ventricle**

*Echocardiographic evaluation of changes in size and
shape of the heart*

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The present study is a partial fulfilment of the requirements for the Master of Science (MSc) Degree in Veterinary Medicine for International Students at the Swedish University of Agricultural Sciences (SLU), in the field of Diagnostic Imaging.

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To my parents

Abbreviations

Ao	aorta
HF	heart failure
DipECVDI	diplomate of European College of Veterinary Diagnostic Imaging
HE	heart enlargement
LA	left atrium
LAE	left atrial enlargement
LA/Ao	left atrial to aortic root ratio
LV	left ventricle
ED	end diastole
ES	end systole
EI	eccentricity index
MR	mitral regurgitation
RV	right ventricle
VD	ventro-dorsal
VHS	Vertebral heart scale
2-D	two-dimensional mode

Abstract

Introduction. Mitral regurgitation (MR) in dogs is characterised on radiographs by increasing size of the heart, called “general heart enlargement.” The appearance suggests that the right heart chambers may be enlarged, but there is no agreement on this, or if present, its cause. Concurrent enlargement of the right heart chambers in MR would have to be explained by pathophysiologic mechanisms that might affect prognosis and treatment.

Aim. To determine presence or absence of echocardiographic changes that indicate right sided heart enlargement in relation to severity of MR.

Materials and methods. Two-dimensional (2-D) echocardiographic frames of 54 dogs with varying degrees of MR were measured to determine ratios of dimensions of left and right sides of the heart: dimensions of right ventricle (RV) and left ventricle (LV) in transverse short axis view above mitral valve (MV) at end diastole (ED), dimension of right ventricle (RV) and left ventricle (LV) on long axis at the MV at ED, on transverse section, the septal-free wall angle (SFWA) at ED and ES where the endocardium of RV joined LV. An eccentricity index (EI) of the LV at end diastole (ED) and end systole (ES) was measured to determine the degree of flattening of the interventricular septum as a measure of RV overload. As the indicator of MR severity, left atrium/aorta root (LA/ Ao) was measured at beginning of diastole. Radiographs of 42 dogs were available. Heart size was measured by the vertebral heart scale (VHS) method. Dimensions were compared with LA/Ao and VHS by regression. The effect of severe LA and heart enlargement on EI were compared with none-moderate enlargement. EI at ED and ES were compared.

Results. The longitudinal and transverse dimensions of right and left side and the SFWA were so variable that although the right side and angle did not increase, no conclusions could be made. ED EI showed no increase in eccentricity with increasing size of LA or VHS. ES EI increased with LA /Ao and VHS, due to increases in some severely enlarged hearts. Five hearts had greater eccentricity at ES, indicating pressure overload on the RV. Three hearts had eccentricity only at ED, indicating volume overload.

Conclusions. No evidence for a consistent effect of increasing severity of MR on the right ventricle was found. In “general heart enlargement” on radiographs, it is unlikely that the right side of the heart enlarges in proportion to severity of MR. The convexity on radiographs is probably caused by the right heart chambers being displaced by enlarged left side of heart. The RV may be volume or pressure overloaded in some cases of MR.

Key words: Mitral regurgitation, radiology, heart enlargement, echocardiography, interventricular septum.

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Contents

Introduction to the research report, 1

Aims of the project. 7

Research Report

Aleksandra Todosijevic, Peter Lord, Jens Häggström, Kerstin Hansson.

Effects of mitral valve regurgitation in the dog on the right ventricle:

Echocardiographic evaluation of changes in size and shape of the heart

Abstract, 11

Introduction, 12

Materials and methods, 13

Results, 17

Discussion, 22

Conclusions, 25

References, 26

Acknowledgements, 30

Introduction

Mitral regurgitation (MR)

MR is also called mitral valve regurgitation, mitral incompetence, mitral insufficiency. MR is leakage of blood backward through the mitral valve from the left ventricle (LV) into the left atrium (LA) each time when the ventricle contracts (systole). This causes the LA and LV to enlarge to accommodate the extra volume needed to maintain the forward flow of oxygenated blood through the body. This enlargement is seen on radiographs, but also are seen signs consistent with enlargement of the right side of the heart, which receives deoxygenated blood from the body and pumps it into the lungs. This has led to differing opinions on the effect of MR on the right side of the heart.

Pathology of MR

MR can be primary, caused by progressive myxomatous mitral valvular degeneration (MMVD), acute rupture of chordae tendinae, or bacterial endocarditis, and secondary, when poor contractions prevent closure as in dilated cardiomyopathy. An abnormality in any component of the mitral valve apparatus (mitral leaflets, annulus of mitral valve, chordae tendinae, ventricular papillary muscle, left atrial and ventricular wall) can cause valve leakage. MMVD is a common disease of small dogs, and a common cause of death by heart failure in old dogs. In MMVD, the spongiosa valve layer of leaflets acidomucopolysaccharide (glucosaminoglycan) accumulates and collagen degenerates. Affected valves become irregularly thickened with plaque-like nodules, deform and become smaller, and may prolapse (bulge) toward the atrial side in systole. Chordae tendinae are thickened, lengthened and fragile. The disease develops over years so many dogs will have murmurs but no clinical signs, while those more severely affected and/or older are likely to develop HF. The Cavalier King Charles spaniel has the highest frequency of MMVD and HF, the murmurs developing at a younger age than in other breeds, and the frequency of HF is greater. For this reason it is commonly used in research on the disease and its treatment (Hägström and others 2004, Kittleson 1998).

Pathophysiology of the heart with MR

In MR, during systole, the LV pumps blood partly into the aorta and partly backwards into the LA. The volume of mitral regurgitant flow depends on the size of the regurgitant orifice and the pressure gradient between the left ventricle and left atrium, which is affected by the strength of the ventricular contraction and the compliance of the LA. As the LA is at low pressure, the valve leaks immediately the ventricle begins to contract, so that the regurgitating volume is ejected into the

LA at low pressure before the aortic valve opens. This means that the load on the heart is not great as the lesions develop slowly, and the large regurgitant volume is well accommodated for years, as both the LV and LA remodel and remain compliant, accommodating the large volumes (Lord 1976, Pape and others 1991, Pizzarello and others 1984, Zile and others 1991). The amount of regurgitant flow is small early in the course of the disease, but as the disease progresses an increasing percentage of stroke volume is ejected into the LA. The size of the LA and the compliance of atrial wall are related to the volume overload and the rate of progression of the severity. The main indication of volume overload is changes in geometry of chambers as consequence of accommodation of large end-diastolic volume, raising the sarcomere length — eccentric hypertrophy. But the eccentric hypertrophy is not normal, it is inadequate to maintain normal pump function (Borgarelli and others 2007, Carabello 2000, Häggström and others 2004, Katz 1995, Lord and others 2003, Urabe and others 1992) and other compensatory mechanisms are activated to maintain cardiac output. It is a vicious circle of worsening heart function, overload, regurgitation, shown by the accelerated heart enlargement up to the time of failure, (Hansson et al., unpublished data¹) when left atrial pressure increases to cause pulmonary capillary pressure to rise which leads to pulmonary edema (transudation of fluid from the capillary spaces into the lung tissues and alveoli). When the normal compliance of the left atrium cannot be maintained to accommodate the regurgitant volume the LA pressure rises. The increased pressures in the left atrium inhibit drainage of blood from the lungs via the pulmonary veins. This causes pulmonary venous hypertension and interstitial edema. As MVD develops slowly, over years, the pulmonary lymphatic drainage increases to accommodate the increased interstitial fluid volume and the clinical effect of the interstitial edema is minimal. When the amount of capillary filtrate exceeds the pumping capacity of the lymphatic drainage, fluid accumulates in the interstitial area around bronchioles arterioles and venules. When the lymphatic drainage cannot cope with the increasing volume of interstitial fluid, the alveoli are flooded. Gas exchange deteriorates causing hypoxemia, and frothy fluid spills from the alveoli into the airways and the lungs become stiffer. This is an acute and life-threatening condition that needs immediate treatment. In acute diseases, edema can form at 20-25mm Hg pressure in the pulmonary capillaries, but in chronic HF when the lymphatic drainage system has enlarged to accommodate the increased fluid (Uhley and others 1969, Uhley and others 1966), as in MR of myxomatous degeneration, the required pressures may be 40-45 mmHg (Ware and Bonagura 1999).

Possible effects of MR on the right ventricle

Filling capacity and output of the RV control systemic venous pressure. The RV pumps blood into the pulmonary vascular bed for oxygenation and the blood then fills the LA during systole. Thus the pressure in the pulmonary vascular bed due to its resistance to flow and the pressure in the pulmonary veins and LA are a load (afterload) on the RV. As the RV has a thin wall it cannot respond well to acute pressure overloads but it can respond well to chronic overloads by remodelling in a similar way to the LV. The response of the RV to chronic pressure overload is remodeling and hypertrophy with a thicker wall and greater curvature to maintain

normal wall stress and pumping capacity (Boxt 1996, 1999). This is seen in congenital pulmonic stenosis and cor pulmonale, which is chronic lung disease causing pulmonary hypertension (PH). In MR the effect of the regurgitant volume on the RV is disputed among authors. Some state that the thin wall of the RV cannot withstand the relatively low increased back pressure from the LV to the LA and lungs (Atkins 1991, Bonagura and Rush 2000, Bonagura and Sisson 2000, Häggström and others 2005). However, the “weakness “ of the RV applies only to an acute pressure load. In chronic pulmonary hypertension RV responds well to the pressure load with hypertrophy and remodeling. On the other hand, Kittleson (1998) considers that pulmonary hypertension secondary to MR is unlikely, because pulmonary artery pressure is only mildly increased because of the maintained compliance of the LV and LA until failure, and even then the developed LA pressure is not enough to affect the RV. If the RV is overloaded in MR, then the cause has to be determined. The cause and the possible deleterious effects on LV function (Boxt 1999, Dong and others 1995, Santamore and Gray 1995) might affect prognosis and treatment.

Radiographic signs in MR

Radiographs are taken in dogs with MR to rule out other diseases with similar clinical signs, to confirm presence of pulmonary edema as evidence of HF, and to assess effectiveness of treatment.

Table 1 lists the radiographic signs of MR. The appearance of the heart is usually called “general heart enlargement,” because the convexity of the cranial and right heart borders are signs of right sided enlargement (Bahr 2007, Dunn and others 1999, Lord and Suter 1999), but in MR the degree of contribution of the RV and RA is not known (Sisson and others 1999). The convex appearance of the cranial and right heart borders in cor pulmonale and MR are shown in Figure 1.

Measurement of heart size

VHS – vertebral heart scale (Buchanan 2000, Buchanan and Bucheler 1995). General heart size can be measured by relating its dimensions to the length of the thoracic vertebrae (Figure 2). Measurements for the VHS are obtained using the lateral view, although the technique also has been described using DV view. Cardiac long axis is measured from the ventral border of the left main stem bronchus to the most ventral aspects of the cardiac apex. This same distance is compared to the thoracic spine beginning at the cranial edge of T4; length is estimated to the nearest 0.1 vertebral body. The maximum short axis is measured in the central third of the heart shadow perpendicular to the long axis; from the middle of the caudal vena cava to the cranial border. The short axis is also measured in number of vertebrae beginning with T4. Two measurement are added to yield the VHS. 8.5-10.5 is considered normal for most breeds. The cavalier King Charles spaniel’s upper limit of normal is about 11.7 (Hansson and others 2005, Lamb and others 2001).

Lateral view	Ventrodorsal view
Increased convexity of cranial heart border. The cranial border is formed by the RA and RV.	Heart is wider and longer, occupies more space of the thorax
Increase sternal contact of cranial heart border.	Heart is more convex on both sides
Trachea displaced dorsally and may be parallel to the spine	Local bulge of heart shadow at 2-3 o'clock position using clock face analogy, formed by LA appendage.
Left main stem bronchus elevated dorsally	
In severe cases compressed left main stem bronchus	
Bulging heart shadow between the bronchus and caudal vena cava indicates left atrium enlargement	

Table 1. Appearance of the heart with MR on radiographs. Textbooks agree on these important radiographic signs.

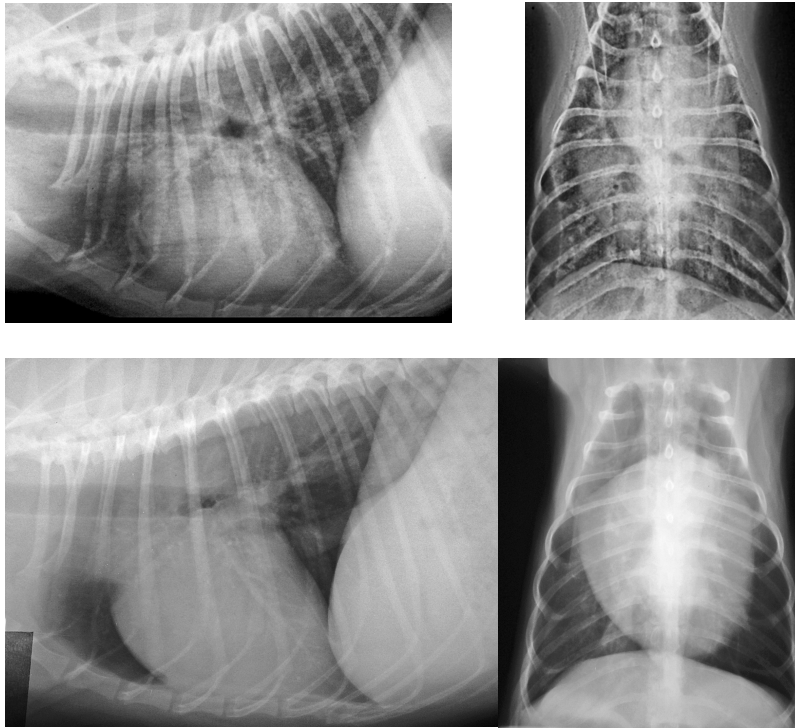


Figure 1. Comparison of radiographs of a dog with only right-sided enlargement, above, caused by chronic lung disease, and a dog with mitral regurgitation, below. They have equal degrees of convexity of the cranial and right heart borders.

$$5.6 + 6.9 = 12.5 \text{ VHS units}$$

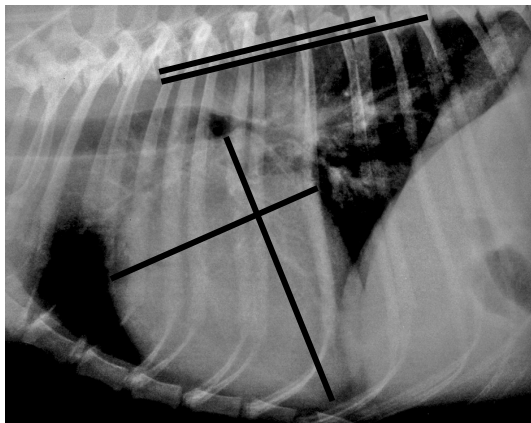


Figure 2. Method of measuring vertebral heart score (VHS) on a lateral radiograph. The two orthogonal dimensions are transferred to the spine and the number of vertebral bodies encompassed by both lengths is the VHS.

Significance of possible right sided overload in MR

Overloaded RV may lead to right heart failure which would give worse prognosis. Pressure-overloaded RV affects LV function (Dong and others 1995), and may lead to a vicious cycle of ventricular inter-action decreasing heart capacity.

Evidence against above possible causes

All moderately enlarged hearts have convex right heart border but no more than 30% of dogs have primary tricuspid regurgitation (TR) due to MMVD (Hägström and others 2005) and only 14 % of dogs with MR have pulmonary hypertension defined as a systolic PA pressure greater than 30 mmHg (Serres and others 2006), although in humans, higher values, 35-45 mm Hg have been used (Dellegrattaglia and others 2007, Reisner and others 1994, Ryan and others 1985). Kittleson (1998) considered that the backpressure developed in heart failure of MR was not sufficient to cause significant right sided enlargement. In experimental chronic MR, the right ventricle was not enlarged (Young et al., 1996).

Echocardiography in MR

As radiographs cannot reveal the internal structure, echocardiography must be used to assess chambers and walls. Dimensions can be measured in the different planes to assess size and function of the individual chambers. Figure 3 shows the measurement of the size of the LA related to the size of the root of the aorta, a ratio (LA/Ao) used in this project to determine the severity of MR. Changes to the right and left ventricles caused by pressure or volume overload can be measured. Pressure and volume overload change the trans-septal pressure gradient which causes the septum to be flattened at different phases of the cardiac cycle, and this can be measured on the short axis view of the left ventricle. The eccentricity index (EI) is a measurement of volume or pressure overload of the RV which flattens the septum and changes the geometry of the LV (Louie and others 1992, Ryan and others 1985).

The size of the LA represents the degree of volume overloading and thus the severity of the MR (Pape et al., 1991; Pizzarello et al., 1984; Häggström et al., 1997; Kittleson & Brown., 2003).

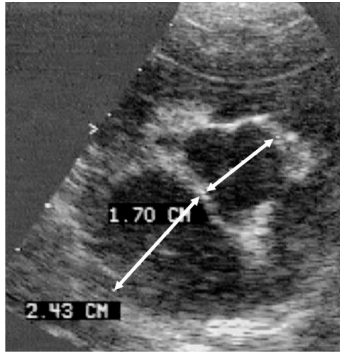


Figure 3. Method of measuring size of left atrium (LA) in early systole. The dimension of the aorta (Ao) is from the convex surface to the junction of two cusps. The LA dimension is an extension of this line to the outside wall of the LA, or if a pulmonary vein enters the LA, as in this case, an extrapolated imaginary line crossing the pulmonary vein.

Aims of the project

The hypothesis of this project was that enlargement of the right side is not essential to the appearance of general heart enlargement seen on radiographs of dogs with MR. Instead the appearance is caused by the enlarged LV pressing into and displacing the RV. This is what was found in experimental chronic MR in dogs by 3-dimensional reconstructions of the heart by magnetic resonance imaging (Young and others 1996). As this was a short period (5-6 months) compared to the natural disease progression, and the MR was produced by an acute procedure, cutting the chordae tendinae, this model may not imitate the natural disease in dogs. The project aimed to answer the questions: Does the right ventricle enlarge as the severity of MR increases and the heart enlarges? Does the septum flatten as the severity of MR increases and the heart enlarges?

¹ Hansson, K., Häggström, J., Kwart, C. & Lord, P. Heart size accelerates before failure in dogs with mitral valve regurgitation.

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Research Report

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Echocardiographic evaluation of changes in size and shape of the heart

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Key words: interventricular septum, mitral regurgitation, heart enlargement, right ventricle, radiography, dog

Abstract

Mitral regurgitation (MR) in dogs is characterised by increasing size of the heart on radiographs. Although MR primarily affects the left side, disease might include both right and left sides, as radiologic interpretation of signs of heart enlargement indicates concurrent right-sided enlargement that increases with increasing size of the heart, called “general heart enlargement.” If the right side is also enlarged, pathophysiologic reasons for this could affect prognosis and treatment. To determine indexes of size and shape of the ventricles in relation to severity of MR, cross section two-dimensional echocardiographic frames from examinations of 54 dogs were measured to determine ratios of left and right side enlargement: left atrium/aorta root (LA/ Ao) at beginning of diastole, eccentricity index (EI) at end diastole (ED) and end systole (ES), dimension of RV and LV transverse short axis above mitral valve (MV), dimension of right ventricle (RV) and left ventricle (LV) on long axis at the MV, at ED, on transverse section, tangential angles at ED and ES of the inside walls where RV joined LV. Heart size was measured by the vertebral heart scale (VHS) method on radiographs of 42 dogs. All dimensions and indexes were related to LA/Ao and VHS by regression. ED and ES show no increase in eccentricity with increasing size of LA. Moderate general heart enlargement was not associated with eccentricity. The largest LA and VHS had significantly greater eccentricity at ES ($p < 0.05$) but not ED, due to eccentricity of 3 hearts. This indicated pressure overload on the RV. 5 hearts had eccentricity only at ED, indicating volume overload. The plots of right/left (R/L) transverse, R/L long and angles showed no relative increase in R side as the left side enlarged. Tangential angles at ED and ES did not give any significant result. In “general heart enlargement” on radiographs, the right side of the heart is not enlarged unless the MR is severe. The RV is probably displaced by the enlarged LA and LV.

Introduction

In the evaluation of dogs with mitral regurgitation (MR), radiographic determination of heart size and shape is important. Although MR volume overloads the left atrium (LA) and left ventricle (LV), the cranial and right heart borders also become more convex, and in the lateral projection, the contact surface of the heart with the sternum increases, creating a more rounded heart than normal, and generating the term “general heart enlargement.” As these are signs of right sided enlargement (Bahr 2007, Dunn and others 1999, Kittleson and Kienle 1998, Lord and Suter 1999), it appears that MR causes right sided enlargement. However, this question is controversial. Some authors consider that MR increases pulmonary vascular pressure, and as the right ventricle (RV) is thin-walled and not able to respond to a pressure overload, dilates and fails, especially if tricuspid regurgitation (TR) is also present.(Atkins 1991, Dunn and others 1999, Häggström and others 2005, Ware and Bonagura 1999) However, it was argued that MR could not generate sufficient backpressure to cause RV enlargement and failure, as RV failure is rare in MR.(Kittleson 1998) Notwithstanding, the universal appearance on radiographs of increased convexity of the “right side” of the heart has to be explained. Clinically significant RV overload would affect prognosis and treatment (Capomolla and others 2000, Louie and others 1995, Moraes and others 2000).

If MR causes pulmonary hypertension (PH) or if tricuspid regurgitation (TR) is concurrently present, the effects of these pressure and volume overloads on the RV should be detectible by echocardiography. Both cause the interventricular septum to become flattened in proportion to the overload (Dellegrottaglie and others 2007, DeMadron and others 1985, Dong and others 1992, Louie and others 1992, Movahed and others 2005, Ryan and others 1985, Weyman and others 1976). If MR causes sufficient pulmonary hypertension to create right heart enlargement that might cause the radiographic appearance of general heart enlargement, it should cause the septum to be flattened in all cases of general heart enlargement. If TR is present, RV and right atrium (RA) will be enlarged to accommodate the volume overload. TR may be primary due to myxomatous degeneration or secondary to PH (Boxt 1996, Häggström and others 2005, Kittleson 1998). Pressure and volume overload cause the interventricular septum to flatten in response to changed transseptal pressures, and the degree of flattening can be measured on two-dimensional (2-D) echocardiograms (Agata and others 1985, Boxt 1996, DeMadron and others 1985, King and others 1983, Louie and others 1995, Portman and others 1987, Reisner and others 1994, Ryan and others 1985) and on magnetic resonance images (Boxt 1996, Dellegrottaglie and others 2007, Dong and others 1992, Roeleveld and others 2005). Pressure overload causes end systolic (ES) septal flattening (SF), and volume overload causes end diastolic (ED) flattening. Of the methods for measuring the severity of SF the simplest is the eccentricity index (EI) (Louie and others 1992, Ryan and others 1985), which is the ratio of the major and minor axes of the LV cavity in cross section.

The specific aims were to: measure relative sizes of the RV and LV on echocardiograms, assess enlargement of the RV by measuring the angle between

wall of the RV and interventricular septum, measure an eccentricity index (EI) at the end of diastole ED and at end of systole ES, as a measurement of septal flattening, and relate any changes of the right side to the degree of enlargement of the LA and the heart, measured by LA/Ao from 2-D echocardiograms and radiographs respectively.

Materials and methods

Materials

The material was taken from:

42 archived videotapes of echocardiograms of Cavalier King Charles spaniels with varying severity of MR from studies of the progression and treatment of MR. The severity of MR was determined by the La/Ao ratio measured by the method of Hansson 2000 and ranged from normal (1.03) to severe (3.44). Those cases were examined by one of two ultrasound machines at different times (Aloka SSD 650, Aloka Co. Ltd, Tokyo, Japan and Interspec, Apogee RX 800, Bothell, Wa, USA), equipped with either a 5 (Aloka) or a 7.5 (Interspec) megahertz sector transducer. A lead II ECG was simultaneously recorded and all studies were archived on video tape. Seven of these dogs had developed heart failure at the time of examination but were not yet treated.

12 echocardiograms of Cavalier King Charles spaniels with varying severity of MR examined at the cardiology clinic, veterinary teaching hospital, SLU. Nine dogs had been treated for heart failure with a diuretic and were stable.

42 corresponding lateral radiographs taken in association with echocardiographic examination. The condition of the dogs was stable between the examinations.

Methods

Relevant parts of videotapes were digitalized (Canopus ADVC-100, Canopus Corporation, 711 Charcot Ave., San Jose, CA 95131, USA) and reviewed using iMovie on a Macintosh computer. They were examined frame by frame to select the correct frame for measuring. End diastole was defined as the frame preceding MV closure and ES for LV measurements as the frame preceding MV opening, which was also the frame with the smallest LV cavity. For transverse measurements across the atrium, ES was the frame after AV closure. Each selected frame was saved in JPEG format and imported and opened in the programme Image J (Rasband, W.S., ImageJ, U. S. National Institutes of Health, Bethesda, Maryland, USA, <http://rsb.info.nih.gov/ij/>, 1997-2007.)

Measurements

Relative size of the RV and LV

Long axis (48 cases). The right parasternal long axis four chamber view was used. Measurements were made at ED, the frame before the A-V valves began to close (Figure 1). The RV dimension was measured across the tricuspid valve (TV) at the annulus. The LV dimension was measured across the MV at the annulus.

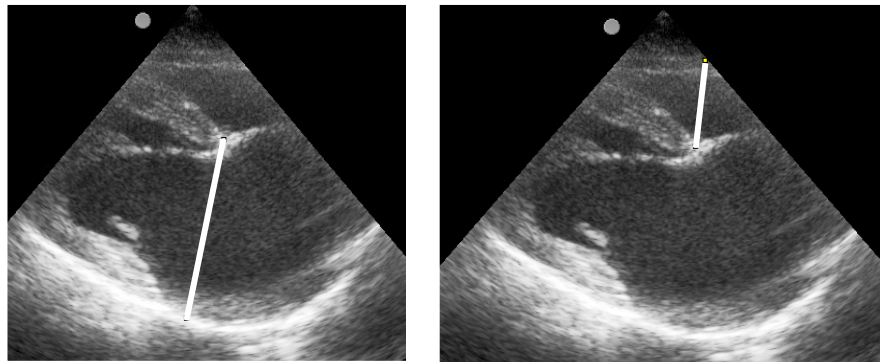


Figure 1. Longitudinal section of the heart at the end of diastole on a 2-dimensional echocardiogram. The placing of the line for the left side dimension at the level of the mitral valve annulus is measured in the left picture and for the right side dimension at the tricuspid valve annulus in the right picture.

Short axis (transverse plane) (54 cases). The right parasternal short axis plane above the A-V valve (Hansson 2002) was used for measuring dimensions of RV and LV at the annulus (Figure 2). The measurements were made at the beginning of diastole, the frame after closure of the aortic valve.

Angle between RV wall and septum (37 cases). This angle was measured on the right parasternal short axis view at the mid ventricular level where the chordae tendinae or papillary muscles just below them were visible at the end of diastole (ED) and the end of systole (ES). The angle was created by two lines which were tangents to the endocardial surface of the RV wall and septal wall (Figure 3). The hypothesis was that if the right ventricular chamber were enlarged by volume overload the angle would increase (Laurenceau and Dumesnil 1976, Louie and others 1992).

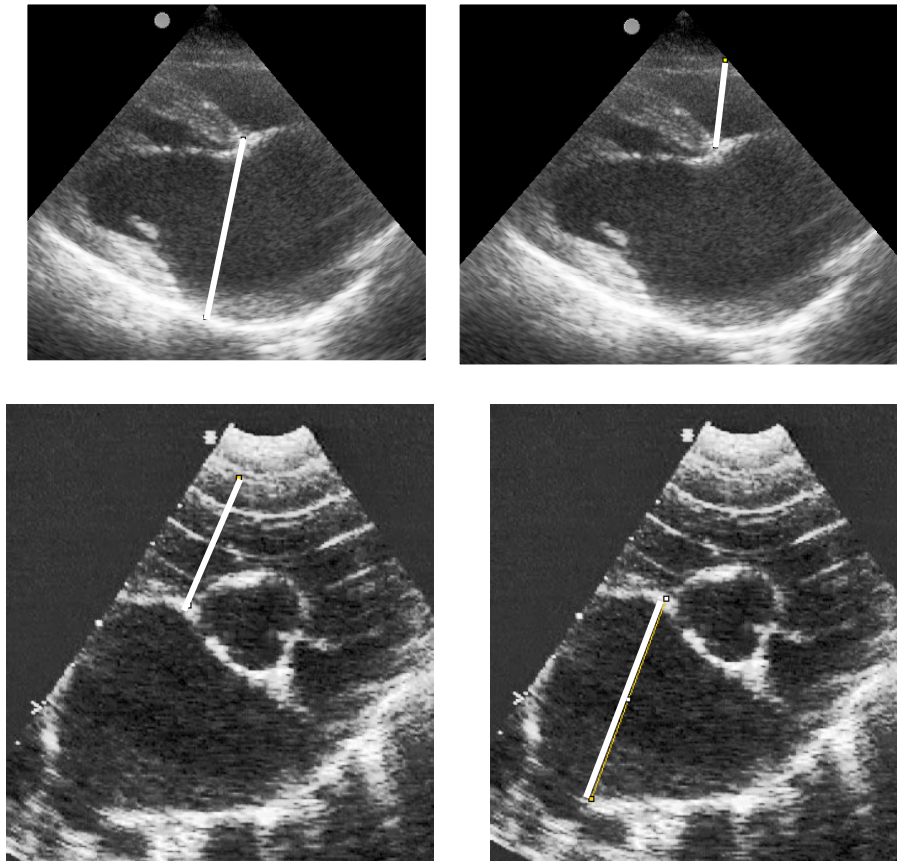


Figure 2. Transverse section of 2-dimensional echocardiogram just above the mitral valve annulus. The aorta (Ao) and left atrium (La) are visible. The picture on the left shows the line measuring the right ventricular dimension from the right ventricular free wall to the left atrium and the picture on the right shows the line measuring the dimension of the LA.

Eccentricity index EI at ED and ES (54 cases). The ellipse tool of Image J was placed on the inner (endocardial) circumference at the same mid ventricular level at ED and ES to measure major and minor axes of the LV cavity. If necessary, the image was rotated to place the septal-free wall axis vertically so that the major axis of the ellipse was aligned with the cranio-caudal axis of the ventricle and the minor axis of the ellipse was aligned with the septal-free wall axis of the ventricle. The minor axis was vertical at 90 degrees to the major axis. The EI was the ratio of major axis to minor axis (Figures 3 and 4).

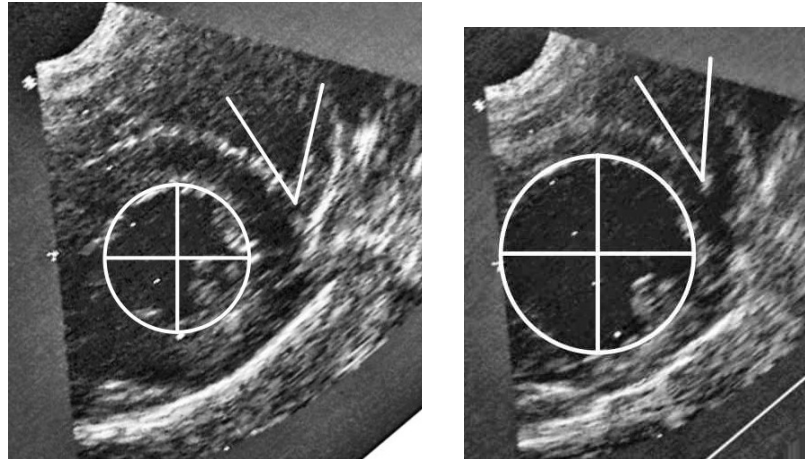


Figure 3. Measurement of eccentricity index and the septal free wall angle at and systole (left) and end diastole (right). The major axis is horizontal and the minor axis is vertical. The images has been rotated to place the axis the axes correctly in relationship to the position of the septum. This heart has a normal septum.

Measurement of Degree of MR and size of heart. The size of the LA is directly related to the degree of MR (Häggström and others 1997, Kittleson and Brown 2003, Pape and others 1991, Pizzarello and others 1984). La/Ao ratio was measured from the same frame as the short axis view for measuring RV and LV dimensions. These dimensions were already recorded on the archived tapes or were made by the cardiologist doing the echocardiogram. This is the most reliable method for measurement of LA size, as it is independent of body weight, and measures the body of the LA (Hansson and others 2002).

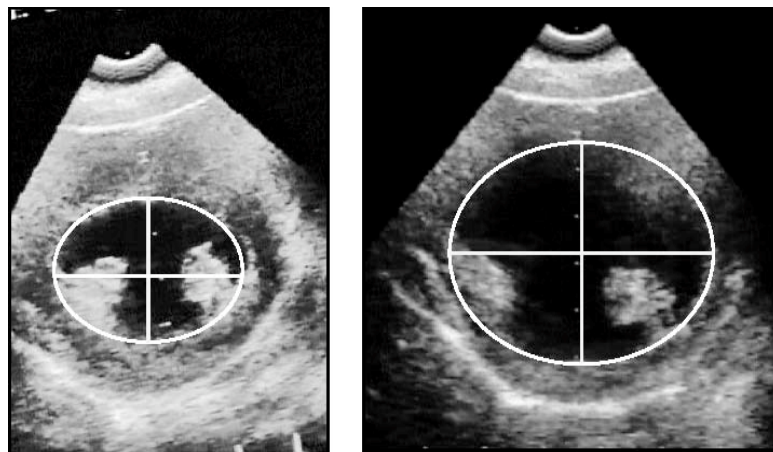


Figure 4. Example of a heart with flattened septum at end systole and end diastole

Vertebral heart scale (VHS) was used as a measure of general heart enlargement. This is the most reliable method for measuring heart size because vertebrae are stable in size whereas comparing size with the thorax is not, because the phase of breathing and chest conformation affect thorax size. Measurements were made on the left lateral projection. The long axis (from the base to apex) of heart and the short axis at 90 degrees to it were measured. The points for measuring followed the original description (Buchanan and Bucheler 1995) but clarified (Hansson and others 2005) by always using the ventral margin of the largest of the main stem bronchi or the most cranial bronchus if they were equal size. The caudal measurement for the short axis was in the middle of the caudal vena cava. The measured long axis and short axis of heart dimensions were transposed onto the vertebral column and recorded as the number of vertebrae beginning with the cranial edge of T4. These values were added to obtain the VHS.

Analysis and statistical methods. All dimensions and ratios were plotted as regressions against LA/Ao and VHS.

To determine if increases of EI at were significantly related to heart size and degree of MR, the EI values were divided into two groups: La/Ao < and >2.5 and VHS < and > 12.5. The groups were subjected to t-test for significant difference of $p < 0.05$.

ED EI and ES EI were plotted on a vertical scale in two columns and a line drawn between each pair of measurements to show whether ED IE was greater or less than ES EI, which can differentiate pressure from volume overload (Ryan and others 1985).

Results

Regression of R/L longitudinal dimension-La/Ao, R/L longitudinal dimension-VHS, R/L transverse dimension-La/Ao, and R/L transverse dimension-VHS (Figure 5).

R/L longitudinal and R/L transverse dimension ratios tended to decrease slightly with increasing LA/Ao, suggesting that the R side did not enlarge as MR increased. However, R/L long and R/L transverse dimensions did not decrease with VHS, suggesting that the R side enlarged in proportion to general enlargement. The data points were spread widely around the mean so the results were inconclusive. The ES RV septal-free wall angle decreased very slightly as left atrium and heart enlarged, but the spread was very large. The other relationships showed no change with LA or heart size.

Regressions of eccentricity on LA and heart size (Figure 6). ED EI did not increase with increasing LA size. ED EI did not increase with increasing heart size. ES EI increased slightly with increasing size of LA and heart, due to increases when the LA and heart were severely enlarged. Severe ED EI was not significantly greater than mild-moderate ED EI, but severe ES EI was significantly greater ($p < 0.05$).

The mean values of even normal-mild LA and heart enlargement were slightly over the expected normal 1.0.

Change of eccentricity between ED and ES. An example of a heart with increased ED EI and ES EI is shown in Figure 4. Figure 7 shows the changes between ED and ES. Most of the hearts hardly changed. But five hearts had high ES EI indicating pressure overload and three hearts had high ED EI, indicating volume overload.

Regression of right ventricular free wall-septal angles to left atrial LA/Ao) and heart size (VHS) (Figure 8). The relationship was weak and the angles were not affected, except that ES angle decreased slightly with VHS.

Radiographic appearance of the heart. The subjective impression of convexity of the cranial heart border and sternal contact, and right side convexity in the VD view, was that the convexities increased in proportion to the VHS. Even mild-moderately increased VHS was accompanied by increased convexity of the right side of the heart. These relationships are the subject of another study.

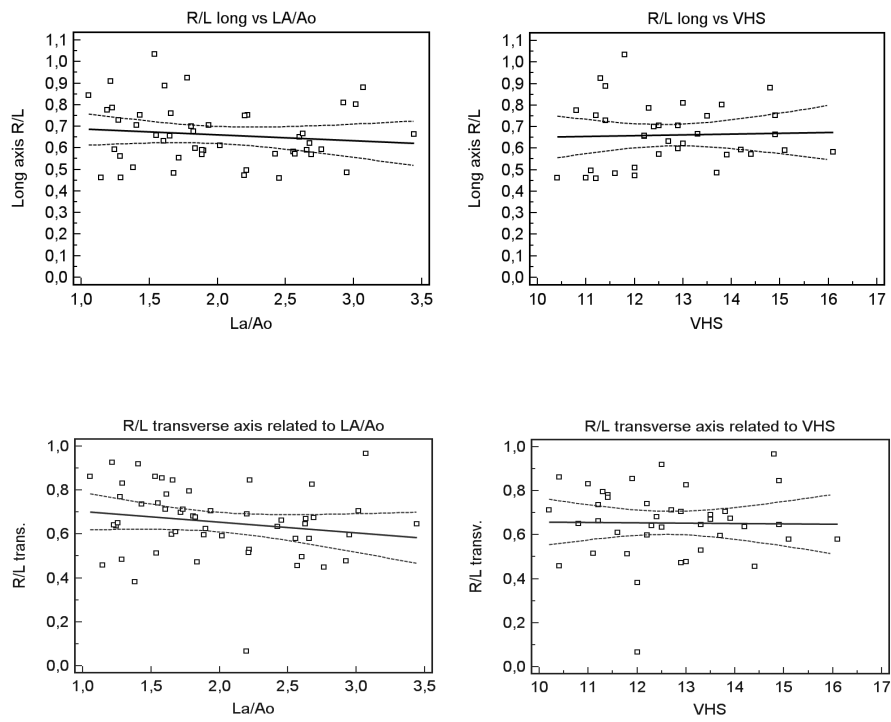


Figure 5. Relationship of relative size of right ventricle to left ventricle (R/L) in long and transverse axes. The ratios seem to be constant, but the 95% confidence limits for the regression lines are wide.

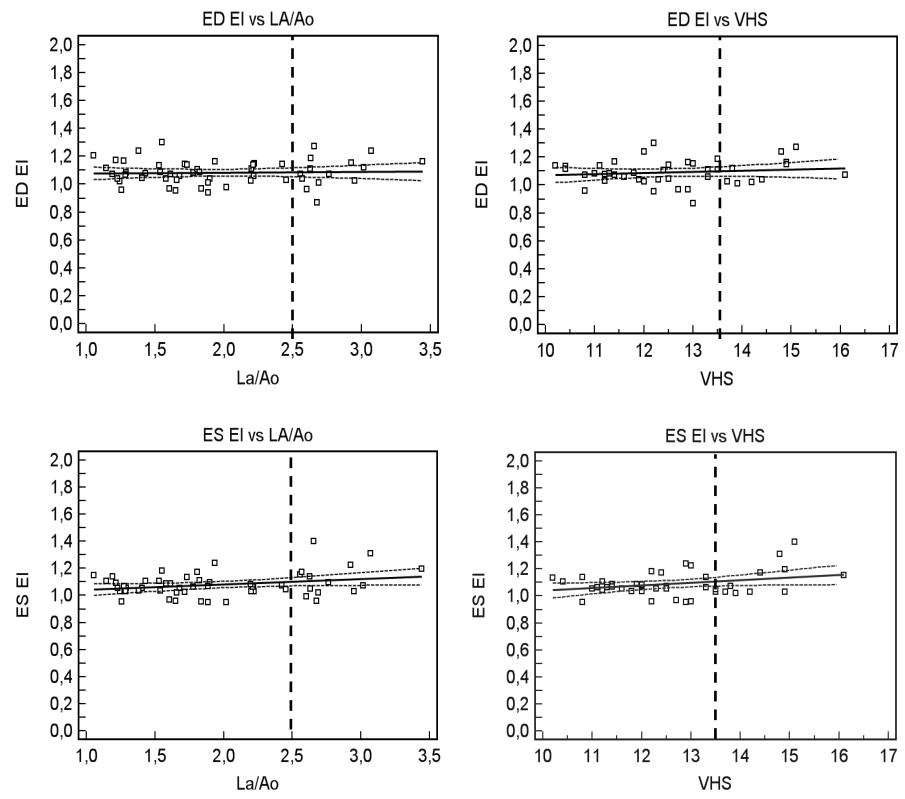


Figure 6. Relationship of end diastolic (ED) and end systolic (ES) eccentricity index (EI) to left atrial size (LA/Ao) and heart size (VHS). The vertical dashed line is the cutoff level between none to moderate enlargement and severe enlargement. The dotted lines are 95% confidence limits of the regression line. The relationship for ES is slightly positive, due to some increases in severely enlarged hearts.

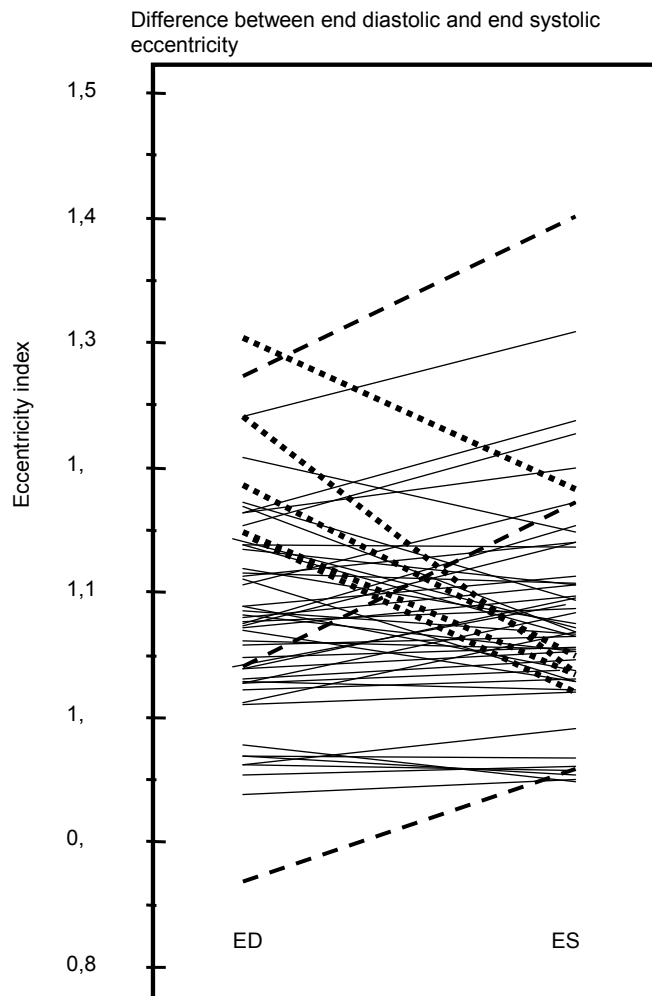


Figure 7. Differences between ED and ES. Most of the lines which were close to the mean were horizontal, with no change between ED and ES. When eccentricity was high, five hearts had high ED EI with lower ES while three increased at ES. No differences were found between the hearts in failure and those not in failure. Using a cut-off difference of 10%, 9/14 of the dogs with HF had minimal difference between ED EI and ES EI, one had ES EI > ED EI, and 3 had ED EI > ES EI. Two hearts without failure had ES EI > ED EI, and two had ED EI > ES EI.

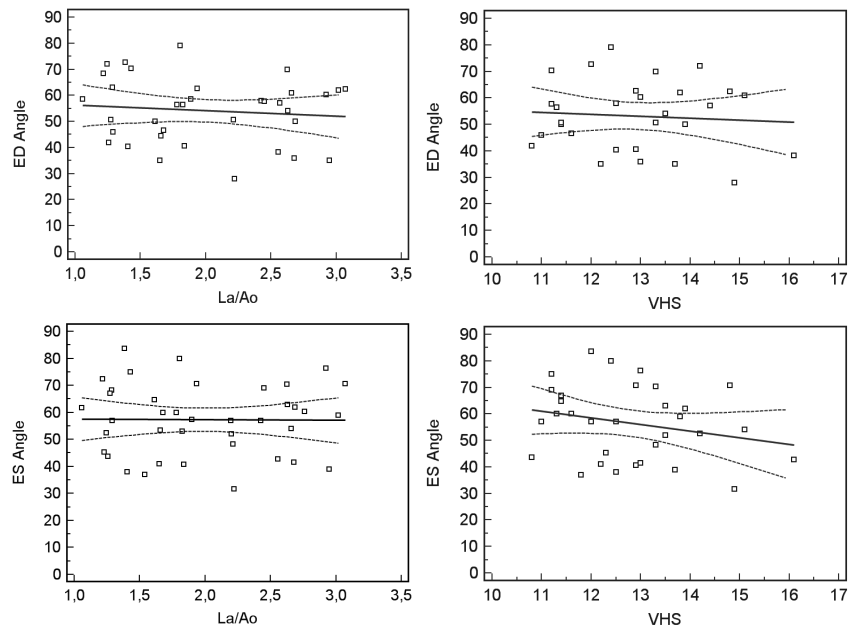


Figure 8. Relationship of right ventricular free wall-septal angle to left atrial LA/Ao) and heart size (VHS). It did not change except in relationship to VHS, when the angle decreased slightly. The 95% confidence limits for the regression line are wide.

Discussion

R/L transverse and R/L long axis. The tendency to relatively smaller right side with increasing size of left atrium suggests that right side does not enlarge in proportion to severity of MR. Right side enlargement in proportion to VHS suggests that a component of the VHS is actually right sided enlargement unrelated to MR, but the wide spread of data points around the mean makes the results inconclusive. The spread of data points is due to difficulties in locating many of them. On many transverse sections the RV wall and cavity were not visible or obscured by near-field artifacts particularly in systole. The exact point of the RV free wall was difficult to determine because near-field artifacts obscured details.

In theory it is possible by M-mode echocardiography to measure RV chamber dimensions from free wall to septum, and thickness of RV wall as an indicator of RV hypertrophy. Nevertheless, we found when trying to measure the angle between the RV free wall and septum, that the appearance of the RV wall and chamber were inconsistent, sometimes not visible at all, and as the videotapes were reviewed, the m-mode recordings confirmed that any attempts to measure RV size by M-mode would have been useless.

Septal-free wall angle. The slight tendency for ES angle to decrease with increasing VHS suggests that the RV is actually compressed by the enlarging LV, but the wide spread of data around the mean makes the results inconclusive. As the study was retrospective, the angle of the transducer could not be controlled to optimize the appearance of the RV free wall, as the examination was directed at the LV. In many cases the RV free wall could not be seen at all, especially at ES, which is why the number of data points is less than the number of hearts examined. The idea that the RV is actually compressed by the enlarging LV is supported by the study of Young et al (1996) who in an experimental model of chronic MR in dogs, found by reconstruction of magnetic resonance images of the heart, that the LV bulged into the RV at ED.

Regression ED EI - LA/Ao; Regression ED EI - VHS. The absence of any increase in ED EI with LA/Ao or VHS and the lack of any significant difference between the groups with none-moderate LA and heart enlargement and the groups with severe enlargement, show that there was no relationship between ED EI and MR or size of the heart. Volume overload was likely to have been caused by concurrent primary TR of myxomatous degeneration rather the secondary TR from PH, as PH causes ES EI which is greater than ED EI even though TR is present (Ryan and others 1985). It is possible that ED EI is insensitive to mild volume overload and that the RV convexity is actually caused by this, but the degree and cause of the volume overload could not be determined as Doppler echocardiographic evaluations of the TV and PV were not done.

The values of ED EI greater than 1.0 with normal-moderate LA and heart enlargement could be explained by presence of mild pressure or volume overload even in these hearts, but as the normal septum configuration is slightly flattened, (Reisner and others 1994) it seems that the normal transmural pressure gradient caused this.

Regression ES EI - LA/Ao; Regression ES EI - VHS. The septum flattens when the trans-septal gradient decreases as RV systolic pressure rises, upsetting the normal relationship between curvature and wall stress (Dellegrottaglie and others 2007, Roeleveld and others 2005). As ES EI increased slightly with increasing size of the LA and heart, and as higher ES EI than ED EI is associated with pressure overload, (Agata and others 1985, Dellegrottaglie and others 2007, DeMadron and others 1985, King and others 1983, Louie and others 1992, Ryan and others 1985, Santamore and Gray 1995) pressure overload could be responsible for increased convexity of RV on radiographs. However, as the increase was caused by a few cases in the severely enlarged LA/Ao and VHS groups, and RV was convex on radiographs even in mild-moderate enlargement there has to be some other reason or the convexity in mild-moderate enlargement. As some hearts had much higher ES EI than ED EI they definitely had pressure overload, but the cause could not be determined. Mild to moderate MR and heart enlargement was not associated with septal flattening, but the significant increase of ES EI in some dogs indicates that RV pressure overload was present in severe MR, as has been reported in humans and dogs (DeMadron and others 1985, Dong and others 1992, King and others 1983, Ryan and others 1985, Serres and others 2006, Weyman and others 1976).

The question arises of the sensitivity of the ES EI to exclude the possibility of mild PH, and whether undetected mild PH could cause the RV convexity seen on radiographs. Unlike with volume overload, there are a number of studies relating PH and septal flattening, using both 2-D echocardiography (Agata and others 1985, King and others 1983, Louie and others 1992, Portman and others 1987, Ryan and others 1985) and more recently, magnetic resonance imaging (Dellegrottaglie and others 2007, Dong and others 1995, Roeleveld and others 2005) and various methods of measurement, with a good correlation between RVP or RVP/LVP and septal flattening, however it was measured. The two papers which used the same method measuring EI as this study found that with RV systolic pressures exceeding 45mm Hg, ES EI averaged 1.44 (Ryan and others 1985) and with a mean pulmonary artery pressure of 53 mm, a mean ES EI of 1.64 was found (Louie and others 1992). A comparison of these results with those of this study (mild-mod LA and heart enlargement: ES EI 1.07 +/- 0.08 (SD); severe heart enlargement, ES EI <1.40), suggests that systolic pressure in the RV of the dogs with MR is unlikely to exceed 45 mm Hg and this is not enough to cause significant right ventricular disease with flattened septum and right side enlargement.

This study confirms the opinion (Kittleson 1998) that sufficient pressure could be not developed to cause RV enlargement. In addition, pressures of over 45 mm should cause pulmonary oedema in chronic MR (Ware and Bonagura 1999) but some of the cases with flattened septum did not have pulmonary oedema, and therefore pulmonary venous pressure would not have been higher than 45mm at the most. Therefore in these cases the PH does not arise from the left side of the heart. PH has been found in 14% of dogs with MR, and was correlated with severity of MR (Serres and others 2006), with RV systolic pressures of 65.0 +/- 22.6 (SD) mm Hg in dogs with severe HF, although no definite cause and effect could be determined. These pressures would be sufficient to flatten the septum. The cause may be endothelin-1-related, due to chronic hypoxia from interstitial pulmonary oedema (Ooi and others 2002) as endothelin-1 is found in dogs with HF.(Prosek and others 2004)

Change of eccentricity between ED and ES. The change of eccentricity between ED and ES can be used to separate volume from pressure overload (Agata and others 1985, Louie and others 1992, Ryan and others 1985, Santamore and Gray 1995). Most of the lines (graph 23) which were close to 1.0 were horizontal: ED and ES EI were close. If the ES EI is higher than the ED EI, pressure overload is present, and may be accompanied by volume overload too (Ryan and others 1985). Five hearts had ED EI which was 10% greater than ES EI, indicating volume overload, but they appeared to be unrelated to severity of MR. Three had ES EI 10% > ED EI, indicating pressure overload. A 10% difference is arbitrary but seemed reasonable in relation to the variability shown in dogs with minimal LA and heart enlargement. As absolute values are subject to more variability because of distortion caused by transducer angle than comparison of ED and ES in the same examination, the more restrictive criteria are justified.

As there was no consistent septal flattening in mild to moderately enlarged hearts there was no evidence that MR consistently causes RV pressure or volume

overload.(DeMadron and others 1985) found no paradoxical wall motion or flattened septum in 14 dogs with left heart disease. It seems unlikely that the convexity of the right side seen in general heart enlargement would be caused by right ventricular enlargement unless the MR was very severe. The enlarged atrium and ventricle push over and even compress the right sided chambers (Young and others 1996).

Study limitations. The echocardiographic study was retrospective, using some already done measurements by another examiner, and the examinations were not optimized for the measurements made of right and left sides in the longitudinal and transverse axes. Echocardiographic artifacts prevented determining the exact or correct point of measurement in many of the transverse and longitudinal images. Variability around the mean of the EI could have been be partly due to varying angle of the transducer causing false eccentricity as evidenced by values of less than 1.0, which are physiologically impossible. Another cause is measurement variability. Sometimes papillary muscles disturbed the border of the ellipse, endocardial borders were partly obscured by echocardiographic artifacts, and the whole LV was not always in the field. The ellipse was placed by estimating the best position. The variations might have hidden mild changes in EI. The variation of distortion could be avoided by another method of measurement (radius of curvature of the septum/radius of curvature of the free wall of the left ventricle). This method could not be used with Image J, and we chose the simplest method. The inability to measure the right ventricle directly means that the conclusion that the RV is not consistently enlarged and thus does not cause the increased radiographic convexity in MR is based on secondary evidence of absence of sufficient RV pressure or voume overload to flatten the septum. It is possible but unlikely that mild PH, < 45mm Hg, could cause hypertrophy of the RV wall and chamber enlargement sufficient to cause the radiographic changes without septal flattening.

Conclusions

Right sided heart enlargement is not necessary for the appearance of general heart enlargement on radiographs. “General heart enlargement” on radiographs should not be interpreted as right sided enlargement or disease. The appearance of convexity of the right heart borders in most cases is caused by the enlarged left atrium and ventricle displacing the right side chambers outwards. The RV may be volume or pressure overloaded in some cases of MR.

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