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Original article

The influence of age, gender and weight on transthoracic echocardiographic evaluation of transmitral and left ventricular outflow tract diastolic parameters in healthy dogs

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Abstract

The aim of this study was to obtain reference values for diastolic cardiac function parameters in healthy dogs and to ascertain if significant differences exist between dogs of various age, weight and sex. The study was performed on 82 healthy dogs of different age and breed. Eleven parameters were analyzed: peak velocity during early diastolic filling, acceleration time of early diastolic filling, deceleration time of early diastolic filling, total time of early diastolic filling, peak velocity during late diastolic filling, acceleration time of late diastolic filling, deceleration time of late diastolic filling, total time of late diastolic filling, total time of early and late diastolic filling, ratio of peak velocities during early and late diastolic filling, isovolumetric relaxation time. The Doppler measurements used for general assessment of diastolic function in healthy dogs were significantly influenced by body weight, heart rate and age. No significant differences were found between males and females. This study described the value of non-invasive echocardiographic assessment of diastolic function in healthy dogs.

Key words: diastolic function, myocardial, transthoracic echocardiography, dog

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Introduction

The development of Doppler and tissue Doppler echocardiography has allowed for a more precise evaluation of myocardial function discerning between systolic and diastolic abnormalities in humans and animals. Recent epidemiological studies in people have revealed that around 30-50% of patients with heart failure have adequate systolic function (Gutierrez and Blanchard 2004). This was a stimulus for clinical research of diastolic myocardial function in human and veterinary medicine. Clinical trials over the last several years in human medicine have established standard criteria for diagnosis of diastolic heart failure. Veterinary clinical research on diastolic dysfunction has also been instigated and some publications are available in worldwide literature dealing with diastolic myocardial function or dysfunction in dogs (Appleton 1991, Chiang et al. 1998, Schober and Fuentes 1998, 2001, 2002, Constable et al. 1999), part of which includes invasive methodology (Blaustein et al. 1981, Refsum et al. 1981, Takaki et al. 1996, Appleton et al. 1998).

Diastolic dysfunction in dogs can be recognized as an isolated state, most likely resulting from physiological aging. It may also be a result of various heart conditions causing structural and geometric heart changes (cardiomyopathies or advanced chronic mitral valve disease) or generalised diseases including non-cardiac pathologies (i.e. hypertension secondary to chronic renal failure, obesity, or lung disease). Lone diastolic dysfunction has not been associated with congestive heart failure in dogs, rather it is a coexisting change that might worsen progression of the primary heart disease.

Recent years have shown a shift in the type of publications on diastolic function assessment to tissue Doppler techniques (Teshima et al. 2005, Kibar 2009, Wess et al. 2010, Killich et al. 2011, Kim and Park 2014), however, this echocardiographic modality is still not readily available for the basic cardiac evaluation in most general practices. This study looked at basic echocardiographic diastolic parameters of left ventricular inflow and outflow and the influence of age, gender and body weight on these parameters.

Materials and Methods

Healthy dogs examined at the Faculty of Veterinary Medicine, Warsaw University of Life Sciences, were included in the study. National and institutional guidelines regarding the use of animals in clinical research according to the Polish legal act of January 21st, 2005 (The law on Animal Experiments of January 21st, 2005) were adhered to. All owners consented to the inclusion of their pet's data in the study, The study included 82 dogs with no clinical signs of heart disease or abnormalities noted on clinical and laboratory examinations including an electrocardiogram, chest radiography, echocardiography and morphological and biochemical blood work. Inclusion criteria included a normal clinical examination without audible heart murmurs or rhythm abnormalities as well as a normal general blood analysis, as well as normal electrocardiographic (ECG) and echocardiographic examinations. Exclusion criteria included any signs of generalized disease or heart condition recognized during the clinical examination. Dogs without signs of disease in the clinical exam were also excluded if blood analysis showed abnormalities, the ECG exam revealed an arrhythmia or echocardiography showed heart disease not heard with a stethoscope.

Echocardiographic examinations were performed using an SC 300 PANDION ultrasound (Pro-Medica) according to standard echocardiographic procedures. Dogs were placed in lateral recumbency for a full echocardiographic examination, which was the basis for ruling out heart disease. Assessment of diastolic function was carried in left lateral recumbency using pulsed wave or continuous wave Doppler (Cohen et al. 1996, Boon 1998, Paulus et al 1998, Yamada et al. 2002, Zile and Brutsaert 2002, Cheitlin et al. 2003). Pulsed wave Doppler, with the gate placed at the tip of the anterior mitral valve leaflet in its' opened position, was used in the left caudal four-chamber view to measure the peak velocity during early diastolic filling in m/s – (E wave velocity), acceleration time of early diastolic filling in ms (E-AT), deceleration time of early diastolic filling in ms (E-DT), total time of early diastolic filling in ms (E time), peak velocity during late diastolic filling m/s (A wave velocity), acceleration time of late diastolic filling in ms (A-AT), deceleration time of late diastolic filling in ms (A-DT), total time of late diastolic filling in ms (A time), total time of early and late diastolic filling in ms (E+A time), and the ratio of peak velocities during early and late diastolic filling (E/A ratio). Continuous wave Doppler was used to assess the isovolumetric relaxation time (IVRT) in ms in the left caudal five-chamber view with the Doppler line placed near the left anterior leaflet tip so that both ventricular inflow and outflow velocities could be measured. The IVRT was measured from the time of aortic valve closure and cessation of LV outflow to the time of mitral valve opening and the onset of LV inflow.

Numerical values were presented as the arithmetic mean with standard deviation (SD), as the median with interquartile range (IQR), and as the range.

There were four independent variables (predictors)

Table 1. Echocardiographic measurements in 82 dogs.

ECHO measurements	Arithmetic mean (SD)	Median (IQR)	Range	Number of outliers
E/A ratio	1.36 (0.23)	1.32 (1.19-1.51)	0.84-1.91	0
E wave	0.66 (0.12)	0.64 (0.57-0.74)	0.38-0.96	0
E-AT	74.65 (20.39)	74.17 (59.33-86.67)	18.33-143.33	0
E-DT	76.64 (21.22)	74.67 (61.33-89.67)	23.67-144.33	0
E time	151.96 (33.16)	149.17 (128-180.33)	94.67-243.33	0
A wave	0.49 (0.1)	0.48 (0.41-0.55)	0.3-0.76	0
A-AT	53.93 (14.58)	53.67 (43.67-61.33)	22.26-130.67	1
A-DT	51.5 (17.83)	48.17 (39.67-56.33)	28.33-148.67	1
A time	112.48 (62.74)	102.5 (88.33-113)	70.33-618	3
A+E time	264.43 (82.93)	252.17 (218-287.67)	170.33-820	1a
IVRT	60.5 (15.62)	58.17 (50-71.67)	23-102.33	0

a A/E time recalculated using modified A time in 2 other dogs

– three numerical: age (in years), body weight (BW, in kg) and heart rate (HR, in bpm), and one categorical: sex. Age, BW and HR were compared between males and females with the Mann-Whitney U test. Correlation between age, BW and HR was assessed using the Pearson's linear correlation coefficient (r). There were 11 numerical dependent variables, which were echocardiographic measurements of transmitral and left ventricular outflow tract diastolic function.

The relationship between 4 independent variables and 11 dependent variables was analyzed using general linear model (GLM) including one interaction, between age and sex.

Before running the model, assumptions were tested separately for independent and dependent variables. For independent variables, normality of residue distribution was tested using normality plots, correlation between residues using Durbin-Watson statistics (considered as uncorrelated if the statistic was between 1 and 3), and multicollinearity using variance inflation factor (VIF), given by the formula $1/(1-R^2)$ where R^2 was the coefficient of determination showing what proportion of variability of a variable was explained by other variables (multicolinearity was found when VIF >10). For dependent variables normality of variable distribution was tested using normality plots, presence of univariate outliers in each group using Box plots with Tukey's fences set as 3×IQR below the lower quartile or above the upper quartile (so identified extreme values were replaced by the next highest observation or recalculated if possible in derived variables), homoscedasticity using the Levene's test, and multicollinearity with VIF.

Multivariate omnibus test (Wilk's lambda) was considered significant if p-value was below significance level (α) of 0.05. Those predictors which proved significant in multivariate omnibus test were included in univariate post-hoc analysis, in which the Holm-Bonferroni correction was applied (corrected p-value = crude p-value × the number from range 11-1 in subsequent comparisons).

Statistical analysis was performed in Statistica 13.3 (TIBCO Software)and IBM SPSS Statistics 24.

Results

The study comprised 82 dogs – 46 females and 36 males of various breeds, including 1 each of Airedale Terrier, Alaskan Malamute, Bearded Collie, Belgian Shepherd, Border Collie, Border Terrier, Borzoj, Bullmastiff, Bullterrier, Bouvier des Floundres, Dalmatian, Giant Schnaucer, Howavart, Maltese, Miniature Pincher, Miniature Schnaucer, Newfoundland, Pekinese, Pug, Saint Bernard and Weimaraner, 2 each of American Staffordshire Terrier, Cairn Terrier, Doberman Pintscher, Fox Terrier, French Bulldog, Labrador Retriever and Polish Lowland Sheepdog, 3 each of German Shepherd and Welsh Cardigan Corgi, 5 each of Boxer and Cane Corso, 6 each of Dachshund and Golden Retriever, 9 mixed breed dogs, and 10 Yorkshire Terriers. Their age ranged from 4 months to 14 years with the median of 2 years and IQR from 1 to 4 years and did not differ between sexes (p=0.460). Their body weight (BW) ranged from 1 to 61 kg with the median of 17 kg and IQR from 7 to 33 kg and did not differ between sexes (p=0.733). HR ranged from 60 to 136 with the median of 91 bpm and IQR from 76 to 112 bpm and did not differ between sexes (p=0.786). There was no linear correlation between age and BW (r=0.15, p=0.185), age and HR (r=0.02, p=0.847) or BW and HR (r=-0.08, p=0.485).

Table 2. Results of univariate GLM analysis.

ECHO measurements	Regression coefficient (SE)	95% CI	t-statistics	p-value
	BW			
E-AT	0.85 (0.12)	0.60 to 1.10	6.79	<0.001*
E-DT	0.73 (0.14)	0.45 to 1.01	5.23	<0.001*
E time	1.58 (0.19)	1.20 to 1.96	8.30	<0.001*
A-AT	0.45 (0.08)	0.28 to 0.61	5.35	<0.001*
A-DT	0.37 (0.10)	0.17 to 0.57	3.60	0.005*
A time	0.77 (0.16)	0.44 to 1.09	4.73	<0.001*
A+E time	2.35 (0.32)	1.71 to 2.99	7.34	<0.001*
	HR			
IVRT	-0.24 (0.08)	-0.39 to -0.09	-3.21	0.022*
A-DT	-0.20 (0.07)	-0.34 to -0.06	-2.88	0.050*
	Age × Sex			
A wave	0.29 (0.01)	0.01 to 0.05	3.53	0.011*

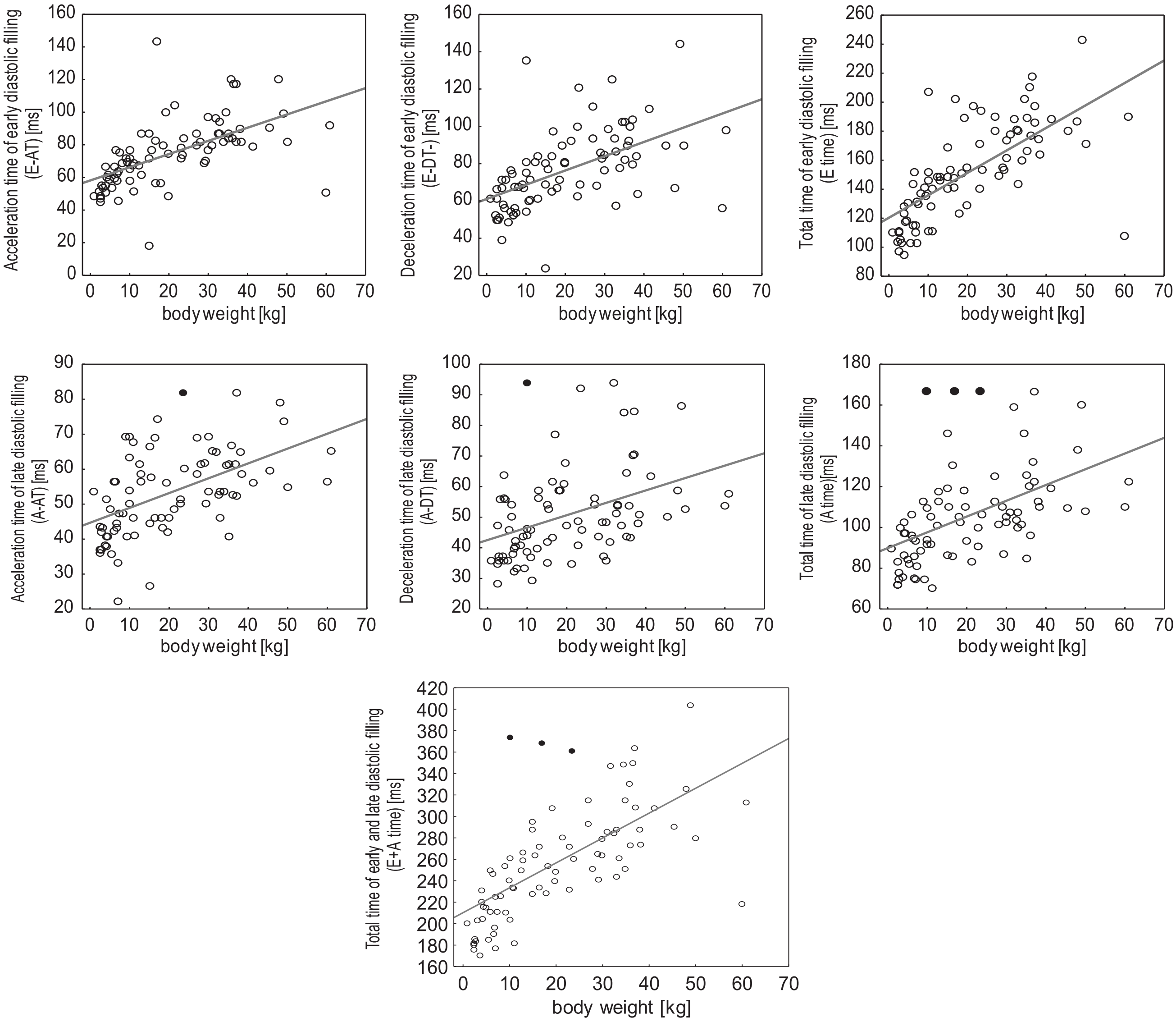

Fig 1. Echocardiographic measurements significantly linked with body weight.

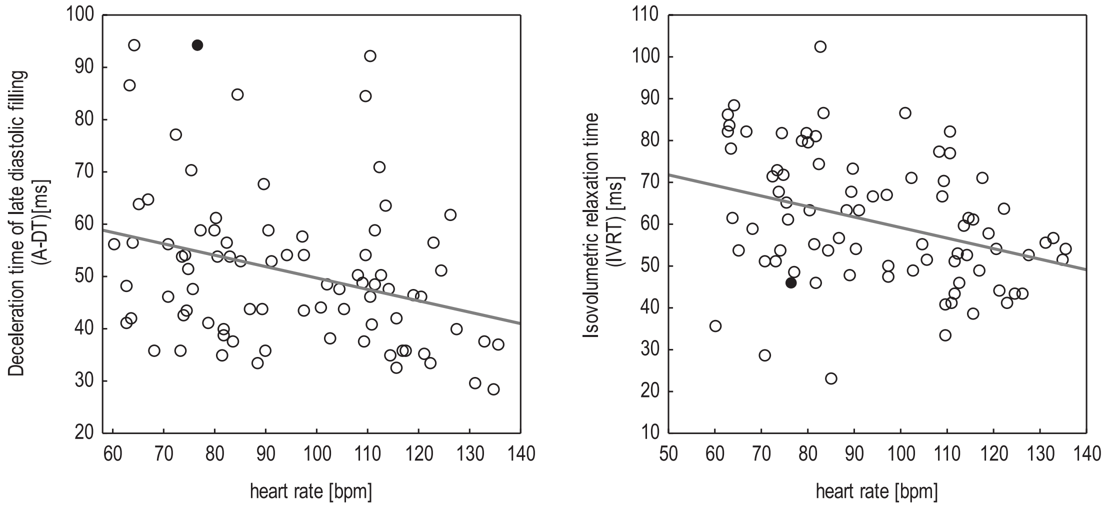

Fig 2. Echocardiographic measurements significantly linked with heart rate.

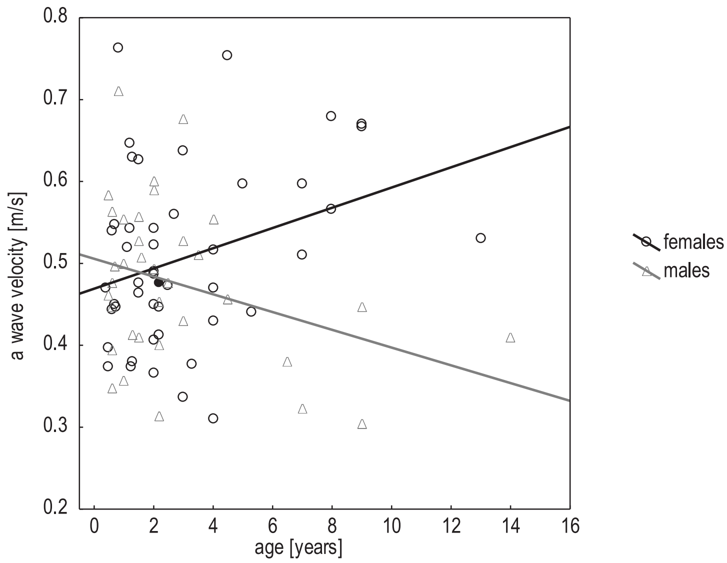

Fig 3. Echocardiographic measurements significantly linked with sex.

Descriptive statistics of echocardiographic measurements (with extreme values included) are presented in Table 1.

Six extreme values were identified in 3 dogs (A-AT and A time in the first, A time and A+E time in the second one, and A-DT and A time in the third one), and replaced with the next highest value (A time and A-DT) or recalculated (A+E time). In 2 dogs A+E time had to be recalculated as A time changed.

Three predictors proved significantly linked with echocardiographic measurements: BW (Wilk's $\lambda = 0.405$, $F_{11,66}=8.80$, $p<0.001$, partial eta = 0.595), HR (Wilk's $\lambda = 0.660$, $F_{11,66}=3.09$, $p=0.002$, partial eta = 0.340), and age (Wilk's $\lambda = 0.711$, $F_{11,66}=2.44$, $p=0.013$, partial eta = 0.289). There was no significant relationship between sex and echocardiographic measurements (Wilk's $\lambda = 0.831$, $F_{11,66}=1.22$, $p=0.292$, partial eta = 0.169). Interaction between sex and age was also insignificant (Wilk's $\lambda = 0.781$, $F_{11,66}=1.69$, $p=0.096$, partial eta = 0.219), however was included in univariate analyses as one component (age) was significantly linked with echocardiographic measurements.

Predictors turned out to be linked with 9 echocardiographic measurements in univariate analysis (Table 2): 7 echocardiographic measurements (E-AT, E-DT, E time, A-AT, A-DT, A time, A+E time) increased with BW (Fig. 1), 2 echocardiographic measurements (IVRT, A-DT) decreased with HR (Fig. 2), and A wave increased with age in females (p=0.030) whereas decreased with age in males (p=0.046) (Fig. 3).

Discussion

Diastolic function has been intensively studied in human medicine. Changes, such as increased LV afterload or hypertrophy or slowing of HR secondary to exclusion of cells from the sinus node and myocardial fibrosis (Cheitlin 2003), lead to a progressive diastolic dysfunction (Kangro et al. 1996, Little et al. 1998). Diastolic echocardiographic changes include a decrease in the E wave velocity and gradual lengthening of the IVRT (Deswal 2005, Prasad et al. 2005). The decrease of the E wave velocity leads to a delay in the time needed for equalization of pressures between the left ventricle and atrium, which in turn causes elongation of the E-DT. Because the volume of blood flow during early diastolic filling decreases, atrial contraction becomes more important in order to ensure a larger volume of blood entering the ventricles during diastole. This is seen as an increase in the A wave velocity and a distinct decline in the E/A ratio values (Cohen 1996**,** Prasad 2005).

Similar changes related to the aging process and diastolic function are found in animals (Schober and Fuentes 2001, Munagala et al. 2005). Our study did not show a decline of a majority of diastolic parameters with age. The most likely reason for this is a small number of dogs over 5 years of age. This is in support of data obtained by Schober and Fuentes (2001) showing the total time of late diastolic filling (A time) in dogs remained unchanged in dogs up to 10 years of age. The only significant change noted in this study was an increase in A wave velocity seen in older females, but not in males (values in males declined with age).

In this study body weight proved to significantly influence the largest number of echocardiographic parameters. With an increase in body weight there was an increase in the times of E-AT, E-DT, E wave, A-AT, A-DT, A wave, E+A wave. This is most likely the result of a generally slower heart rate in heavier dogs (Hezzel et al 2013,).

The IVRT in healthy dogs was not significantly influenced by age in this study, but rather by HR. In people the value of IVRT lengthens with age (Cohen et al. 1996, Witkowska 2002). Another study performed in healthy dogs also did not show significant differences in IVRT except in the oldest group of dogs, which had the highest IVRT value (Schober and Fuentes 2001). It is possible that the IVRT physiologically lengthens as a result of aging after the 8^{th}–10^{th} year of life, yet this would have to be analyzed more thoroughly in a larger group of older, healthy dogs. The IVRT time in our study clearly shortens with a faster HR which is in line with other publications in people (Witkowska 2002) and dogs (Pereira 2009).

No significant differences were noted in any of the diastolic parameters between male and female dogs. The significant interaction between gender and age was seen with the values of the A wave velocity, which behaved differently in males and females with increased age. One study in humans did show a gender influence in healthy 50-year-old individuals, where the values of E wave velocity and E/A ratio were higher in women than in men (Kangro et al. 1996). However, in this study the E/A radio was not affected statistically and there was only 12 dogs over 5 years of age, making the authors believe that a larger population of healthy older dogs must be studies to make a more sound conclusion.

Routine non-invasive examinations of diastolic parameters have been implemented in human medicine (Naqvi 2003) enabling recognition of a possible dysfunction in the elderly that could lead to other cardiac problems (Pedersen et al. 2005).

This study shows that body weight and heart rate in healthy dogs influence some diastolic parameters obtained non-invasively with Doppler echocardiography. The echocardiographic data presented in this study for the 11 Doppler parameters of diastolic function can be used as a reference range for dogs (Table 2), however data for geriatric dogs should be collected in a larger study.

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References

Appleton CP (**1991**) Influence of incremental changes in heart rate on mitral flow velocity: assessment in lightly sedated conscious dogs. J Am Coll Cardiol 17: 227-236.

Appleton, CP, Hatle LK, Popp RL (**198**) Relation of transmitral flow velocity patterns to left ventricular diastolic function: new insight from a combined hemodynamic and Doppler echocardiographic study. J Am Coll Cardiol 12: 426-440.

Blaustein AS, Gaasch WH, Adam D, Levine HJ (**1981**) Myocardial relaxation. V. Postextrasystolic contraction-relaxation in the intact dog heart. Circulation 64**:** 345-351.

Boon JA (**1998**) Evaluation of Size, Function, and Hemodynamics. In: Boon JA (ed) Manual of Veterinary Echocardiography, Williams and Wilkins, Philadelphia, pp 151-260.

Cheitlin MD (**2003**) Cardiovascular physiology – changes with aging. Am J Geriatr Cardiol 12**:** 9-13.

Cheitlin MD, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, Davis JL, Douglas PS, Faxon DP, Gillam LD, Kimball TR, Kussmaul WG, Pearlman AS, Philbrick JT, Rakowski H, Thys DM, Antman EM, Smith SC Jr, Alpert JS, Gregoratos G, Anderson JL, Hiratzka LF, Hunt SA, Fuster V, Jacobs AK, Gibbons RJ, Russell RO; American College of Cardiology, American Heart Association, American Society of Echocardiography (**2003**) ACC/AHA/ASE 2003 Guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). Circulation 108: 1146-1162.

Chiang C, Hagio M, Yoshida H, Okano S (**1998**) Pulmonary Venous flow in normal dogs recorded by transthoracic echocardiography: techniques, anatomic validations and flow characteristics. J Vet Med Sci 60: 333-339.

Cohen GI, Pietrolungo JF, Thomas JD, Klein AL (**1996**) A practical guide to assessment of ventricular diastolic function using Doppler echocardiography. J Am Coll Cardiol 27: 1753-1760.

Constable P, Muir P 3rd, Sisson D (Clinical Assessment of left ventricular relaxation. J) Clinical Assessment of left ventricular relaxation. J Vet Intern Med 13: 5-13.

Deswal A (**2005**) Diastolic dysfunction and diastolic heart failure: mechanisms and epidemiology. Curr Cardiol Rep 7**:** 178-183.

Gutierrez C, Blanchard DG (**2004**) Diastolic heart failure: challenges of diagnosis and treatment. Am Fam Physician 69: 2609-2616.

Hezzel MJ, Dennis SG, Humm K, Agee L, Boswood A. (**2013**) Relationships between heart rate and age, bodyweight and breed in 10,849 dogs. J Small Anim Pract 54: 318-324.

Kangro T, Henriksen E, Jonason T, Nilsson H, Ringqvist I (**1996**) Factors of importance to Doppler indices of left ventricular filling in 50-year-old healthy subjects. Eur Heart J 17: 612-618.

Kibar M, Markovic M, Kolm US, Thalhammer J (**2009**) Determination of diastolic dysfunction by conventional and Doppler tissue echocardiography in dogs. Turk J Vet Anim Sci 33: 501-507.

Killich M, Harmtann K, Wess G (**2011**) Measuring myocardial velocity using tissue Doppler imaging in healthy dogs. Tierarztl Prax. Ausg K, Kleintiere Heimtiere 39: 69-78.

Kim JH, Park HM (**2014**) Usefulness of Conventional and Tissue Doppler Echocardiography to Predict Congestive Heart Failure in Dogs with Myxomatous Mitral Valve Disease. J Vet Inter Med 29: 132-140.

Little WC, Warner JG Jr, Rankin KM, Kitzman DW, Cheng CP (**1998**) Evaluation of left ventricular diastolic function from the pattern of left ventricular filling. Clin Cardiol 21: 5-9.

Munagala VK, Hart CY, Burnett JC Jr, Meyer DM, Redfield MM (2005) Ventricular structure and function in aged dogs with renal hypertension: a model of experimental diastolic heart failure. Circulation 111: 1128-1135.

Naqvi TZ (**2003**) Diastolic Function assessment incorporating new techniques in Doppler echocardiography. Rev Cardiovasc Med 4: 81-99.

Paulus WJ, Brutsaert DL, Gillebert TC, Rademakers FE, Stanislas U, Moreira AL, Hess OM, Jiang ZH, Kaufmann P, Mandinov L, Matter CM, Marino P, Gibson DG, Henein MY, Manolas J, Smiseth OA, Stugaard M, Hatle L, Spirito P, Betocchi S, Villari B, Goetzsche O, Shah AM, . (**1998**) How to diagnose diastolic heart failure European Study Group on Diastolic Heart Failure. Eur Heart J 19: 990-1003.

Pedersen F, Raymond I, Mehlsen J, Atar D, Hilderbrandt PR (**2005**) Prevalence of diastolic dysfunction as a possible cause of dyspnea in the elderly. Am J Med 118: 25-31.

Pereira GG, Petrus LC, Santos AL, Yamaki FL, Larsson MH (**2009**) Evaluation of left ventricular diastolic echocardiographic parameters in healthy dogs by pulsed-wave Doppler. Pesq Vet Bras 29: 291-294.

Prasad A, Okazaki K, Zadeh AA, Dijk E, Fu Q, Thomas JD, Levine BD (**2005**) Abnormalities of Doppler measures of diastolic function in the healthy elderly are not related to alterations of left atrial pressure. Circulation 111: 1499-1503.

Refsum H, Junemann M, Lipton MJ, Skioldebrand C, Carlsson E, Tyberg JV (**1981**) Ventricular diastolic pressure-volume relations and the pericardium. Effects of changes in blood volume and pericardial effusion in dogs. Circulation 64: 997-1004.

Schober K, Fuentes VL (**1998**) Doppler echocardiographic assessment of left ventricular diastolic function in dogs. Tierarztl Prax Ausg K Klientiere Heimtiere 26: 13-20.

Schober KE, Fuentes VL (**2001**) Effects of age, body weight, and heart rate on transmitral and pulmonary venous flow in clinically normal dogs. Am J Vet Res 62: 1447-1454.

Schober KE, Fuentes VL (**2002**) Doppler echocardiographic assessment of left ventricular diastolic function in 74 boxer dogs with aortic stenosis. J Vet Cardiol 4: 7-16.

Takaki A, Katayama K, Sakai H, Tanaka N, Matsuzaki M (**1996**) Assessment of Pulmonary venous and transmitral flow in closed-chest dogs under various loading conditions by transesophageal Doppler echocardiography. Jpn Circ J 60: 115- 123.

Teshima K, Asano K, Sasaki Y, Kato Y, Kutara K, Edamura K, Hasegawa A, Tanaka S (**2005**) Assessment of Left Ventricular Function Using Pulsed Tissue Doppler Imaging in Healthy Dogs and Dogs with Spontaneous Mitral Regurgitation. J Vet Med Sci 67: 1207-1215.

Wess G, Killich M, Hartmann K (**2010**) Comparison of Pulsed Wave and Color Doppler Myocardial Velocity Imaging in Healthy Dogs. J Vet Inter Med 24: 360-366.

Witkowska M (**2002**) Diastolic function of the left ventricle in the elderly. In: Głębocka L (ed) Diastolic dysfunction of the heart (Polish: Zaburzenia czynności rozkurczowej serca), Wydawnictwo Lekarskie PZWL, Warsaw, pp 162-166.

Yamada H, Goh PP, Sun JP, Odabashian J, Garcia MJ, Thomas JD, Klein AL (**2002**) Prevalence of left ventricular diastolic dysfunction by Doppler echocardiography: clinical application of the Canadian consensus guidelines. J Am Soc Echocardiogr 15: 1238-1244.

Zile MR, Brutsaert DL (**2002**) New concepts in diastolic dysfunction and diastolic heart failure: Part I, diagnosis, prognosis, and measurements of diastolic function. Circulation 105: 1287-1293.