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# Meta-analysis of normal canine echocardiographic dimensional data using ratio indices

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## KEYWORDS

Indexing;  
Echocardiography;  
Measurement;  
Breed;  
Age

**Abstract** *Objectives:* To investigate the dependence of echocardiographic ratio indices (ERIs) on age, body weight (BW) and breed/study group using individually contributed and published summarized data in dogs.

*Background:* ERIs allow for narrow prediction intervals of M-mode echocardiographic measurements in generic adult dogs. Breed and age-specific differences have not been examined systematically using ERI methods.

*Animals, materials and methods:* Individual M-mode measurements were contributed by 15 published investigators from 661 dogs, allowing direct calculation of ERIs and summary statistics for each of these breed/study groups. M-mode ERI summary statistics were estimated from published summaries of 22 additional groups that included 527 adult and 36 growing dogs. Individual two-dimensional (2DE) left atrial (LA) and aortic root (Ao) measurements were contributed from 36 dogs. ERIs were analyzed for dependence on BW, breed/study group and age.

*Results:* The majority of variation among ERIs was due to differences in the breed or study technique with comparatively little dependence on BW. Age dependence of ERIs was seen in the early growth phases of young dogs, but expected values for each ERI became static long before maturity, roughly at 10–12 weeks of age. ERIs derived from individual 2DE LA and Ao measurements showed no significant dependence on BW.

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**Conclusions:** ERIs are well normalized for body size and may be useful for clinical evaluation of individuals, prediction of expected M-mode and 2DE cardiac dimensions, and investigation of age or breed-specific cardiac shape changes.  
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Interpretation of the echocardiogram relies on both qualitative and quantitative assessment of cardiac structures as seen on two-dimensional (2DE) and M-mode evaluation. Quantitative evaluation of 2DE or M-mode measurements for any given individual is subject to sources of variability inherent within the echocardiographic examination. Logically, sources of observed variation may arise from operator techniques,<sup>1</sup> as well as true quantitative differences between normal animals that may be affected by age,<sup>2</sup> genetics/breed,<sup>3</sup> body size, level of training (physiological hypertrophy),<sup>4</sup> or determinants of cardiac performance (heart rate, preload, afterload, contractility and atrial or ventricular chamber synergy).<sup>5</sup> Indexing methods may be employed to normalize for one or more sources of variation, and thus help determine whether a quantitative measurement is appropriate for an individual.

Most of the echocardiographic ratio indices (ERIs) described here result from the division of linear M-mode or 2DE measurements by a weight-based aorta ( $Ao_w$ ), a characteristic length equivalent to  $0.795(BW)^{1/3}$  as determined from 53 dogs of varying body size and breed.<sup>6</sup> It should be noted that Doberman pinschers and Boxer dogs were excluded from this original study due to overrepresentation in the initial sample population and concern that they may be atypical as compared with other dogs. Brown et al.<sup>6</sup> demonstrated little or no correlation of linear M-mode ERIs with body weight (BW). The current study was done to further investigate the dependence of ERIs on age, BW and breed/study groups using individually contributed and published summarized data from different sources.

In this report, normal canine ERI summary statistics are calculated directly from individually contributed data or estimated from published M-mode summary statistics for a wide range of body sizes and breeds. Tabulated ERIs are then used to examine unique shape characteristics between dogs of varying breed, size and age. To the authors' knowledge this is the first descriptive metastudy using the ERI method to summarize much of the existing available data on normal dogs.

## Animals, materials and methods

**Table 1** defines the characteristics of the study population as well as M-mode measurements,

nomenclature and ERI calculations. Data were obtained from publications available to the authors that included a minimum of 10 individuals. Echocardiographic measurement techniques varied somewhat between investigators; details may be found in the original publications.

Individualized data from raw measurements supplied by the investigators were available for 15 breed/study groups ( $n = 625$ ) while summarized data were compiled from 20 additional breed/study groups ( $n = 527$ ).<sup>2-4,6-26</sup> Summarized data were collected from recurrently referenced or known publications of echocardiographic data with additional studies included from indexed literature searches (PubMed) using keywords such as "dog", "echocardiography", and "reference". A total of 1152 clinically normal adult dogs, ranging in size from 1.4 to 97.7 kg, are represented (**Table 2**). Twenty two breed-specific and six groups of mixed or unspecified breed were included. Some measurements were not available for every group.

Summarized data on growing dogs were available for 16 English Pointer<sup>2</sup> and 20 Spanish Mastiff dogs.<sup>24</sup> Body weight and standard M-mode measurements were included for both groups. English Pointers were measured at 1, 2, 4 and 8 weeks of age, and 3, 6, 9 and 12 months of age, with all measurements done for each of the 16 dogs at each time period. Spanish Mastiffs were measured monthly from 1 month to 1 year, and then at 2 years. The number of dogs measured at each age varied from 10 to 20.

Individualized 2DE left atrial (LA) and aortic root (Ao) measurements from 36 healthy adult dogs were supplied by Rishniw and Erb<sup>27</sup> (**Fig. 1**).

When individual measurements were available, ERIs were tested for normality within each breed/study group using the Kolmogorov–Smirnov test

**Table 1a** Study population characteristics<sup>2-4,6-26</sup>

Data source	Adult dogs	Growing dogs	2D LA and Ao	Total
Individualized	625		36	661
Summarized	527	36		563
Total	1152	36	36	1224

Individualized data were gathered from raw echocardiographic measurements contributed by investigators. Summarized data were estimated from published statistics. All dogs were clinically healthy. LA, left atrial diameter; AO, aortic diameter.

**Table 1b** M-mode and 2DE echocardiographic ratio indices

Weight-based calculation	Description
$wAo = Ao_m / Ao_w$	Index of aortic root dimension, M-mode
$wIVSd = IVSd / Ao_w$	Index of interventricular septal thickness, diastole, M-mode
$wLVIDd = LVIDd / Ao_w$	Index of left ventricular internal dimension, diastole, M-mode
$wLVWs = LVWs / Ao_w$	Index of left ventricular wall thickness, diastole, M-mode
$wIVSs = IVSs / Ao_w$	Index of interventricular septal thickness, systole, M-mode
$wLVIDs = LVIDs / Ao_w$	Index of left ventricular internal dimension, systole, M-mode
$wLVWs = LVWs / Ao_w$	Index of left ventricular wall thickness, systole, M-mode
$wLA = LA / Ao_w$	Index of left atrial dimension, M-mode
$wSaxLAD = SaxLAD / Ao_w$	Index of short axis LA diameter, 2DE
$wSaxAoD = SaxAoD / Ao_w$	Index of short axis aortic root diameter, 2DE
$wLaxLAD = LaxLAD / Ao_w$	Index of long axis LA diameter, 2DE
$wSaxLAC = SaxLAC / Ao_w$	Index of short axis LA circumference, 2DE
$wSaxLAA = SaxLAA / (\pi(Ao_w/2)^2)$	Index of short axis LA area, 2DE
$wSaxAoC = SaxAoC / Ao_w$	Index of short axis aortic root circumference, 2DE
$wSaxAoA = SaxAoA / (\pi((Ao_w/2)^2))$	Index of short axis aortic area, 2DE

$Ao_w$ , weight-based aortic root dimension calculated as  $0.795(BW)^{1/3}$ , where BW is the body weight (kg). Linear weight-based indices are calculated by dividing the corresponding echocardiographic measurement by  $Ao_w$ .

or, for sample sizes  $\leq 50$ , the Shapiro–Wilk test. The Kruskal–Wallis test was used to compare breed-specific ERI means between these groups due to non-normally distributed data (Table 2). ERI means from multiple groups supplied by the same investigator were also compared using the Kruskal–Wallis test. Summary statistics for each breed/study group (mean  $\pm$  standard deviation) were computed directly from individual ERIs.

It was necessary to estimate ERI means and standard deviations ( $\overline{ERI}_{est}$ ,  $\sigma_{est}$ ) from published or estimated summary statistics of raw echocardiographic data and body weight ( $\overline{Y}$ ,  $\sigma_Y$ ,  $\overline{BW}$ ) when individualized echocardiographic measurements were not available. If the standard deviation of the echocardiographic dimension was not available, it was estimated from the published range and sample size.<sup>28,29</sup> If the mean was not

available, then the median was substituted as a measure of central tendency. We chose the following estimation formulas:  $\overline{ERI}_{est} = \overline{Y} / (k\overline{BW}^{1/3})$  and  $\sigma_{est} = \sigma_Y / (k\overline{BW}^{1/3})$ , where  $k = 0.795$  in the dog.<sup>6</sup> The accuracy of these estimates was investigated by computing values for  $\overline{ERI}$  and  $\sigma_{ERI}$  directly, for breed/study groups where individualized data was available, and comparing to the estimate values as a percent variation.

Weighted least squares (WLS) linear regressions were performed on the means of each adult ERI, treating each study group as a single data point with mean BW set as the independent predictor variable. The weighting factor was set to the reciprocal of the standard error ( $SE = \sigma_{ERI} / \sqrt{n}$ ). We define a global mean for each ERI ( $\overline{ERI}_G$ ) as the weighted average of the group means; consequently  $\overline{ERI} / \overline{ERI}_G$  characterizes the deviation of each group ERI from the global mean. The coefficient of variation of the means ( $CV_{\overline{ERI}} = \sigma_{\overline{ERI}} / \overline{ERI}_G$ ) is reported as a standardized measure of variation of each  $\overline{ERI}$  between breed/study groups while individual group coefficient of variation ( $CV_{ERI} = \sigma_{ERI} / \overline{ERI}$ ) is a standardized measure of the variation of ERIs within each group. Cook's distance was evaluated to determine whether there were outliers in the regression procedure, i.e. whether individual breed/study groups diverged from the regression model. Simple (unweighted) linear regressions were compared with the WLS method to ensure that the data weighting procedure did not affect the results appreciably.

ERI values on growing dogs were analyzed to examine the variation with age. This was accomplished by regressing group mean values against age with an exponential function,  $Y = B + A(1 - e^{-Ct})$ , where  $B$  is the projected value at age 0,  $A$  is the total change in the ERI during growth and  $C$  describes the rate of change of the ERI with time;  $A + B$  is the final ERI value at the end of growth. Total change over the study interval and estimated age to achieve 85, 90 and 95% of the final ERI value were computed from the regression. The overall median age and interquartile range (IQR) at which ERIs from both groups reached 95% of their final value were also determined.

Simple descriptive statistics were computed directly from individual 2DE LA and Ao ERIs. Correlation with body weight was performed by the Pearson product moment. All statistical analyses were done using SPSS software,<sup>d</sup> with significance reported at  $P < 0.05$ .

<sup>d</sup> SPSS software, version 14.0.

**Table 2** ERI results and summary statistics from 1152 adult dogs

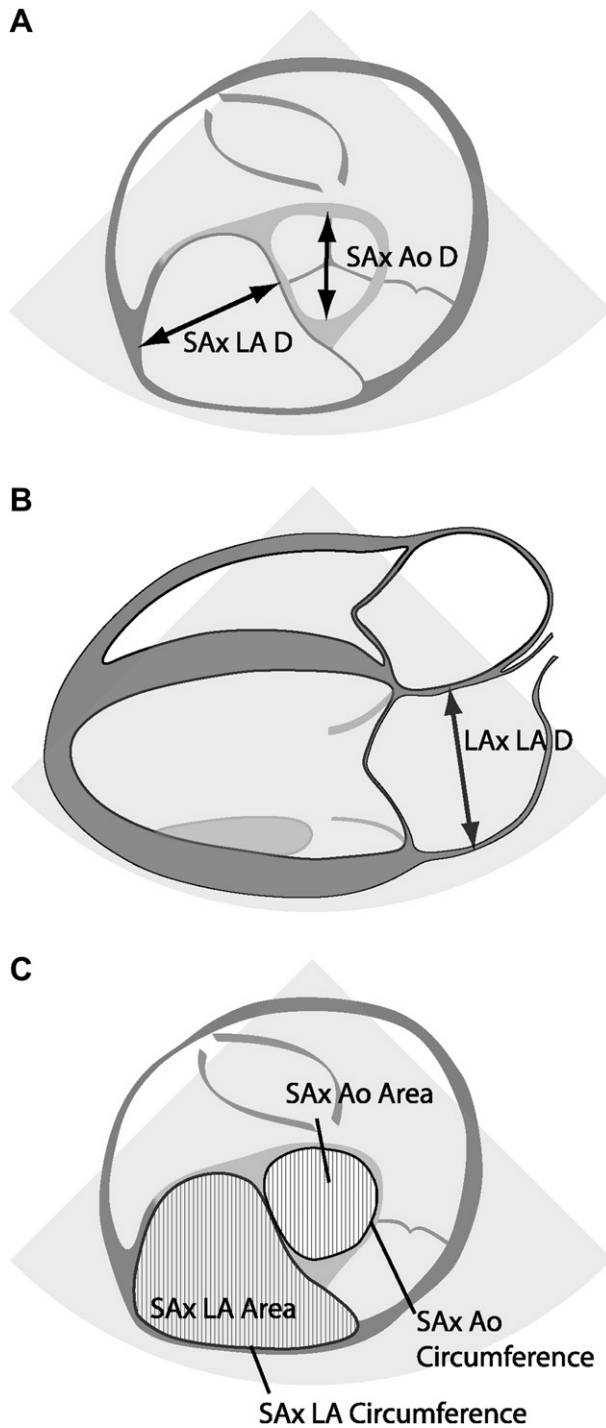
Reference	Breed	n	Weight (Kg)	wIVSd	wLVIDd	wLVWd	wIVSs	wLVIDs	wLVWs	wAo	wLA	FS
Morrison <sup>3</sup>	Miniature poodle	20	3.0 ± 2.0	0.44 ± 0.05 1.06 (0.11)	1.74 ± 0.28 1.01 (0.16)	0.44 ± 0.05 1.09 (0.11)	0.70 ± 0.09 1.23 (0.13)	0.87 ± 0.19 0.76 (0.21)	0.70 ± 0.09 1.20 (0.13)	0.87 ± 0.12 0.88 (0.13)	1.05 ± 0.23 1.03 (0.22)	0.47 ± 0.06 1.38 (0.13)
Yamato <sup>7</sup>	Miniature poodle	30	4.5 ± 1.4	0.39 ± 0.05 0.96 (0.12)	1.76 ± 0.20 1.02 (0.12)	0.39 ± 0.05 0.99 (0.12)	0.65 ± 0.08 1.14 (0.12)	1.04 ± 0.15 0.91 (0.14)	0.64 ± 0.08 1.11 (0.13)	1.00 ± 0.10 1.01 (0.10)	1.08 ± 0.09 1.06 (0.09)	0.41 ± 0.04 1.21 (0.10)
Della Torre <sup>4,a</sup>	Italian GH	20	5.4 ± 1.5	0.46 ± 0.06 1.12 (0.13)	1.61 ± 0.18 0.93 (0.11)	0.51 ± 0.05 1.29 (0.10)	0.66 ± 0.07 1.16 (0.11)	0.93 ± 0.17 0.81 (0.18)	0.74 ± 0.07 1.28 (0.09)			0.43 ± 0.07 1.26 (0.16)
Crippa <sup>8</sup>	Beagle	20	8.9 ± 1.5	0.41 ± 0.07 0.99 (0.18)	1.60 ± 0.22 0.92 (0.14)	0.50 ± 0.12 1.25 (0.25)	0.58 ± 0.10 1.02 (0.17)	0.95 ± 0.22 0.83 (0.23)	0.69 ± 0.12 1.19 (0.18)			0.40 ± 0.10 1.18 (0.24)
Haggstrom <sup>9,a</sup>	CKCS	57	8.9 ± 1.4		1.78 ± 0.16 1.03 (0.09)	0.42 ± 0.05 1.06 (0.12)		1.19 ± 0.14 1.04 (0.12)		0.98 ± 0.09 0.98 (0.09)	0.97 ± 0.10 0.96 (0.10)	0.33 ± 0.05 0.97 (0.14)
Pedersen <sup>9,a</sup>	Dachshund	33	9.5 ± 1.9	0.42 ± 0.05 1.03 (0.13)	1.70 ± 0.19 0.98 (0.11) <sup>b</sup>	0.41 ± 0.07 1.02 (0.16)	0.57 ± 0.06 0.99 (0.11) <sup>b</sup>	1.12 ± 0.16 0.98 (0.14)	0.61 ± 0.08 1.04 (0.13)	1.08 ± 0.09 1.09 (0.09)	0.98 ± 0.14 0.96 (0.14)	0.34 ± 0.07 0.99 (0.22)
Une <sup>10</sup>	Japanese beagle	19	9.9 ± 2.6	0.38 ± 0.05 0.94 (0.14)	1.82 ± 0.23 1.05 (0.13)	0.37 ± 0.04 0.92 (0.11)	0.55 ± 0.08 0.96 (0.14)	1.21 ± 0.18 1.05 (0.15)	0.52 ± 0.07 0.89 (0.13)	0.89 ± 0.08 0.90 (0.09)	0.91 ± 0.09 0.90 (0.10)	0.33 ± 0.03 0.97 (0.09)
Baade <sup>11</sup>	Westie	24	10.3 ± 0.9	0.40 ± 0.08 0.97 (0.21)	1.66 ± 0.34 0.96 (0.20)	0.37 ± 0.07 0.93 (0.19)	0.59 ± 0.15 1.04 (0.25)	1.16 ± 0.22 1.00 (0.19)	0.57 ± 0.08 0.98 (0.14)			0.35 ± 0.07 1.03 (0.21)
Gooding <sup>12,a</sup>	Eng cocker	12	12.2 ± 2.4	0.45 ± 0.08 1.10 (0.19)	1.85 ± 0.14 1.07 (0.07)	0.44 ± 0.08 1.10 (0.19)		1.22 ± 0.14 1.06 (0.12)				0.34 ± 0.05 1.01 (0.14)
Della Torre <sup>4</sup>	Whippet	20	14.5 ± 2.1	0.44 ± 0.05 1.08 (0.12)	1.86 ± 0.12 1.07 (0.06)	0.46 ± 0.05 1.16 (0.10)	0.64 ± 0.06 1.12 (0.10)	1.25 ± 0.14 1.09 (0.11)	0.67 ± 0.10 1.15 (0.15) <sup>b</sup>			0.33 ± 0.05 0.96 (0.15)
Morrison <sup>3</sup>	Welsh corgi	20	15.0 ± 2.9	0.41 ± 0.04 1.00 (0.10)	1.63 ± 0.16 0.94 (0.10)	0.41 ± 0.05 1.02 (0.13)	0.61 ± 0.05 1.08 (0.09)	0.97 ± 0.15 0.84 (0.16)	0.61 ± 0.07 1.05 (0.11)	0.92 ± 0.10 0.92 (0.10)	1.07 ± 0.16 1.06 (0.15)	0.44 ± 0.06 1.29 (0.15)
Mashiro <sup>13,a</sup>	Generic	16	1.76 ± 3.1	0.31 ± 0.04 0.75 (0.12)	1.81 ± 0.12 1.04 (0.07)	0.30 ± 0.03 0.76 (0.11)		1.25 ± 0.10 1.08 (0.08)				0.31 ± 0.04 0.91 (0.13)
Sisson <sup>2</sup>	Pointer	16	19.2 ± 2.8	0.32 ± 0.05 0.79 (0.16)	1.84 ± 0.11 1.06 (0.06)	0.33 ± 0.03 0.83 (0.10)	0.50 ± 0.05 0.88 (0.09)	1.19 ± 0.11 1.03 (0.09)	0.54 ± 0.06 0.93 (0.11)	1.13 ± 0.08 1.14 (0.07)	1.06 ± 0.09 1.05 (0.09)	0.36 ± 0.04 1.04 (0.11)
Wey <sup>9,a</sup>	Generic	47	20.8 ± 13.0	0.40 ± 0.06 0.99 (0.15)	1.75 ± 0.16 1.01 (0.09)	0.40 ± 0.05 1.00 (0.12)	0.56 ± 0.11 0.98 (0.20) <sup>b</sup>	1.16 ± 0.19 1.01 (0.16) <sup>b</sup>	0.57 ± 0.09 0.99 (0.15)			0.34 ± 0.09 0.99 (0.27) <sup>b</sup>
Morrison <sup>3</sup>	Afghan	20	23.0 ± 5.1	0.57 ± 0.12 1.40 (0.21)	1.86 ± 0.22 1.07 (0.12)	0.40 ± 0.05 1.00 (0.12)	0.57 ± 0.12 1.01 (0.21)	1.24 ± 0.20 1.08 (0.16)	0.53 ± 0.11 0.91 (0.20)	1.15 ± 0.17 1.16 (0.14)	1.15 ± 0.20 1.13 (0.18)	0.33 ± 0.06 0.97 (0.19)
de Madron <sup>14,a</sup>	Generic	27	24.4 ± 19.2	0.36 ± 0.08 0.88 (0.21)	1.91 ± 0.16 1.10 (0.08)	0.33 ± 0.07 0.82 (0.20)	0.52 ± 0.07 0.91 (0.14)	1.29 ± 0.16 1.12 (0.12)	0.51 ± 0.09 0.87 (0.17)	1.06 ± 0.15 1.07 (0.15)	1.05 ± 0.17 1.03 (0.16) <sup>b</sup>	0.33 ± 0.06 0.96 (0.18)
Brown <sup>6,a</sup>	Generic	50	25.2 ± 17.4	0.44 ± 0.06 1.06 (0.14)	1.59 ± 0.15 0.92 (0.10) <sup>b</sup>	0.41 ± 0.06 1.02 (0.14)	0.59 ± 0.09 1.04 (0.15)	1.04 ± 0.16 0.91 (0.15)	0.60 ± 0.08 1.04 (0.14)	1.00 ± 0.12 1.01 (0.12)	1.01 ± 0.11 0.99 (0.11)	0.34 ± 0.07 1.01 (0.19) <sup>b</sup>
Page <sup>15</sup>	Greyhound	16	26.6 ± 3.5	0.45 ± 0.07 1.09 (0.16)	1.86 ± 0.12 1.07 (0.07)	0.51 ± 0.07 1.28 (0.14)	0.56 ± 0.11 0.99 (0.19)	1.37 ± 0.15 1.19 (0.11)	0.64 ± 0.09 1.11 (0.15)			0.25 ± 0.06 0.75 (0.25)
Della Torre <sup>4,a</sup>	Greyhound	20	26.9 ± 3.3	0.50 ± 0.04 1.22 (0.09)	1.79 ± 0.13 1.04 (0.07)	0.54 ± 0.04 1.36 (0.07)	0.66 ± 0.04 1.16 (0.07)	1.35 ± 0.10 1.17 (0.07)	0.72 ± 0.05 1.24 (0.07) <sup>b</sup>			0.25 ± 0.04 0.72 (0.15)
Goncalves <sup>16,a</sup>	Generic	70	27.7 ± 19.5	0.52 ± 0.08 1.28 (0.14) <sup>b</sup>	1.52 ± 0.14 0.88 (0.09)	0.41 ± 0.06 1.02 (0.15)	0.70 ± 0.09 1.24 (0.13)	0.95 ± 0.13 0.82 (0.13)	0.63 ± 0.10 1.08 (0.15)	0.93 ± 0.12 0.94 (0.12) <sup>b</sup>	1.13 ± 0.14 1.12 (0.12)	0.38 ± 0.06 1.11(0.16) <sup>b</sup>
Herrtage <sup>17</sup>	Boxer	30	28.0 ± 7.1	0.37 ± 0.08 0.91 (0.22)	1.66 ± 0.21 0.96 (0.13)	0.41 ± 0.08 1.04 (0.20)	0.54 ± 0.08 0.95 (0.15)		0.62 ± 0.08 1.07 (0.13)	0.91 ± 0.08 0.92 (0.09)	0.95 ± 0.08 0.94 (0.09)	0.33 ± 0.08 0.97 (0.24)

Snyder et al. <sup>18,a</sup>	Greyhound	11	29.1 ± 3.7	0.55 ± 0.07	1.92 ± 0.12	0.48 ± 0.06		1.37 ± 0.11					0.29 ± 0.04
				1.34 (0.12)	1.11 (0.06)	1.19 (0.13)		1.19 (0.08)					0.85 (0.14)
Schober <sup>19</sup>	Boxer	66	30.0 ± 4.0	0.39 ± 0.06	1.76 ± 0.19	0.39 ± 0.06	0.54 ± 0.08	1.20 ± 0.15	0.56 ± 0.09				0.32 ± 0.06
				0.96 (0.15)	1.02 (0.11)	0.98 (0.15)	0.95 (0.15)	1.04 (0.12)	0.96 (0.16)				0.94 (0.19)
Lombard <sup>9,a</sup>	Generic	23	30.1 ± 7.8		1.76 ± 0.17	0.42 ± 0.04		1.10 ± 0.13		1.01 ± 0.08	0.98 ± 0.13		0.38 ± 0.05
					1.02 (0.10)	1.05 (0.11)		0.95 (0.12)		1.02 (0.08)	0.97 (0.13)		1.11 (0.14)
Muzzi <sup>20</sup>	German shepherd	60	30.2 ± 4.0	0.39 ± 0.04	1.68 ± 0.20	0.36 ± 0.04	0.57 ± 0.04	1.25 ± 0.21	0.53 ± 0.05	1.02 ± 0.06	0.98 ± 0.08		0.29 ± 0.07
				0.95 (0.09)	0.97 (0.12)	0.89 (0.13)	0.99 (0.06)	1.09 (0.16)	0.90 (0.09)	1.02 (0.06)	0.97 (0.09)		0.84 (0.23)
Vollmar <sup>9,a</sup>	Boxer	75	31.0 ± 4.8	0.39 ± 0.06	1.66 ± 0.14	0.40 ± 0.05	0.55 ± 0.08	1.12 ± 0.12	0.59 ± 0.07	0.92 ± 0.08	0.99 ± 0.11		0.33 ± 0.04
				0.95 (0.15)	0.96 (0.09)	0.99 (0.12)	0.97 (0.15) <sup>b</sup>	0.97 (0.11)	1.01 (0.12)	0.92 (0.09)	0.97 (0.12)		0.96 (0.11)
Morrison <sup>3</sup>	Golden Retriever	20	32.0 ± 4.8	0.40 ± 0.05	1.78 ± 0.15	0.40 ± 0.04	0.55 ± 0.07	1.07 ± 0.18	0.59 ± 0.10	0.95 ± 0.14	1.07 ± 0.17		0.39 ± 0.07
				0.97 (0.13)	1.03 (0.08)	0.99 (0.11)	0.98 (0.13)	0.93 (0.17)	1.02 (0.16)	0.96 (0.15)	1.05 (0.16)		1.15 (0.19)
Kayar <sup>21</sup>	German shepherd	50	34.6 ± 2.7	0.38 ± 0.06	1.74 ± 0.18	0.37 ± 0.05	0.55 ± 0.06	1.32 ± 0.13	0.52 ± 0.04	1.05 ± 0.07	0.95 ± 0.09		0.31 ± 0.03
				0.92 (0.15)	1.00 (0.10)	0.92 (0.13)	0.96 (0.11)	1.15 (0.10)	0.90 (0.08)	1.06 (0.07)	0.94 (0.10)		0.92 (0.11)
Calvert <sup>22</sup>	Doberman pinscher	21	36.0 ± 2.9	0.37 ± 0.02	1.78 ± 0.14	0.37 ± 0.01	0.54 ± 0.02	1.17 ± 0.11	0.54 ± 0.02	1.14 ± 0.07	1.01 ± 0.06		0.34 ± 0.02
				0.89 (0.06)	1.03 (0.08)	0.91 (0.03)	0.96 (0.04)	1.02 (0.09)	0.93 (0.04)	1.15 (0.06)	1.00 (0.06)		1.00 (0.05)
Vollmar <sup>23</sup>	Deerhound	21	41.3 ± 4.9	0.33 ± 0.10	1.86 ± 0.18	0.36 ± 0.07	0.53 ± 0.15	1.24 ± 0.19	0.56 ± 0.08	1.08 ± 0.13	1.03 ± 0.14		0.34 ± 0.06
				0.81 (0.31)	1.08 (0.10)	0.91 (0.18)	0.93 (0.28)	1.08 (0.15)	0.96 (0.14)	1.08 (0.13)	1.02 (0.14)		0.98 (0.17)
Bayon <sup>24</sup>	Spanish Mastiff	12	52.4 ± 3.3	0.33 ± 0.05	1.60 ± 0.16	0.33 ± 0.04	0.53 ± 0.06	0.97 ± 0.12	0.51 ± 0.05	0.93 ± 0.09	0.96 ± 0.11		0.39 ± 0.02
				0.80 (0.15)	0.93 (0.10)	0.82 (0.13)	0.92 (0.11)	0.85 (0.13)	0.88 (0.10)	0.93 (0.10)	0.94 (0.11)		1.15 (0.04)
Koch <sup>25</sup>	Newfoundland	27	61.0 ± 5.6	0.37 ± 0.06	1.60 ± 0.13	0.32 ± 0.04	0.48 ± 0.07	1.13 ± 0.12	0.48 ± 0.04	0.93 ± 0.06	0.96 ± 0.07		0.30 ± 0.04
				0.90 (0.17)	0.92 (0.08)	0.80 (0.13)	0.84 (0.15)	0.99 (0.11)	0.83 (0.08)	0.93 (0.06)	0.94 (0.08)		0.88 (0.13)
Koch <sup>25</sup>	Great dane	15	62.0 ± 6.6	0.46 ± 0.04	1.68 ± 0.14	0.40 ± 0.05	0.52 ± 0.05	1.26 ± 0.10	0.51 ± 0.07	0.94 ± 0.05	1.05 ± 0.16		0.25 ± 0.05
				1.12 (0.08)	0.97 (0.08)	0.99 (0.14)	0.92 (0.09)	1.09 (0.08)	0.88 (0.14)	0.94 (0.06)	1.03 (0.16)		0.73 (0.21)
Vollmar <sup>26,a</sup>	Irish WH	144	63.5 ± 8.3	0.35 ± 0.06	1.60 ± 0.12	0.33 ± 0.05	0.49 ± 0.07	1.06 ± 0.11	0.50 ± 0.06	1.04 ± 0.09	1.01 ± 0.11		0.34 ± 0.04
				0.86 (0.17)	0.93 (0.08)	0.84 (0.15)	0.86 (0.14)	0.92 (0.10)	0.86 (0.12) <sup>b</sup>	1.05 (0.08) <sup>b</sup>	0.99 (0.11)		1.00 (0.12)
Koch <sup>25</sup>	Irish WH	20	68.5 ± 8.0	0.37 ± 0.05	1.54 ± 0.11	0.31 ± 0.03	0.46 ± 0.05	1.11 ± 0.10	0.43 ± 0.05	0.92 ± 0.02	0.95 ± 0.11		0.28 ± 0.04
				0.90 (0.12)	0.89 (0.07)	0.77 (0.11)	0.81 (0.11)	0.96 (0.09)	0.74 (0.11)	0.93 (0.02)	0.94 (0.11)		0.82 (0.13)
Global mean ± SD				0.410 ± 0.062	1.731 ± 0.109	0.399 ± 0.059	0.569 ± 0.061	1.151 ± 0.131	0.581 ± 0.076	0.994 ± 0.083	1.014 ± 0.061		0.340 ± 0.051

Results are presented as two rows for each group. The first row represents the mean group ERI ± SD. The second row represents the group ERI compared to the global mean with the group coefficient of variation in parentheses. The global mean ± SD is listed in the bottom row. GH, Greyhound; CKCS, Cavalier King Charles Spaniel; Eng Cocker, English Cocker; Irish WH, Irish Wolfhound; FS, fractional shortening. See Table 1b for key.

<sup>a</sup> Individualized data.

<sup>b</sup> Non-normal distribution.

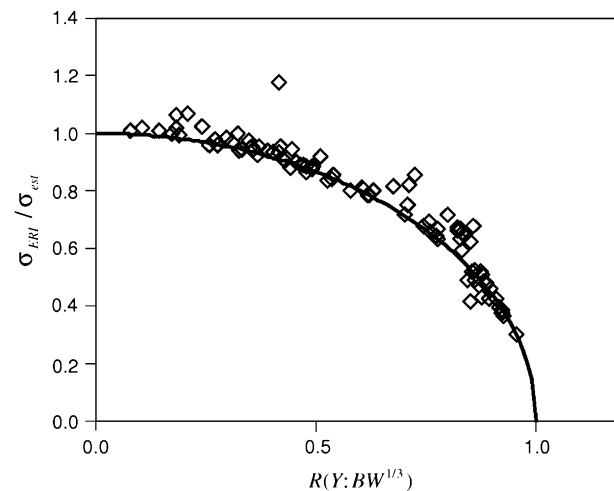


**Figure 1** Right parasternal 2DE LA and Ao measurements, from Rishniw et al. (A) SAX Ao D = short axis aortic root diameter, SAX LA D = short axis left atrial diameter. (B) LAX LA D = long axis left atrial diameter. (C) SAX Ao circumference = short axis aortic root circumference, SAX Ao area = short axis aortic root area, SAX LA circumference = short axis left atrial circumference, SAX LA area = short axis left atrial area.

## Results

### Estimation of summary statistics

The accuracy of estimation procedures for ERI summary statistics is expressed here as ratios of actual to estimated,  $\overline{\text{ERI}}/\overline{\text{ERI}}_{\text{est}}$  and  $\sigma_{\text{ERI}}/\sigma_{\text{est}}$ , computed for breed/study groups where individualized data were available. The estimated means,  $\overline{\text{ERI}}_{\text{est}} = \overline{Y}/(k\overline{\text{BW}}^{1/3})$ , were very accurate and differed from the actual value by only a few percent at most; these will not be discussed further. However, standard deviation estimates are highly dependent on the correlation between the raw measurement,  $Y$ , and  $\text{BW}^{1/3}$  (or  $\text{BW}$ ). Fig. 2 depicts this relationship, indicating that  $\sigma_{\text{est}} = \sigma_Y/(k\overline{\text{BW}}^{1/3})$  systematically overestimates  $\sigma_{\text{ERI}}$  with increasing correlation ( $R$ ). The ratio  $\sigma_{\text{ERI}}/\sigma_{\text{est}}$  is close to 1.0 ( $\pm 0.075$ ) at low correlation, indicating accurate estimation, but decreases approximately as  $\sqrt{1 - R^2}$ , approaching 0 at  $R = 1.0$ . The larger values of  $R$  in Fig. 2 result from breed/study groups in which there was a wide variation in body size (i.e., the generic breed groups); all data shown with  $R > 0.7$  are due to these groups.  $R$  values  $< 0.7$  resulted for all breed-specific groups. For these groups, the estimation procedure is justified with the understanding that  $\sigma_{\text{ERI}}$  is systematically overestimated for groups where individualized data were not available (Table 2).



**Figure 2** The relationship of actual to estimated SD ratios with the correlation,  $R$ , between  $Y$  (linear echocardiographic measurement) and  $\text{BW}^{1/3}$ . The data are collected from adult dogs in which individualized data were available ( $n = 625$ ). As  $R$  decreases the estimated SD becomes more accurate. Values of  $R > 0.7$  only resulted from groups with a wide range in body size (i.e., generics).

## Adult dog ERIs

ERI summary statistics from 1152 clinically normal adult dogs are presented in Table 2, grouped by breed/study and ordered by mean BW. Group ERI results are presented in two rows with the first row representing  $\bar{ERI} \pm SD$  and the second row representing  $\bar{ERI}/\bar{ERI}_G (CV_{ERI})$ .  $\bar{ERI}_G$  values are listed in the bottom row of Table 2. Using data from Vollmar et al., for example,  $\bar{ERI} \pm SD$  of wLVId for Boxer dogs was found to be  $1.66 \pm 0.14$ , compared to a global mean of  $1.73 \pm 0.109$ . Consequently wLVId of Boxer dogs from Vollmar et al. was 96% of the global mean ( $1.66/1.73$ ) with a group coefficient of variation of 9.0%.

Deviations from normality are indicated in Table 2 for breed/study groups where individualized data were available. Evaluation of ERI expectations from the raw measurement studies revealed highly significant differences for every ERI (Kruskal–Wallis). Differences between breed/study groups from the same investigator were also significant except for wLA in Boxers and Irish wolfhounds contributed by Vollmar et al. ( $P = 0.32$ ), and for wIVSs in Greyhounds, Whippets, and Italian greyhounds contributed by Della Torre et al. ( $P = 0.62$ ). Evaluation of breed groups examined by the same investigator(s) with Kruskal–Wallis yielded higher  $P$  values as compared to those when the investigator and breed were different.

The results of WLS regression of each ERI value against BW are presented in Table 3. All correlations were negative indicating that ERIs tended to decrease with body weight, but the correlations were not always significant. Minor, but significant correlations were found for wLVId ( $R^2 = 0.198$ ) and fractional shortening (FS) ( $R^2 = 0.117$ ). Additional significant correlations were apparent for

wLVWs ( $R^2 = 0.518$ ), wIVSs ( $R^2 = 0.457$ ) and wLVWd ( $R^2 = 0.266$ ).  $1 - R^2$  quantifies the dependency of each ERI on factors other than BW (i.e., breed/study group).  $1 - R^2$  was  $> 0.5$  for all ERIs and  $> 0.8$  in 6/9 ERIs, indicating that the majority of variation was due to breed/study.  $CV_{ERI}$  ranged from 0.060 to 0.152, suggesting a consistent level of ERI variation within breed/study groups. Cook's distance was  $< 1$  in all cases indicating that none of the breed/study groups constituted an outlier in the regression procedure. Simple linear regression did not result in any substantive changes compared with the WLS procedure.

The rate of change of each ERI with BW is tabulated also as a percentage (%  $\Delta/kg$ , Table 3). wIVSd, for example, decreased 0.19% for each kilogram increase corresponding to a 19% decrease in the expected value over the entire 100 kg range. Wall thicknesses, both wIVS and wLVW in systole and diastole, exhibited greater dependency on BW than did FS while wLVIDs, wAo, and wLA exhibited less dependency.

## Growing dog ERIs

Mean ERI values from two published studies of growing dogs were regressed against age using the exponential function described above. Age dependence was demonstrated for each ERI during the early growth phase, particularly for wLVId, wLVIDs, wAo and wLA which increased with age. Conversely, wIVSs, wLVWs, and FS decreased with age in both groups. Mean values for wIVSd and wLVWd increased with age in Pointers and decreased in Spanish Mastiffs. Table 4 shows the ages at which 85, 90 and 95% of the final value occurred for each ERI. The majority of ERI values reached 95% of their final value by 12 weeks; median 10.9 weeks (IQR: 8.9–12.2 weeks).

**Table 3** Results of WLS regression of ERIs against BW (kg)

ERI	<i>n</i>	Mean	SD	<i>R</i>	<i>P</i>	$R^2$	$1 - R^2$	<i>B</i>	<i>M</i>	% $\Delta/kg$	$CV_{ERI}$
wIVSd	33	0.410	0.062	-0.252	0.079	0.063	0.937	0.424	-0.001	-0.186	0.152
wLVId	35	1.731	0.109	-0.445	0.004	0.198	0.802	1.797	-0.003	-0.156	0.063
wLVWd	35	0.399	0.059	-0.515	0.001	0.266	0.734	0.435	-0.002	-0.399	0.149
wIVSs	30	0.569	0.061	-0.676	0.000	0.457	0.543	0.633	-0.002	-0.393	0.107
wLVIDs	34	1.151	0.131	0.000	0.500	0.000	1.000	1.148	0.000	0.000	0.114
wLVWs	30	0.581	0.076	-0.720	0.000	0.518	0.482	0.655	-0.003	-0.482	0.131
wAo	24	0.994	0.083	-0.205	0.169	0.042	0.958	1.010	-0.001	-0.070	0.083
wLA	24	1.014	0.061	-0.187	0.191	0.035	0.965	1.021	-0.001	-0.054	0.060
FS	35	0.340	0.051	-0.341	0.022	0.117	0.883	0.364	-0.001	-0.247	0.151

Descriptive statistics of weight-based indices as determined by WLS of group means against BW including weighted global mean, standard deviation of the means (SD), correlation (*R*) and coefficient of determination ( $R^2$ ). *B* = intercept *b* of the linear equation  $Y = mX + b$ ; *M* = slope *m*. %  $\Delta/kg$  represents the rate of change of each ERI with BW.  $CV_{ERI}$  = coefficient of variation of the means, reported as a standardized measure of variation of each ERI between breed/study groups. See Table 1b for key.

**Table 4a** ERI age dependence in growing Spanish Mastiffs

% Final value	wIVSd (13%)	wLVIDd (23%)	wLVWd (7%)	wIVSs (-4%)	wLVIDs (31%)	wLVWs (-8%)	wAo (21%)	wLA (15%)	FS (-20%)
85%	0.8	4.1	—	—	6.8	—	6.1	1.0	2.5
90%	1.4	7.0	—	—	10.1	0.0	11.6	4.6	4.8
95%	2.5	11.9	—	—	15.7	2.7	21.0	10.9	8.6

FS, fractional shortening. See Table 1b for key.

—, value is too constant to be computed.

**Table 4b** ERI age dependence in growing English Pointers

% Final value	wIVSd (-21%)	wLVIDd (13%)	wLVWd (-24%)	wIVSs (-24%)	wLVIDs (29%)	wLVWs (-31%)	wAo (13%)	wLA (3%)	FS (-33%)
85%	5.4	3.4	6.4	6.2	7.1	7.8	3.9	—	6.4
90%	6.8	6.8	8.2	7.8	8.8	9.7	5.0	—	7.5
95%	9.2	12.5	11.3	10.5	11.7	13.0	7.0	—	9.3

In Table 4a, b the ages in weeks at which 85, 90 and 95% of the final ERI value occur are listed under each ERI. In parentheses is the overall % and direction of change over the course of the study. FS, fractional shortening. See Table 1b for key.

—, value is too constant to be computed.

## 2DE LA and Ao ERIs

Descriptive statistics for 2DE LA and Ao ERIs are shown in Table 5. There was no significant dependence on BW seen with any of these ERIs.

## Discussion

The principle aim of this study was to summarize and analyze a large set of echocardiographic dimensional data using the ratio indexing method. Potentially, the method allows characterization of shape differences between dogs of widely varying body size, age, and "somatotype". This characterization is not dependent on statistical or biological assumptions, but resides in the similarity principle which defines geometric similitude. The importance of this work is that it serves as a basis

for the quantification of variation across much of the canine echocardiographic literature.

Weight-based ratio indices of this report were calculated as  $ERI = Y/(kBW^{1/3})$  where  $Y$  is any of the linear measurements and the numerical value of  $k$  is arbitrary. The choice used for  $k$ , 0.795, imparts an obvious visual interpretation to the ratios, i.e. each dimension expressed specifically in terms of the average M-mode aortic root diameter from the original study.<sup>6</sup> The choice of the value for  $k$  has no effect whatsoever on the accuracy or conclusions described herein and expectations for  $ERI = Y/BW^{1/3}$ , i.e. with  $k$  removed, may be derived simply by multiplying each statistic of Table 2 by 0.795; there is no advantage in seeking an improved value for  $k$  using additional data. Nevertheless it is noteworthy that this value remains consistent, whether computed from all the individualized data of the study ( $k = 0.7931 \pm 0.0887$ ) or the means of all the groups ( $k = 0.7902 \pm 0.0658$ , 25 breed/study groups). Furthermore the value of the exponent computed from power regression of Ao against BW (individualized data) is almost exactly 1/3 (0.344) and the correlation of Ao<sub>w</sub> with BW is extremely low ( $R = 0.13$ ). This indicates that the M-mode aortic root dimension obeys the similarity principle closely over the full range of size for dogs. Nevertheless breed/group-specific variation is readily apparent.

ERIs of adult dogs from a wide range of body sizes and somatotypes showed little deviation from the global mean (Table 2). For all ERIs, the majority of variation over the available range of BW was due to differences between breed/study

**Table 5** Correlation of 2D LA and Ao ERIs with body weight

ERI	Mean ± SD	R	P
wSaxLAD	1.23 ± 0.16	-0.028	0.436
wSaxAoD	0.96 ± 0.12	-0.036	0.418
wLaxLAD	1.54 ± 0.30	0.123	0.237
wSaxLAC	6.46 ± 0.65	-0.185	0.140
wSaxLAA	2.49 ± 0.48	-0.078	0.325
wSaxAoC	3.29 ± 0.29	0.066	0.351
wSaxAoA	0.93 ± 0.22	0.042	0.403

Summary statistics for 2DE LA and Ao ERIs. Descriptions of weight-based indices are listed in Table 1. See Table 1b for key.



groups, as indicated by  $1 - R^2 > 0.5$ . Some mild shape changes were noted with increasing body weight; i.e., the % decreases/kg for wall thickness measurements in systole and diastole were all greater than for chamber diameter measurements in systole and diastole (Table 3). Taken in whole, these findings indicate that ERIs are well normalized for body size and that the observed variation is due principally to breed/study group-dependent factors, including both differences in echocardiographic technique and actual changes in shape.

Variability of breed/study group ERIs from the same investigator was significant but less than the overall variability between groups. Two investigators, Vollmar and Della Torre et al.,<sup>4</sup> submitted individualized data for more than one study group. Comparison of  $\bar{E}RI$ s between investigator-specific groups showed significant differences, but to a lesser degree (higher  $P$  values) than groups from different investigators. Deviation of these group  $\bar{E}RI$ s from  $\bar{E}RI_G$  was similar to those seen within four additional breed groups (Miniature poodle, Welsh Corgi, Afghan and Golden Retriever) calculated using summarized data from Morrison et al.<sup>3</sup> While a statistical comparison of  $\bar{E}RI$ s between these four breeds in the current study was not possible, due to lack of individualized data, Table 2 demonstrates that these  $\bar{E}RI$ s are similar suggesting that breed-specific differences may be less important than previously indicated. It is important to note that Morrison et al. regressed linear measurements from different sized breeds against BW which resulted in significantly differing slopes and intercepts for these breeds; this led to the interpretation of breed- or body size-dependent aberrancy of cardiac structure. In addition to statistical anomalies arising from indexing geometrically dissimilar dimensions, this conclusion likely is limited by the ranges of BW within each breed group. Correlations of BW with linear measurements are not available from this study for further evaluation.

The six generic groups used in the current study each included dogs of mixed breed and body size.<sup>6,9,13,14,16</sup> If breed or somatotype does have a significant effect on M-mode values, one might expect ERI values from these six groups to show greater similarity to each other than to other breed-specific groups. In fact, the variation between these groups was of similar magnitude to that seen between all 34 groups, suggesting that differences in the measurement technique and study design may be largely responsible. This conclusion cannot be confirmed, however, due to the retrospective nature of the investigation.

There were significant correlations noted for some of the ERI means with BW in adult dogs (Table 3). Dependencies were similar quantitatively to FS, a well-known ratio index employed across wide ranges of body size and breed. Such correlations suggest body size-dependent shape changes that are greater than those previously published.<sup>6</sup> One explanation for this finding is that breed/study-specific differences may have affected correlations with BW since the original study was done using generic dogs and examination methods were more uniform than for the current study. Removal of breed-specific groups from our analysis resulted in lower correlations with BW than shown in Table 3. Also, the greatest regression weighting factors always occurred in large breed groups over 30 kg. Simple linear regression however did not result in any substantive changes compared with the WLS procedure, indicating that these weighting factors could not have played an overly influential role.

Age dependence of ERIs suggests that cardiac shape changes occur during the early growth phase (Table 4). The direction of change indicates whether a cardiac dimension grows proportionally faster (positive change) or slower (negative change) than the dog's linear growth rate. In both growing Pointers and Spanish Mastiffs,<sup>2,24</sup> ERIs changed in the same direction except for the diastolic wall thickness measurements. This may indicate different growth rates between breeds, or additional study-dependent factors. Indices of left ventricular internal dimension increased with age in both groups. Prior studies of postnatal changes in the dog have shown that physiologic changes such as an increase in systemic pressure and decrease in pulmonary pressure lead to faster growth of the left ventricle as compared to the right, and ultimately a shift from right to left ventricular dominance.<sup>30–32</sup> ERIs were found to be constant long before adolescent growth was complete. The change in individual ERIs over the entire growth phase was 3–31%, compared with 20–33% for FS. This analysis suggests that continuing changes in ERI values beyond 3–4 months may be pathologic in dogs and that ERIs may be beneficial in assessing cardiac disease progression apart from changes due to growth. Additional data from other adolescent breed/study groups would be expected to produce a more accurate prediction interval.

Two dimensional LA and Ao linear, area and circumferential ERIs showed no significant correlation with body size, indicating that they are well normalized for BW. The LA/Ao ratio is an accepted indicator of LA dilation in dogs across a wide range

of BW but can be affected by changes in the Ao that occur with specific disease states or breeds. Our findings indicate that both weight-based 2DE LA and Ao ERIs may be used independently to generate narrow prediction intervals for normal LA and Ao size.

The ERI values in Table 2 are readily employed to estimate expected values and ranges for native echocardiographic measurements. Using data from Vollmar et al.,<sup>9</sup> for example,  $Ao_w$  for a 25 kg Boxer dog is 2.32 (i.e.,  $0.795 \times 25^{1/3}$ ) and the LVIDd expectations are derived by multiplying the tabulations ( $1.66 \pm 0.14$ ) by this value yielding  $3.86 \pm 0.32$  cm. These values differ from the LVIDd summary statistics of the original dataset ( $4.13 \pm 0.38$  cm) because the estimation occurs at a specific BW, which allows for the generation of a more specific prediction interval; this is especially true for individuals at the lower extreme of a breed/group weight range (Fig. 3). However, the use of Table 2 to generate expected dimensions for breeds where only summarized data were available should be done with greater caution as the resulting prediction intervals are no longer BW-specific. This is not a shortcoming of the ERI approach but results from our estimation procedure for  $\sigma_{ERI}$  that was necessitated by the lack of individual data for these groups.

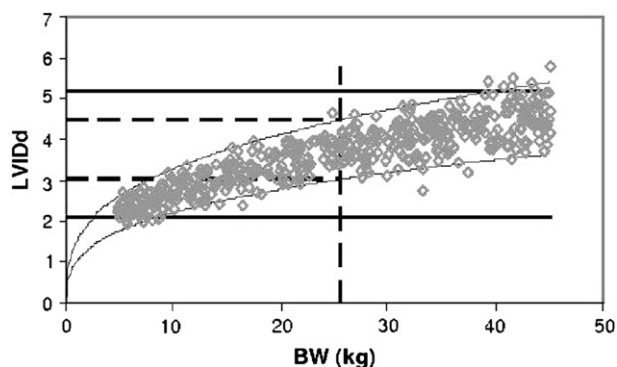
A close relationship exists between power regressions of the form  $Y = A(BW)^B$ , and weight-based ratio indices.<sup>9,33</sup> Dividing both sides of the above equation by  $(BW)^B$  yields  $Y/(BW)^B = A$ . We refer to this construction as a ratio index when the value of  $B$  is determined based on the principles of geometric relations (i.e., length is proportional to  $BW^{1/3}$ ), or a power index when  $B$  is the statistically optimal value determined from regression. Consequently ERIs can be rearranged to the same form as power equations. Using a 20 kg dog as an example, let  $Y = \text{LVIDd}$  and  $BW = 20$ . From Table 2, the mean value for wLVIDd is 1.731, which equals  $\text{LVIDd}/Ao_w$ . Rearranging the equation gives:

$$\begin{aligned} \text{LVIDd} &= 1.731(Ao_w) = 1.731 * 0.795(BW)^{1/3} \\ &= 1.376(BW)^{1/3} = 3.7 \text{ cm.} \end{aligned}$$

The equation derived by Cornell et al.<sup>9</sup> is:

$$\text{LVIDd} = 1.53(BW)^{0.294} = 3.7 \text{ cm.}$$

The power regression formula includes two undetermined regression parameters,  $A$  and  $B$  above, whereas the ratio index approach has only one since the value of  $1/3$  is assumed for parameter  $B$  to predict linear dimensions. While the two equations



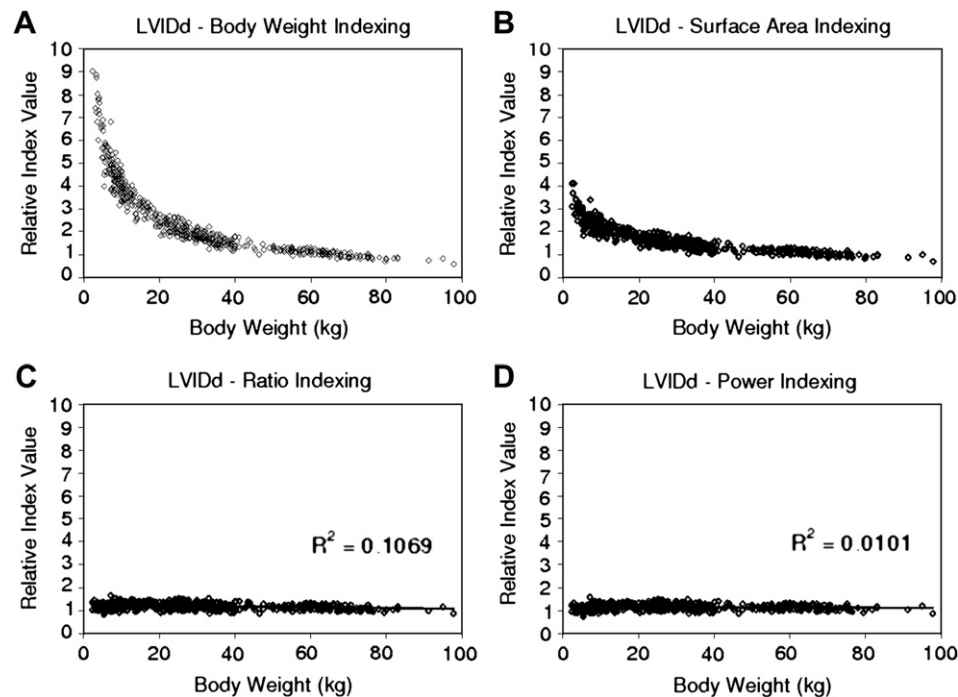
**Figure 3** Random data (gray diamonds) are generated to illustrate a prediction interval for LVIDd based on a specific body weight (dashed lines). The solid gray lines represent 95% confidence intervals across a wide range of BW. Any prediction interval (solid lines) that is generated from a group of dogs with varying BW will be increasingly broad, especially at higher extremes of BW.

give very similar results over a large range of BW, the power regression yields a better estimate of  $Y$  at extreme BWs or whenever the optimal value of  $B$  is significantly different from the ratio index assumption.

Shortcomings of alternative indexing methods also are revealed by this analysis. While the optimal regression value for the exponent  $B$  in a power index may be very close to, or statistically indistinguishable from, the ratio index value of  $1/3$ , indexing a linear dimension by BSA employs a BW exponent of  $2/3$  which differs from the statistically optimal value by a factor of two or more. Indexing by BW ( $B = 3/3$ ) results in even greater disparity. Indices of the latter two forms are highly dependent on BW, particularly at low BW, thereby failing as body size normalization methods (Fig. 4). Viewed as regression procedures, they are also statistically invalid and should not be condoned for peer-reviewed publication.<sup>6</sup>

There are several important limitations inherent in the current study. This was an uncontrolled metastudy with multiple potential sources of variation in physiologic parameters and data acquisition that have been shown to affect M-mode measurements. The ability of the ratio index method to quantify shape characteristics decreases as these sources of variation increase. Variation due to these uncontrolled factors also decreases the apparent dependence of ERIs on BW. This impairs our ability to make inferences about shape changes that may actually be breed- or BW-dependent.

The authors acknowledge the potential for publication bias due to differences in data



**Figure 4** Comparison of four alternative normalizations of LVIDd using individualized data from this study ( $n = 625$ ) displayed at comparable levels of variation. Indexing LVIDd by either body weight (A) or body surface area (B) fails to achieve size normalization; indices are highly correlated with BW due primarily to inherent non-linear relationships between length, area, and volume. ERI (C) and power indexing (D) normalize effectively for BW and with similar BW independence.

collection methods that may occur when there is a pre-existing intent to publish.

M-mode data collection methods varied between the breed/study groups of this report. Known observer-dependent sources of variability include patient positioning and long versus short axis measurement.<sup>1,34,35</sup> Our study precluded analysis of these factors except for a subset of groups derived from reports where inter-observer variability was controlled.<sup>4,23,26</sup> Hence an unknown percentage of variation between breed/study groups is due to technical differences, not actual shape changes; actual breed/group-dependent ERI variation is less than depicted. A previous study reported intra- and inter-observer variability as coefficients of variation<sup>1</sup> with minimum values ranging from 3.1 to 13.8% for M-mode values in the dog. We calculated  $CV_{\overline{ERI}}$  as a standardized measure of variation of each ERI between breed/study groups and found it to be of similar range. It is not possible to make significant inferences on this similarity however due to an inherent difference in the study design from the aforementioned report.

It was necessary to estimate ERI summary statistics ( $\overline{ERI}_{est}$ ,  $\sigma_{est}$ ) from published summaries of echocardiographic measurements ( $\overline{Y}$ ,  $\sigma_Y$ ,  $\overline{BW}$ ) when individualized data were not available.

While the estimation procedure for  $\overline{ERI}$  was excellent,  $\sigma_{ERI}$  was systematically overestimated in a way that increased with the correlation between the raw echocardiographic measurement and body weight. This is expected to have relatively little impact on the statistics depicted in Table 2 since the estimation procedure was restricted to breed/study groups with narrow body weight ranges, thereby limiting the effect. It is important to recognize, however, that correlation of echocardiographic measurements with body size is the very reason that normalization is required.

Weight-based ERIs are not normalized for body condition score and values from individuals that are significantly over or underweight should be interpreted with caution. The authors suggest that ERIs from such individuals should be determined based on an estimate of ideal BW when generating expected echocardiographic values.

In comparison to previous indexing methods, ERIs show little variation over a wide range of body sizes. Variation that may occur is more likely due to breed/study differences between groups. Findings between individualized and summarized groups in this study appeared to be robust, considering the estimation methods used to generate summarized statistics. ERIs can be a useful clinical tool for

evaluation of unique shape characteristics related to specific breeds or disease states. Allometric scaling relies on the same geometric principle as the ERI method, and is a useful clinical tool in generating narrow confidence intervals for expected echocardiographic measurements from a given BW.

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