Effects of age, body weight, and heart rate on transmitral and pulmonary venous flow in clinically normal dogs

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Objective—To determine the influence of age, body weight (BW), heart rate (HR), sex, and left ventricular shortening fraction (LVSF) on transmitral and pulmonary venous flow in clinically normal dogs.

Animals—92 client-owned dogs 3 months to 19 years old.

Procedure—Transthoracic Doppler echocardiography recordings of transmitral flow and pulmonary venous flow were obtained in conscious unsedated dogs. Influence of age, BW, HR, sex, and LVSF on diastolic variables was assessed, using statistical methods such as ANOVA on ranks and univariate and multivariate forward stepwise linear regression analyses.

Results—Age significantly influenced isovolumic relaxation time (IVRT; $r = 0.56$), ratio between peak velocity of the early diastolic mitral flow wave-to-peak velocity of late diastolic mitral flow wave (E:A; $r = -0.44$), deceleration time of early diastolic mitral flow (DT_E; $r = 0.26$), and peak velocity of atrial reversal pulmonary venous flow wave (AR-wave; $r = 0.37$). Significant changes of mitral inflow and pulmonary venous flow variables were evident only in dogs > 6 and > 10 years old, respectively. Body weight significantly influenced DT_E ($r = 0.63$), late diastolic flow duration ($r = 0.60$), and AR duration ($r = 0.47$), whereas HR significantly affected DT_E ($r = -0.34$), IVRT ($r = -0.33$), and peak velocity of AR ($r = 0.24$). Sex or LVSF (range 22 to 48%) did not influence any echocardiographic variables.

Conclusions and Clinical Relevance—Age, BW, and HR are important factors that affect filling of the left atrium and left ventricle in clinically normal dogs. (*Am J Vet Res* 2001;62:1447–1454)

Left ventricular diastolic dysfunction is evident in a wide number of cardiac abnormalities and may play a major role in the pathogenesis and clinical manifestation of heart failure in human beings[1-3] as well as dogs.[4,5] Pulsed-wave Doppler echocardiography of transmitral flow and pulmonary venous flow has been used to assess left atrial and left ventricular filling and, indirectly, left ventricular diastolic function in clinically normal dogs.[4,6-16] Reasonable correlations have been found between Doppler-derived indices of diastolic cardiac function and invasively derived diastolic variables (diastolic pressures, the time constant of ventricular relaxation, ventricular compliance, and myocardial stiffness) in a number of studies in dogs.[6-11,17,18] Therefore, Doppler-derived indices of left ventricular diastolic function can be considered useful for the noninvasive evaluation of diastolic events in dogs. However, velocity patterns of transmitral and pulmonary venous flow are dependent on intrinsic myocardial diastolic properties as well as external factors such as loading conditions, left atrial and left ventricular systolic function, **heart rate (HR)** and rhythm, pericardial restraint, and right ventricular performance.[6,7,10,17,19-21] In addition, age, sex, phase of respiration, and **body weight (BW)** all have a noticeable influence on Doppler-derived variables of diastolic function in human beings.[22-36] Despite some experimental invasive studies on age-related changes in left ventricular diastolic properties in dogs,[16,37,38] the effect of most physiologic variables on diastolic function has not been systematically evaluated in dogs. To the authors' knowledge, there are few reports on the effect of these variables on Doppler indices of left ventricular diastolic function in clinically normal dogs.

Therefore, the purposes of the study reported here were to determine the effect of age, BW, HR, sex, and **left ventricular shortening fraction (LVSF)** on Doppler-derived indices of left atrial and left ventricular filling, to test the hypothesis that Doppler-derived variables of transmitral flow and pulmonary venous flow are affected primarily by age and HR in healthy dogs, and to generate age-related reference values for Doppler variables of left atrial and left ventricular filling in clinically normal dogs.

Materials and Methods

Animals—Data were obtained from 92 clinically normal dogs that represented a wide range of BW, breeds, and ages. Data were obtained between 1995 and 1999. Dogs were included in the study when they fulfilled the following criteria: medical history did not include evidence of heart disease, coughing, dyspnea, or syncope; normal results of physical examination; normal sinus rhythm or sinus arrhythmia; and normal results of **2-dimensional (2-D)** and M-mode echocardiography. Data were collected in consecutive dogs, although dogs were selected for use in the study on the basis of having high-quality echocardiographic images that would allow for accurate quantitative measurements.

Echocardiography—All dogs underwent a complete echocardiographic examination that included transthoracic

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2-D, M-mode, spectral, and color-flow Doppler echocardiographic evaluations,[a] using a transducer array of 2.25 to 7.50 MHz, depending on the size of the dog. Examinations were performed in conscious unsedated dogs during a period of quiet respiration. The 2-D echocardiograms were obtained in accordance with techniques described elsewhere[39] and by use of recommended standardized transthoracic imaging planes.[40] Left ventricular parasternal M-mode recordings were obtained from short-axis views with dogs positioned in right lateral recumbency. Doppler echocardiography of mitral inflow and pulmonary venous flow was performed from the left parasternal apical 4-chamber view with dogs positioned in left lateral recumbency.[13,41] All patterns of pulmonary venous flow were recorded from the pulmonary vein of the left caudal lung lobe.[12] Doppler echocardiographic evaluation of optimal sample volume position and alignment with flow was guided by simultaneous display of real-time 2-D echocardiographic images. Oblique or angled views were avoided. Sweep speed during recordings was 50 or 100 mm/s. In all instances, a simultaneous 1-lead ECG was recorded. Data were stored on a system-integrated workstation, videotape, or magnetic optical disc for subsequent analysis.

Measurements and calculations—All measurements were made by 1 investigator (KES). Measurements and computations on left ventricular parasternal M-mode echocardiograms were performed in accordance with standards established by the Committee on M-mode Standardization of the American Society of Echocardiography.[42] The mean of 5 consecutive measurements was considered the average of each variable, irrespective of the respiratory phase. Left ventricular **isovolumic relaxation time (IVRT**; interval from closure of the aortic valve to opening of the mitral valve) was calculated as the difference between the intervals from the Q-wave on the ECG to opening of the mitral valve (start of early diastolic flow on the Doppler recording) and from the Q-wave to closure of the aortic valve (sound commensurate with valve closure on Doppler recording of aortic flow) obtained from nonsimultaneous recordings.[43] Measurement of variables of mitral inflow and pulmonary venous flow were made in accordance with recommendations for measurement of those variables in human beings.[19,41] Doppler curves of mitral inflow were created to determine peak velocities of **early diastolic mitral flow wave (E-wave)**, **late diastolic mitral flow wave (A-wave)**, **ratio of peak velocity of E-wave to peak velocity of A-wave (E:A)**, **deceleration time of the E-wave (DT_E)**, and duration of the A-wave. Velocity curves of pulmonary venous flow were created for the instantaneous highest velocity spectra to determine peak velocities of **systolic pulmonary venous flow wave (S-wave)**, **early diastolic pulmonary venous flow wave (D-wave)**, and **late diastolic atrial reversal of pulmonary venous flow wave (AR-wave)**. In the case of biphasic systolic flow, the tallest wave was used for determination of peak velocity. Duration of the AR-wave was measured from onset to termination of negative flow in late diastole. In addition, the **ratio of duration of the A-wave to duration of the AR-wave (A duration:AR duration)** was calculated. Heart rate was calculated from the interval between successive R-waves.

Dogs were arbitrarily allocated into 5 age groups (< 2 years old, ≥ 2 but < 4 years old, ≥ 4 but < 6 years old, ≥ 6 but < 10 years old, and ≥ 10 years old) to determine age-dependent reference values of transmitral flow and pulmonary venous flow for Doppler-derived variables.

Statistical analysis—Descriptive statistics were determined for age, BW, HR, sex, LVSF, and all Doppler-derived variables of diastolic function. Data were reported as median and 10th and 90th percentiles, except when stated otherwise. Differences between age groups were detected, using a Kruskal-Wallis ANOVA on ranks test.[b] When significant differences were observed, pairwise comparisons were performed, using the Dunn test. An ANOVA was used to evaluate differences in Doppler-derived indices between females and males with correction for other factors that could be explained by differences in sex. Possible relationships between Doppler-derived indices for left atrial and left ventricular filling and age, BW, HR, sex, and LVSF were tested, using simple linear regression analysis. Scatter plots of predicted values of E:A, peak velocity of the AR-wave, and IVRT in relation to age and DT_E in relation to BW were reported as means and 95% confidence intervals.

Multiple linear regression analysis was used to predict Doppler-derived values from physiologic independent variables. A forward stepwise procedure allowed evaluation of the contribution of each independent variable (age, BW, HR, sex, and LVSF) in the total variance of Doppler-derived indices of left ventricular diastolic function. The **partial correlation coefficient (R^2)** indicated the proportion of variance explained by inclusion of a single variable in the regression analysis. Statistical power for the reported tests was calculated at ≥ 0.80 for all described values, and values of $P \leq 0.05$ were regarded as significant.[44]

Results

Animals—Ninety-two dogs (56 males and 36 females) representing 27 breeds were included in the study. The BW of these dogs ranged from 2 to 43 kg (mean, 19 kg). Doppler recordings of mitral flow and pulmonary venous flow were obtained for analysis (**Fig 1**).

Univariate analysis—Values of echocardiographic variables for dogs in various age groups were reported as median and 10th and 90th percentiles and can be used as reference values (**Table 1**). Correlation coefficients and their significance were evaluated by linear regression analysis of each echocardiographic index against the independent variables (**Table 2**).

Effects of age—An association was found between age and IVRT, peak velocities of the E-, A-, and AR-waves, E:A, DT_E, and AR duration. Range of

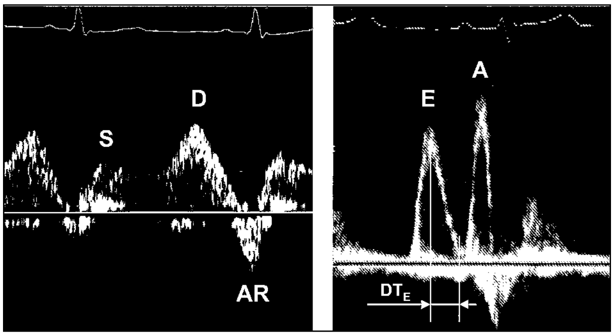

Figure 1—Doppler echocardiograms of pulmonary venous flow (left) and transmitral flow (right) obtained from a left apical 4-chamber view of the heart in a clinically normal 12-year-old dog. Notice the prominent late diastolic atrial reversal of pulmonary venous flow wave (AR-wave), prolonged deceleration time (DT_E) of the early diastolic mitral flow wave (E-wave), and the ratio of peak velocity of the E-wave to peak velocity of the late diastolic mitral flow wave (A-wave), which is < 1.0. Measurement of DT_E is indicated (arrows). S = Systolic pulmonary venous flow wave (S-wave). D = Early diastolic pulmonary venous flow wave (D-wave).

Table 1—Median (10th to 90th percentile) values for body weight (BW), heart rate (HR), and echocardiographic variables of left ventricular systolic and diastolic function in 92 clinically normal dogs categorized on the basis of age

	Age (y)				
Variable	< 2 (n = 30)	≥ 2 to < 4 (n = 30)	≥ 4 to < 6 (n = 13)	≥ 6 to < 10 (n = 11)	≥ 10 (n = 8)
BW (kg)	11^{a} (4–29)	26^{b} (8–33)	28^{b} (7–36)	11^{a} (8–40)	10^{a} (9–23)
HR (bpm)	112 (67–162)	103 (74–120)	105 (73–138)	113 (93–134)	115 (69–129)
LVSF (%)	37^{a} (30–43)	31^{b} (25–42)	36 (27–43)	35 (28–43)	36 (28–44)
IVRT (ms)	46^{a} (31–62)	47 (40–65)	43 (43–63)	47 (41–65)	63^{b} (41–73)
Peak E (m/s)	0.77^{a} (0.63–0.93)	0.72 (0.54–0.92)	0.73 (0.52–0.91)	0.69^{b} (0.52–0.82)	0.69^{b} (0.52–0.81)
Peak A (m/s)	0.48^{a} (0.37–0.68)	0.52 (0.35–0.67)	0.49 (0.39–0.64)	0.57^{b} (0.45–0.70)	0.65^{b} (0.45–0.78)
E:A	1.65^{a} (1.16–1.98)	1.35 (0.93–1.86)	1.44 (1.10–1.60)	1.08^{b} (0.98–1.70)	1.28^{b} (0.68–1.42)
DT_E (ms)	67^{a} (53–79)	73^{a,b} (53–107)	90^{b,c} (54–110)	80 (49–98)	80^{c} (73–98)
A duration (ms)	87 (63–112)	87 (77–109)	93^{a} (77–123)	90 (68–106)	80^{b} (61–99)
Peak S (m/s)	0.41 (0.30–0.60)	0.40 (0.31–0.53)	0.45 (0.30–0.60)	0.34 (0.24–0.70)	0.40 (0.34–0.75)
Peak D (m/s)	0.57 (0.44–0.69)	0.55 (0.39–0.82)	0.51 (0.38–0.82)	0.50 (0.36–0.75)	0.57 (0.41–0.86)
S:D	0.72 (0.46–1.23)	0.68 (0.53–1.18)	0.75 (0.55–1.38)	0.79 (0.47–1.17)	0.93 (0.53–1.09)
Peak AR (m/s)	0.21^{a} (0.16–0.26)	0.21 (0.16–0.29)	0.21 (0.15–0.29)	0.24 (0.19–0.30)	0.26^{b} (0.22–0.28)
AR duration (ms)	67^{a} (53–80)	70^{a} (53–87)	70^{a} (53–103)	67^{a} (57–80)	57^{b} (48–60)
A duration:AR duration	1.19 (1.05–1.64)	1.35 (1.05–1.70)	1.47 (0.92–1.64)	1.33 (1.03–1.73)	1.42 (1.26–1.65)

bpm = Beats per minute. LVSF = Left ventricular shortening fraction. IVRT = Isovolumic relaxation time. Peak E = Peak velocity of the early diastolic mitral flow wave (E-wave). Peak A = Peak velocity of late diastolic mitral flow wave (A-wave). E:A = Ratio between Peak E to Peak A. DT_E = Deceleration time of E-wave. A duration = Duration of A-wave. Peak S = Peak velocity of systolic pulmonary venous flow wave (S-wave). Peak D = Peak velocity of early diastolic pulmonary venous flow wave (D-wave). S:D = Ratio of Peak S to Peak D. Peak AR = Peak velocity of late diastolic atrial reversal of pulmonary venous flow (AR-wave). AR duration = Duration of AR-wave. A duration: AR duration = Ratio of A duration to AR duration. ^{a,b,c}Within a row, values with different superscript letters differ significantly ($P \leq 0.05$).

Table 2—Correlation coefficients determined during univariate analysis between age, BW, HR, sex, and LVSF and Doppler-derived variables of left ventricular diastolic function

Variable	Age	BW	HR	Sex	LVSF
IVRT	0.56	NS	–0.33	NS	NS
Peak E	–0.23	NS	NS	NS	NS
Peak A	0.31	NS	0.30	NS	NS
E:A	–0.44	NS	NS	NS	NS
DT_E	0.26	0.63	–0.34	NS	NS
A duration	NS	0.60	NS	NS	NS
Peak S	NS	NS	0.30	NS	NS
Peak D	NS	NS	NS	NS	NS
Peak AR	0.37	NS	0.24	NS	NS
S:D	NS	NS	NS	NS	NS
AR duration	NS	0.47	NS	NS	NS
A duration :AR duration	NS	NS	NS	NS	NS

NS = Not significant at a value of $P < 0.05$.

values for IVRT was between 30 and 74 milliseconds and increased with age (**Fig 2**; Table 2). The lowest values were in dogs < 2 years old, and the highest values were in dogs > 13 years old. We did not detect significant differences in median IVRT among groups, except for comparison between the oldest and youngest groups of dogs (Table 1). There was a progressive decrease in E-wave peak velocity with age, although a significant difference was detected only when values for dogs > 6 years old were compared with values for dogs < 2 years old. A progressive increase in A-wave peak velocity was seen with age, with significant differences between values for dogs > 6 years old, compared with values for dogs < 2 years old. Accordingly, E:A decreased with age (**Fig 3**). The range of values for E:A was 0.64 to 2.21, with 4 (5%) dogs having E:A values > 2.0 (2.21, 2.40, 2.52, and 2.61, respectively). These 4 dogs were < 2.5 years old (median, 1.35 years). Seven (8%) dogs had E:A < 1.0. These 7 dogs were 3 to 15 years old (median, 3.2 years), and the oldest of these dogs had the lowest E:A value (0.64). Two dogs may have had a pseudonormal mitral inflow pattern (defined in human beings[19,21] as an E:A value between 1 and 2, normal DT_E, and AR duration > A duration) that may have represented a moderate stage of diastolic dysfunction. Duration of the A-wave changed with age, but we did not detect a uniform pattern among age groups. The DT_E was between 40 and 120 milliseconds and also was correlated with age. **Ratio of peak velocity of the S-wave to peak velocity of the D-wave (S:D)** was between 0.40 and 1.63. Six (7%) dogs had S:D < 0.50. These dogs were between 8 months and 6 years old, (median, 1.3 years). Thirteen (15%) dogs between 4 months and 10 years old (median, 3.0 years) had S:D > 1.0. Peak

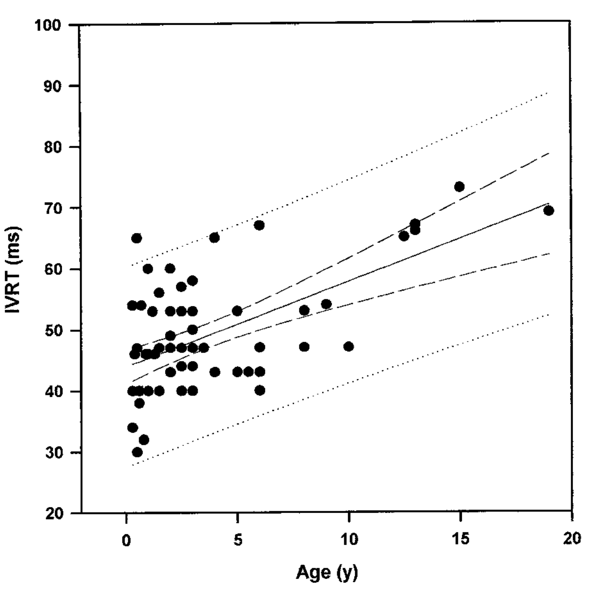

Figure 2—Scatter plot of left ventricular isovolumic relaxation time (IVRT) versus age in 92 clinically normal dogs. The solid line represents the linear regression line, dashed lines represent the 95% confidence intervals, and dotted lines represent the prediction lines for the dependent variable (ie, IVRT) predicted by the regression model. Equation for the regression line ($r = 0.56$; $P < 0.05$) is as follows: IVRT = 43.874 + (1.384 X age).

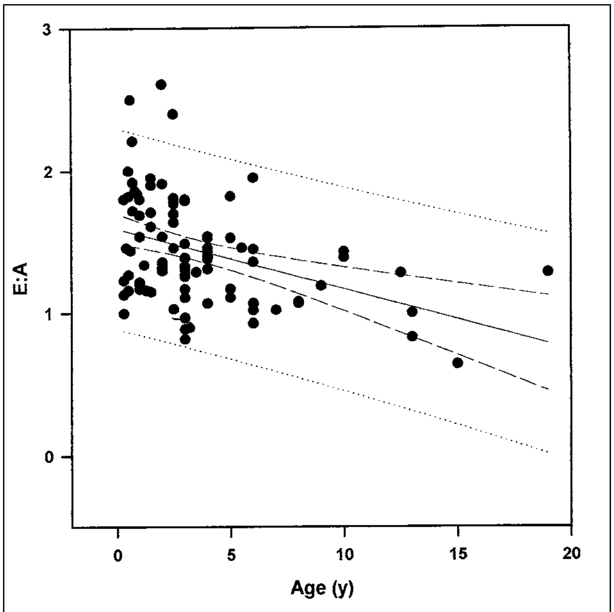

Figure 3—Scatter plot of the ratio of peak velocity of the E-wave to peak velocity of the A-wave (E:A) versus age in 92 clinically normal dogs. Notice the linear relationship between both variables. Equation for the regression line ($r = -0.44$; $P < 0.001$) is as follows: E:A = 1.607 + (0.0473 X age). *See* Figure 2 for key.

velocity of the AR-wave ranged from 0.11 to 0.32 m/s and was higher in older dogs (**Fig 4**). Dogs ≥ 10 years old had a significantly greater peak velocity for the AR-wave, compared with values for younger dogs. Two dogs (4 and 6 years old) had peak velocities for the AR-wave that were > 0.30 m/s (0.31 and 0.32, respectively). Duration of the AR-wave was significantly less in dogs ≥ 10 years old. The A duration:AR duration was between 0.87 and 2.13, and 2 dogs (6 months and 5 years old) had an A duration:AR duration < 1.0 (0.99 and 0.87, respectively).

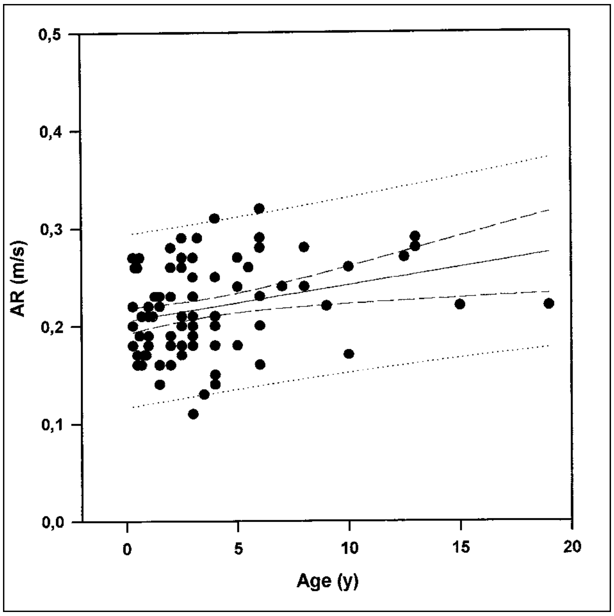

Figure 4—Scatter plot of peak velocity of the AR-wave versus age in 92 clinically normal dogs. Equation for the regression line ($r = 0.37$; $P < 0.05$) is as follows: AR = 0.201 + (0.00494 X age). *See* Figure 2 for key.

Effects of BW—The DT_E, duration of the A-wave, and duration of the AR-wave increased with an increase in BW (**Fig 5**; Table 2).

Effects of HR—Values for IVRT and DT_E decreased, but peak velocities for the A-, S-, and AR-waves increased with an increase in HR (Table 2).

Effects of sex and LVSF—Sex or LVSF (range, 22 to 48%) did not have an effect on any echocardiographic variables (Table 2).

Independent variables—Significant relationships were detected between BW and LVSF ($r = -0.49$), BW and HR ($r = -0.27$), and LVSF and HR ($r = 0.20$).

Multivariate analysis—Results of the stepwise multiple linear regression analysis were recorded (**Table 3**). For each echocardiographic variable, we reported the variable that was entered into the regression at each step, the **correlation coefficient (*r*)**, R^2, the **increase in R^2 attributable to the entered variable (ΔR^2)** and the *P* value.

Age alone accounted for up to 28% of the variance in IVRT, 11% of the variance in peak velocity of the A-wave, 16% of variance in E:A, 12% of variance in DT_E, and 16% of variance in peak velocity of the AR-wave. Body weight alone accounted for 39% of the variance in DT_E, 37% of the variance in A-wave duration, 8% of the variance in S:D, and 22% of the variance in duration of the AR-wave. Heart rate alone accounted for 15% of the variance in peak velocity of the A-wave, 10% of the variance in E:A, 13% of the variance in peak velocity of the S-wave, and 5% of the variance in peak

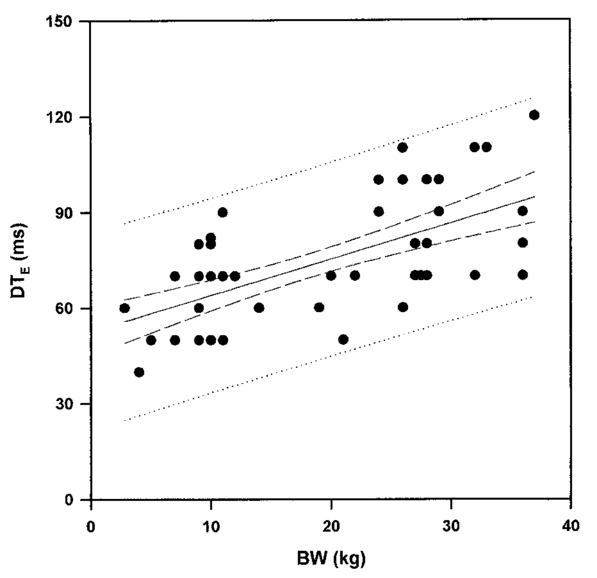

Figure 5—Scatter plot of DT_E versus body weight (BW). Equation for the regression line ($r = 0.63$; $P < 0.001$) is as follows: $DT_E = 52.452 + (1.134 \times BW)$. *See* Figure 2 for key.

Table 3—Results of multivariate forward stepwise regression analysis between independent factors (age, BW, and HR) and Doppler-derived variables of left ventricular diastolic function

Variables	r	R^2	ΔR^2	P
IVRT	NA	NA	NA	NA
Age	0.53	0.28	0.28	< 0.001
Peak A	NA	NA	NA	NA
HR	0.39	0.15	0.15	< 0.001
Age	0.51	0.26	0.11	< 0.01
E:A	NA	NA	NA	NA
Age	0.40	0.16	0.16	< 0.001
HR	0.51	0.26	0.10	< 0.05
DT_E	NA	NA	NA	NA
BW	0.63	0.39	0.39	< 0.001
Age	0.72	0.51	0.12	< 0.001
A duration	NA	NA	NA	NA
BW	0.61	0.37	0.37	< 0.001
Peak S	NA	NA	NA	NA
HR	0.36	0.13	0.13	< 0.01
Peak AR	NA	NA	NA	NA
Age	0.40	0.16	0.16	< 0.001
HR	0.46	0.21	0.05	< 0.001
S:D	NA	NA	NA	NA
BW	0.28	0.08	0.08	< 0.05
AR duration	NA	NA	NA	NA
BW	0.47	0.22	0.22	< 0.001

r = Correlation coefficient. R^2 = Partial correlation coefficient. ΔR^2 = Increase in R^2 attributable to the entered variable. NA = Not applicable.

velocity of the AR-wave. Sex and LVSF did not enter into the regression.

Discussion

To our knowledge, the influence of age, BW, HR, sex, and LVSF on diastolic function in clinically normal unsedated dogs has not been characterized. Earlier invasive studies in dogs have suggested that the aging heart has increased ventricular stiffness and delayed relaxation and, thus, altered diastolic function.[16,37,38] In addition, HR,[6,11,15,45] loading conditions,[7-10,17,18,20] and phase of respiration[11] can affect left ventricular diastolic function or Doppler-derived filling patterns in dogs. Findings of the study reported here for a large population of healthy dogs confirmed that age and HR significantly affect Doppler-derived variables of left ventricular diastolic function. Moreover, BW was an additional independent variable that influenced left ventricular filling patterns.

Normal age-associated changes of left ventricular diastolic function in human beings include myocardial remodeling with decreased myocardial compliance, elastic recoil, and ventricular diastolic suction, blunted myocardial responsiveness to β-adrenergic agents, and asynchronous regional function of the left ventricle that cause impaired relaxation and a shift from early to predominantly late diastolic filling.[19,21,27,29] Findings in our study revealed that there was a prolonged IVRT and DT_E, decreased E:A, and increased velocity of the AR-wave associated with increasing age, indicating a gradual decrease in the rate of left ventricular relaxation, increased myocardial stiffness, and enhanced late diastolic filling, which are in agreement with findings of invasive studies in dogs[16,18,37,38] and Doppler studies in cats[46] and human beings.[21-25,28-31,34] However, closer correlations between age and Doppler-derived indices, including pulmonary venous flow in particular, have been documented in human beings.[24,25,29] Potential reasons that age had less of an effect in the study reported here were the wide range of BW and HR with the consequence of a wide scatter of normal values, compared with normal values in people, and the relatively small number of older dogs included in our study.

Analysis of the findings in our study indicated that changes in transmitral and pulmonary venous flow patterns may be seen in older dogs, which should not be confused with diastolic filling abnormalities associated with primary cardiac disease. This distinction may not be easy, but it is important, because many animals with cardiac disease are old animals, diastolic abnormalities may precede detectable systolic dysfunction,[4,23] and abnormal Doppler-derived diastolic variables may yield prognostic information for dogs[c] and human beings with myocardial diasease.[47,48]

Young healthy dogs may have a short IVRT (commonly used as a measure of relaxation) and E:A > 2.0, although this pattern of flow also has been associated with restrictive filling in people with cardiac disease.[19,21,49] In young domestic animals,[37] children,[50] and athletes,[21] left ventricular elastic recoil is vigorous, and myocardial relaxation is swift. Therefore, most filling may be completed during early diastole with only a small contribution during atrial contraction. A significant age-related decrease of the E:A may be expected for animals ≥ 6 years old. However, the E:A had noticeable variation within the age groups, which may have been the result of hemodynamic differences among the dogs, technical factors that affected flow recordings,[34,41,51,52] or undetermined factors, making it difficult to interpret a single E:A value.[33] A reversal of the E:A (< 1.0), which is suggestive of a relaxation abnormality,[19,21,49] is rare in healthy dogs and was seen in only 7 of 92 (8%) dogs in our study. The lowest E:A was in a 15-year-old dog. There did not appear to be a distinct age above which the E:A was < 1.0, in contrast to human beings, in which one would expect to detect an E:A of < 1 in individuals > 60 years old.[19,25]

Patterns of pulmonary venous flow have been used to estimate left ventricular filling pressures, left ventricular stiffness, and left atrial function and to determine whether patterns of mitral inflow are abnormal.[11] In the study reported here, velocity of the pulmonary venous atrial reversed flow was increased in dogs ≥ 10 years old, compared with values for dogs < 2 years old, suggesting increased atrial systolic function or decreased left ventricular compliance with advanced age, similar to the situation in human beings.[30] However, peak velocity of the AR-wave was < 0.35 m/s in all dogs, which is an echocardiographic cutoff value commonly used in people to define a relevant increase in ventricular stiffness.[31] The A duration:AR duration, a specific variable used to assess left ventricular end-diastolic pressure in people,[21,53] was not affected by age, suggesting normal filling pressures or left ventricular compliance in these dogs. The fact that the A duration:AR duration was not affected by age also was reported in a study of 72 clinically normal people.[30] In our study, 2 of 92 (2%) dogs had an A duration:AR duration < 1.0, possibly indicating decreased left ventricular compliance. However, these 2 dogs were < 5 years old, and in both dogs, the difference between the A duration and the AR duration was small (1 and 13 milliseconds). A similar proportion of patients (3/72 [4%]) with an A duration:AR duration < 1.0 has been reported in healthy people.[30] In another study in human beings,[54] it was suggested that an A duration:AR duration < 1.0 may be more common in younger people. Specificity of the A duration:AR duration < 1.0 for use in the prediction of left ventricular end-diastolic pressure ≥ 15 or ≥ 20 mm Hg has been reported in people as 79%[55] and 85%,[53] respectively.

In the study reported here, we documented that BW is an important determinant for selected Doppler-derived variables of left ventricular filling. The DT_E as well as the duration of the A- and AR-waves were prolonged with increasing BW. Higher peak velocities of the mitral E-wave have been reported in dogs that weigh ≥ 19 kg, compared with values for dogs that weigh ≤ 10 kg,[d] but they were not found in this study. Conflicting results have been reported in healthy human beings. Some investigators did not find a significant relationship between body mass[56] or body surface area[23,25,28] and left ventricular filling, whereas others[26,32] reported that increased body surface area or body mass index may affect Doppler-derived left ventricular diastolic properties. However, potential explanations for these findings were not discussed. Association between BW or body surface area and variables for mitral inflow and pulmonary venous flow was not found in healthy cats.[46] The finding of the dependence of DT_E on BW is clinically important, because this variable is frequently used to obtain information on left ventricular compliance[9,18] as well as prognosis.[57,58,c] Reference values for DT_E in dogs do not mention BW,[4,12,18] yet the BW may vary widely in dogs with heart disease. Prolonged DT_E with increased BW may partially be explained by the correlation between BW and HR or BW and LVSF. Larger dogs had lower HR, which may have prolonged DT_E.[36] Systolic and diastolic function are closely related; therefore, decreased LVSF in larger dogs may, hypothetically, be accompanied by prolongation of DT_E. Mild effects of systolic function on variables of mitral inflow also have been reported in healthy people.[25] However, in other studies in human beings, a relationship between LVSF or LV ejection fraction and variables for left ventricular filling was not found.[24,28] Of less importance is the finding of the dependence of A duration and AR duration on BW, because neither of these variables is used as a single indicator of diastolic function. Because both variables changed in the same direction and to a comparable degree with changes in BW, the diagnostically important A duration:AR duration was not affected.

In the range of physiologic HR in our population of clinically normal dogs (54 to 186 beats/min), HR was found to be a determinant of Doppler-derived variables for left atrial and left ventricular diastolic filling, although the effect of HR was relatively low. With increasing HR, the IVRT decreased, peak velocities of the A-, AR-, and S-waves increased, and DT_E decreased. These findings indicate that, with a decrease of cycle length, early diastolic filling starts earlier and becomes briefer. As a consequence, active atrial contraction contributes more to diastolic filling to maintain stroke volume. Similar results were reported in studies of dogs[6,11,15,17] and healthy human beings.[22,24-27,35,36] Thus, when HR is not controlled in clinical and laboratory studies to assess diastolic function, influence of HR on these Doppler-derived variables must be considered. Peak velocities of the E- and D-waves were not affected by HR in the dogs of our report, similar to results for human beings.[24,32]

We did not detect any significant difference in left atrial and left ventricular Doppler-derived diastolic variables in clinically normal dogs between males and females, which is consistent with studies in human beings.[23,24,27,28] In contrast, higher values for IVRT, peak velocity of the E- or A-waves, DT_E, E:A, or A duration and AR duration have been found in women, compared with men, which may be related predominantly to differences in BW or body size,[22,25,26] and a separate Doppler assessment for female and male human beings has been recommended.[29]

The M-mode echocardiographic index of LVSF was not significantly associated with any Doppler-derived diastolic variable. Considering that the LVSF was within the reference range in all dogs, we can reasonably state that changes in diastolic flow pattern as a result of age, BW, and HR are not attributable to the coexistence of abnormalities in systolic function. Minor effects of LVSF on peak velocity of the E- or A-waves, E:A, DT_E, and atrial filling fraction have been found in 477 clinically normal people,[24,25] but in 143 other clinically normal people, LV ejection fraction did not have an effect on pulmonary venous flow.[28] However, because sympathetic stimulation improves diastolic function,[17,18,45] shortened IVRT and DT_E and increased E:A and S:D may be anticipated in excited dogs.

The study reported here did have limitations. We assumed that the dogs were healthy as determined on the basis of clinical data. However, some dogs may have had occult myocardial disease, especially those at increased risk as a result of advanced age. Classification of the dogs into 5 age groups was arbitrary; however, effects of the independent variables also were analyzed as continuous variables. Although only 19 dogs were ≥ 6 years old, we believe this is the largest study of pulmonary venous and left ventricular inflow velocities in older dogs. This study lacks concurrent Doppler-derived and direct hemodynamic measures, which would be important for corroborating abnormal diastolic filling patterns.[19] Doppler-derived indices are reflective of flow and are not synonymous with function.[23] We only recorded patterns of pulmonary venous flow from the pulmonary vein of the left caudal lung lobe, assuming that it would be representative of flow in all pulmonary veins. The study of left ventricular diastolic function is complex, and many factors can influence left atrial and left ventricular filling measured by Doppler echocardiography, including age, BW, HR, sex, and LVSF as well as loading conditions, phase of respiration, blood pressure, left ventricular mass, thickness of the ventricular wall, systolic function of the long axis of the left ventricle, ventricular interference, pericardial restraint, and numerous technical factors.[10,11,29,31,34,41]

The study reported here revealed that transmitral flow and pulmonary venous flow in clinically normal dogs are significantly influenced by age, which underlines the importance of reference values for various age groups. Body weight and HR are additional important determinants of left atrial and left ventricular filling, whereas sex and LVSF did not affect Doppler-derived diastolic variables in clinically normal dogs. Thus, age, BW, and HR should be taken into account when interpreting left ventricular filling abnormalities in apparently healthy dogs. Age, BW, and HR explained ≤ 51% of the variation of the Doppler-derived variables. This suggests that there are other physiologic relationships that should be investigated. Additional studies are needed to investigate the extent to which the factors described in this study influence Doppler-derived diastolic variables of left ventricular filling in dogs with various heart diseases.

[a]Sequoia 512, Acuson Corp, Mountain View, Calif.
[b]Sigma Stat, version 2.0 for Windows 95, Jandel Scientific, San Rafael, Calif.
[c]Borgarelli M, Tarducci A, Santilli RA, et al. Echo prognostic indicators for DCM (abstr), in *Proceedings*. 18th Annu Meet Vet Med Forum, 2000;78–80.
[d]Gaber C. Normal pulsed Doppler velocities in adult dogs (abstr), in *Proceedings*. 5th Annu Meet Vet Med Forum, 1987;923.

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