Two-dimensional echocardiographic left-atrial-to-aortic ratio in healthy adult dogs: a re-examination of reference intervals

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Running Title: LA:Ao in healthy dogs

The preliminary results of this study were presented at the 2018 ECVIM Congress in Rotterdam, Netherlands.

Acknowledgements

No authors received any research support for this study.

ABSTRACT

Introduction: Left-atrial-to-aortic ratios (LA:Ao) provide a body-weight independent estimate of left atrial size. However, reference intervals were established with small sample populations, and for only single points in the cardiac cycle. More robust reference intervals are warranted.

Animals: 238 apparently healthy adult dogs

Materials and Methods: LA:Ao measurements were obtained at 3 points in the cardiac cycle – maximal dimension, at the closing of the aortic valve (or just before opening of the mitral valve) ($LA:Ao_{MAX}$); minimal dimension, at the onset of the QRS complex ($LA:Ao_{MIN}$) and at the onset of atrial systole ($LA:Ao_{P}$). $LA:Ao_{MAX}$ was obtained from right parasternal short and long axis views, $LA:Ao_{MIN}$ and $LA:Ao_{P}$ were obtained from the right parasternal short axis view. Dogs were excluded from analyses of reference intervals if weight-based left atrial and left ventricular diastolic dimensions exceeded reference interval limits. Effects of breed and bodyweight on LA:Ao measurements were examined.

Results: Upper LA:Ao reference limits mostly agreed with previously published limits, although 10% of dogs had $LA:Ao_{MAX}$ in the short-axis view exceeding 1.6. These dogs had smaller aortae than expected for their bodyweight, and included mostly boxers and English setters. Reference limits for $LA:Ao_{MIN}$ and $LA:Ao_{P}$ were smaller than those for $LA:Ao_{MAX}$ in either view. No LA:Ao measurements were associated with bodyweight.

Conclusions: Reference limits were either confirmed or established for the common two-dimensional methods of assessing relative left atrial size in healthy dogs. Clinicians

should use caution when diagnosing mild left atrial enlargement in certain dog breeds, and should examine the weight-based aortic dimensions in such cases.

KEYWORDS: ultrasound, cardiac mensuration, cardiac enlargement, cardiomegaly, canine

Abbreviation Table

LA:Ao	ratio of the left atrial dimension to the aortic valve dimension
LA:Ao$_{MAX}$	ratio of the left atrial dimension to the aortic valve dimension at onset of ventricular diastole
LA:Ao$_{P}$	ratio of the left atrial dimension to the aortic valve dimension at onset of atrial systole
RPSA	right parasternal short-axis view
wAo	Aortic-to-weight-based aortic ratio
wLA	left atrial-to-weight-based aortic ratio
wLVIDd	left ventricular internal dimension at end-diastole ratioed to weight-based aortic measurement

Measurement of left ventricular and left atrial chamber dimensions forms a cornerstone of echocardiography, allowing estimation of left heart volume overload. In veterinary cardiology, these measurements are commonly indexed to bodyweight or another cardiac structure, such as the aorta, because of the marked disparity in body sizes within dogs [1]. The left-atrial-to-aortic ratio (LA:Ao) is one such indexed measurement. It is independent of bodyweight [2,3], easily measured, and clinically useful. Most cardiologists use two-dimensional imaging for these measurements and obtain them from either a right parasternal short-axis (RPSA) or long-axis view. Alternatively, investigators index the left atrial measurement to either bodyweight [4], or to a weight-adjusted aortic measurement [1,5].

Approximately 20 years ago, two independent studies, examined LA:Ao in healthy dogs [2,3]. These studies have been collectively cited over 300 times, however, the data were based on 36 healthy dogs of various size in one study [2] and 56 Cavalier King Charles Spaniels in the other [3]. Furthermore, the reference intervals proposed by the two groups of investigators differed considerably and used different methods to establish the reference limits. Subsequent studies ruled out differences in the methods used to measure the aorta as a cause for these discrepancies [6]. More recently, investigators have examined left atrial measurements using a long-axis view [7], expanding on the original publications by Rishniw and Erb [2].

Adding to the different methods and reference limits are differences in the timing of the left atrial and aortic measurements. Both structures are dynamic and change apparent or actual size throughout the cardiac cycle [8,9]. While both original studies used the onset of ventricular diastole (closure of the aortic valve) as the time-point for measurements, other cardiologists prefer to measure the left atrium and aorta at different points in the cardiac cycle – usually at the P wave, or, alternatively, at the onset of ventricular systole. However, no reference intervals have been proposed for measurements obtained at these points in the cardiac cycle.

The Clinical Laboratory Standards Institute recommends measuring at least 120 individuals to establish reference intervals or reference limits, because this allows non-parametric calculation of the 90% confidence intervals around the reference limits [10]. With smaller sample sizes, "robust" methods can be used to estimate the confidence intervals.

Therefore, we sought to reassess the LA:Ao reference limits for dogs using a larger cohort and multiple investigators. Furthermore, we hoped to provide reference limits for measurements obtained at various points in the cardiac cycle, and from two right-sided views. As secondary aims, we also examined left atrial dimensions, indexed to bodyweight, or a weight-adjusted aortic dimension.

Animals, materials and methods

Cardiologists and clinicians with practice limited to cardiology provided data from apparently healthy adult dogs (> 1 year). All dogs underwent a full echocardiographic evaluation after obtaining a brief history and a performing a physical examination. Most dogs were presented for evaluation in cardiac screening clinics, or for other studies of cardiac health and disease; 52 dogs were included from a previously published prospective study of left atrial function [9]. Data were collected prospectively from all dogs and included breed, age at examination, sex, weight, all left atrial measurements, aortic measurements and left ventricular diastolic measurements. Dogs had no history of cardiac disease or any other disease that would be expected to affect cardiac function. Body condition scores were not recorded for any dogs.

Echocardiography

Measurement planes. All left atrial and aortic measurements were obtained from two-dimensional images from three cardiac cycles and averaged; all left ventricular dimensions were measured from M-mode images from three cardiac cycles and averaged. The left atrium was imaged from the right parasternal short-axis and right parasternal long-axis 4-chamber view; the aorta was imaged only from the short-axis view at the level of the valve cusps as described previously [2]. The left atrium in short axis was measured along a line extending from, and parallel to, the commissure of the aortic valve separating the left coronary and non-coronary cusps, as described previously [2]. The left atrium in long axis was measured mid-way between the mitral valve annulus and the roof of the left atrium, along a line that extended from the inter-atrial septum to the lateral left atrial wall, approximately parallel to the mitral annulus, as described previously [2]. Left ventricular diastolic dimensions were obtained from the short-axis view at the tips of the papillary muscles, just apical to the chordal insertions at the onset of the QRS complex. Cursors for all measurements were placed at the tissue-blood interface [11], as described previously [2].

Measurement timing. All studies were performed with simultaneous ECG monitoring, using a variety of ultrasound machines and probes. Left atrial and aortic measurements were obtained at three points in the cardiac cycle: at the onset of ventricular diastole, defined as the first measurable frame after aortic valve closure (in the short-axis view) (LA_{MAX} and Ao_{MAX}), the onset of atrial systole (LA_P and Ao_P), defined as the peak of the P wave on the ECG, and at the onset of ventricular systole (LA_{MIN} and Ao_{MIN}), defined as the onset of the QRS complex. In the right parasternal long-axis view, the left atrium was measured only at the onset of ventricular diastole (LA_{MAX}), defined as the last measurable frame before mitral valve opening [2].

We used two measures of cardiac size to define “normality” for our cohort. First, we calculated the weight-indexed left ventricular (wLVIDd), left atrial (wLA) and aortic (wAo) dimensions as previously described [1]. We then ascribed each dog a value of “0” if wLVIDd and wLA were within previously defined limits (1.95 for wLVIDd and 1.56 for wLA), and “1” if they exceeded one of these limits. Dogs were excluded if they scored “2” (i.e., exceeded the limits for both measurements), but were included if they scored “0” or “1”.

We then calculated the LA:Ao for the three points in the cardiac cycle defined above. We used the aortic measurement obtained at that same point for calculating the respective LA:Ao, e.g., both the left atrial and aortic measurements for the onset of atrial systole (LA_P) were obtained at the peak of the P wave. We calculated the LA:Ao for the right parasternal long-axis view using the aortic measurement obtained at the onset of ventricular diastole (Ao_{MAX}) in the short-axis view.

Statistical analyses

We first examined whether investigators submitted similar LA:Ao estimates by plotting and visually comparing the LA:Ao data provided by each investigator. We further compared the LA:Ao, including wLA estimates, with Kruskal Wallis tests and post-hoc multiple comparison tests where indicated. We did not adjust the nominal alpha value (0.05) for these 4 comparisons. Because wAo measurements appeared to be impacted by breed, but because data for those breeds were provided largely by one investigator (Investigator 1), we examined whether Investigator 1 provided smaller Ao measurements than the other investigators with an ANOVA, followed by a Dunnett's test, comparing each of the other investigators to Investigator 1. We did this with and without the "impacting breeds" included in the analysis under the assumption that, if the Investigator, and not the breed, was responsible for our observations, we would detect differences between Investigator 1 and the other investigators in both instances.

To further assess whether Investigator 1 inadvertently biased the dataset by measuring differently from other investigators, we performed an inter-observer agreement analysis. Four investigators submitted right parasternal short axis images from 10 cases (3 images per case; total 120 images) to an online repository as DICOM files. All investigators then measured the aortic and left atrial dimensions, and investigators' average measurements for each image set were compared via a repeated measures ANOVA with post-hoc multiple comparisons. We calculated the average coefficient of variation between all investigators and the maximum difference for each image set.

Because cardiologists commonly index left atrial measurements to bodyweight using an allometric scaling approach, we examined the relationships between LA, or Ao dimensions (at each time point) and bodyweight, and provided the scaling constants and exponents for each of these relationships [12].

We then used an open-source application to calculate reference intervals for all variables [13]. We chose the non-parametric method to determine reference intervals using the entire eligible data set. However, because Investigator 1 contributed approximately 50% of the observations, we also calculated upper reference limits (which are most often used clinically) after excluding the data provided by Investigator 1, to determine whether Investigator 1 excessively biased the reference intervals.

We also examined associations between LA:Ao measurements and bodyweight by scatterplots and correlation analyses, and between LA:Ao measurements and breeds by visually examining the data. We additionally examined the relationship between weight-based aortic measurements and maximal LA:Ao ($LA:Ao_{MAX}$). All statistical analyses were performed using commercially available statistical software.[g]

Results

Six investigators submitted data from 238 healthy adult dogs for the study. We excluded five dogs based on our echocardiographic criteria (wLVIDd and wLA both exceeded reference limits), although none of these dogs appeared to have cardiac disease. These five dogs were all examined by the same investigator. Three were young, small mixed-breed dogs and two were middle-aged English setters. Data for these five dogs are provided as an online supplement **(Supplemental Table 1)**. Therefore, we ultimately analyzed data from 233 dogs. We did not have a weight for one dog, and lacked the long-axis measurements for one dog – these two dogs were excluded from the relevant analyses. Of the dogs included in the analyses, six had

wLA_{MAX} >1.56 and 26 had wLVIDd >1.95, but no dogs had both variables above the reference limits.

The remaining 233 dogs comprised 56 breeds and mixed breed dogs (**Supplemental Table 1**), weighed a median of 18.5 kg (range: 2.5 to 62 kg, IQR: 11 to 28 kg) with approximately equal sex distributions (female: 78, spayed female: 44, male: 91, neutered male: 25).

Investigators did not differ between LA:Ao measurements that they submitted, except for LA:Ao measured at the P-wave ($LA{:}Ao_P$).For this variable, one investigator submitted slightly higher $LA{:}Ao_P$ measurements than three other investigators (P=0.02) (**Figure 1, Table 1**).

The reference intervals for the four LA:Ao measurements, and for wLVIDd are provided in **Table2**. The regression coefficients for LA measurements, indexed to bodyweight, and the upper reference limits derived from these, are provided in **Table 3**.

Twenty-eight dogs had $LA{:}Ao_{MAX\ (RPSA)}$ >1.6, and seven dogs had $LA{:}Ao_{MAX\ (RPSA)}$ >1.7 (**Figure 2A**). When we examined the $LA{:}Ao_{MAX}$ data by breed, we identified 3 breeds which appeared to account for 50% of high $LA{:}Ao_{MAX\ (RPSA)}$ values: Beagles (2/3), Boxers (7/16) and English setters (5/19) (**Figure 2B**), although 3 of the English setters were excluded from the initial analyses because they exceeded the wLA and wLVIDd limits. We re-calculated the reference intervals after removing these three breeds. This decreased the upper limit from 1.73 to 1.66 (90% CI: 1.63-1.75).

None of the LA:Ao variables or weight-based left atrial (wLA) or aortic (wAo) variables showed any association with bodyweight (largest *r* for any association = 0.17; **Supplementary Figure 1**).

We found that $LA:Ao_{MAX\ (RPSA)}$ had a modest negative relationship with weight-indexed aortic measurements (wAo) – dogs with smaller aortae for their weight tended to have larger $LA:Ao_{MAX\ (RPSA)}$ measurements (r=0.49, P<0.05; **Figure 3**). All dogs (n=28) with LA:Ao>1.6 had wAo <1.0; 25/28 had wAo≤0.9. However, many dogs with wAo <1.0 had LA:Ao<1.6. When plotted against bodyweight, the wAo were consistently < 0.9 in two breeds identified as having large $LA:Ao_{MAX}$ – Beagles and Boxers. English setters had wAo that were scattered across the range of values (**Supplementary Figure 2**). However, all the English setters with LA:Ao exceeding 1.6 had wAo < 0.9, similar to Boxers and Beagles.

Because a single investigator (Investigator 1) provided most of the data for Boxers and English setters, we examined whether this investigator simply imaged and measured aortic valves differently from the other investigators. We found that measurements of investigator 1 were smaller only than those of investigator 4, who had the largest measurements (on average). Furthermore, after measurements obtained from Boxers were removed from the analysis, we observed no differences in measurements between Investigator 1 and the other investigators.

Additionally, Investigator 1 did not measure the same images differently from other investigators. Investigator 5 measured aortae larger than all other investigators (P<0.05 for all pairwise comparisons). The average inter-observer coefficient of variation for measuring aortic dimensions was 5.3% (median 4.9%). The average maximum difference for measurements between investigators was 1.1 mm (median 1.0 mm) with the largest maximum difference for any image being 2.63mm (for an aorta that measured 24 mm).

Discussion

Our study suggests that the previous upper reference limit for two-dimensionally measured LA:Ao_{MAX} of 1.6, obtained from the right parasternal short-axis view, is reasonable, but might slightly underestimate the true range, resulting in misdiagnosis of some healthy dogs with LA:Ao_{MAX} slightly exceeding this limit as having left atrial enlargement. In our current study, approximately 10% of apparently healthy dogs exceeded this limit. Our study augments previous research by providing reference limits for LA:Ao measurements obtained during different points in the cardiac cycle, provides more robust data for left atrial dimension indexed to the weight-based aortic dimension (wLA), and provides novel data for the left atrial dimensions indexed to bodyweight. We identified at least two breeds in which the LA:Ao measurements exceeded traditional reference limits [2,3] in a moderate proportion of the individuals: boxers and English setters. Therefore, clinicians should perhaps interpret LA:Ao measurements cautiously when examining individuals of these breeds. Whether similar issues exist with breeds absent from our study, or represented by too few individuals (e.g. Beagles), remains to be determined.

Our study also provides reference limits for LA:Ao measured during different points in the cardiac cycle, and from the right parasternal long-axis view. Some clinicians have proposed that the right parasternal long-axis view is superior to the short-axis views, because it avoids measurement into the pulmonary venous ostia, especially in dogs with left atrial enlargement [7]. Others have suggested that measuring the left atrium and aorta in the short axis view at the end of ventricular diastole, or onset of atrial systole provide clearer images of the aorta and left atrium (Luis Fuentes, personal communication). Therefore, our study provides reference intervals for clinicians who prefer to use time points or views that differ from the traditional method ($LA:Ao_{MAX(RPSA)}$).

Our finding that $LA:Ao_{MAX}$, obtained from the right parasternal short-axis view, might exceed 1.6 in approximately 10% of dogs has clinical implications. Several studies have used reference limits of 1.5 or 1.6 when determining left atrial enlargement [14–18]. This would tend to increase the number of dogs falsely identified as having mild left atrial enlargement. Indeed, a recent study defined "mild enlargement" as LA:Ao between 1.5 and 1.7 [14]. The authors of that study, however, did not examine the agreement or accuracy of identifying "normal" vs "mildly enlarged" left atria – our data suggest that such accuracy would be low. Other studies have shown an increased risk of cardiac death in dogs with mitral valve disease when LA:Ao exceeds 1.7 [16] – that would seem intuitive given our data suggesting that LA:Ao <1.7 can be (and most probably is) normal in many dogs.

Whilst many of veterinary cardiologists use $LA:Ao_{MAX}$, other investigators routinely report the use of the minimal LA:Ao [19,20], or $LA:Ao_{P}$, and some do not report the exact technique used [21].

As previous studies [8] and our data show, these measurements are not interchangeable and inconsistency in acquisition or reporting could lead to scientific and clinical confusion. Because of this lack of interchangeability, clinicians should report the view and timing of their measurements of LA:Ao to avoid confusion and to maintain consistency. This should be done both for clinical cases and studies describing LA:Ao measurements submitted for publication.

Recently, investigators examined the LA:Ao$_{MAX}$ from the right parasternal long-axis view in 80 healthy dogs using two-dimensional echocardiography [7]. They measured the aorta from a long-axis view, rather than short-axis view, and obtained reference intervals slightly larger than those of our study or the original study by Rishniw and Erb (2.4 vs 2.1) [2]. However, in the figures from that paper, the authors appeared to measure the aorta during systole (valve cusps appear open in the representative figure) and the line of measurement appears to extend from cusp to cusp, rather than wall to wall. This would result in a potentially smaller aortic diameter than that obtained from the short-axis view, and therefore, would increase the resultant LA:Ao measurement.

Our data support and augment those of another recent study, where investigators determined left atrial and left ventricular reference intervals in 122 healthy adult dogs [4]. Our data are remarkably similar to those obtained by Visser and colleagues, with few exceptions. The upper reference limits for LA:Ao$_{MAX}$ are virtually identical. The scaling exponents for left atrial and left ventricular dimensions indexed to bodyweight in that study (0.309 and 0.299, respectively) mirror those from our study (0.31 and 0.295) and those of the left ventricular dimensions measured by Cornell and colleagues (0.294) [12]. The upper reference limits for left ventricular dimensions indexed to bodyweight are almost identical to those proposed by Cornell and colleagues (1.89 vs 1.85). However, the upper reference limits for LV and LA indexed to bodyweight proposed by Visser and colleagues (1.67 and 1.65 respectively) are smaller than those in our study (and those proposed by Cornell and colleagues). Several reasons exist for these differences. First, Visser and colleagues had a single investigator perform all the imaging, and another single investigator perform all the measurements. Any inherent, systematic measurement bias (or imaging bias) would remain undetected with such an approach. Second, inter-observer variability is generally greater than intra-observer variability, which would result in a less variable data set from which to generate reference limits. Finally, the two studies used different methods to determine reference intervals – Visser and colleagues used a parametric approach that discarded the upper and lower 2.5th percentiles, while we used a non-parametric approach, which tends to give slightly wider reference intervals than parametric methods.

We had multiple investigators submit data. We did not examine all aspects of inter-observer or intra-observer variability, as this has been examined for various echocardiographic variables previously, and for several of the investigators involved in our study [7,9,22–24]. Furthermore, unpublished data suggest that most cardiologists or clinicians routinely performing echocardiographic examinations obtain similar measurements for LA:Ao when measuring the same image from healthy dogs.[h] In only one primary analysis (LA:Ao_P) did one investigator (Investigator 1) provide measurements that differed statistically from three other investigators, but the magnitude of the difference was small (approximately 0.1 units), and not clinically important. Furthermore, when we examined the source of variation for this investigator, the wLA_P and LA_P were both smaller, rather than larger than most of the other investigators. Therefore, the reason for the larger LA:Ao_P was not a larger LA measurement, but a smaller Ao_P measurement. We examined the wAo and Ao_P measurements between investigators, and confirmed these suspicions. However, the other aortic measurements did not differ between investigators. When we examined whether Investigator 1 consistently measured aortic valve dimensions smaller than other investigators, we found that this investigator differed only from one other observer, who tended to measure the dimensions larger than the other investigators. Because we could not all image the same dogs and compare images, we cannot rule out the possibility that Investigator 1 imaged dogs differently. However, this investigator did provide measurements for 12/16 Boxers and 9/15 English setters. Of these, all 12 Boxers and three English setters had wAo<0.91. Importantly, the remaining four Boxers, imaged by other investigators, also had wAo<0.91, and two other English Setters also had wAo<0.91. Consequently, the small difference between data submitted by the investigators could represent differences in aortic size of the sample populations, rather than biased measurement. When we excluded this investigator from the calculation of reference intervals, we found a small decrease in the upper reference limit for $LA:Ao_P$ (from 1.70 to 1.65). Similarly, excluding these two breeds also decreased the upper reference limit for $LA:Ao_P$ from 1.70 to 1.66. However, given that LA:Ao estimates are commonly reported to one decimal point, these differences would be abolished by "rounding" of the values (producing an upper limit for $LA:Ao_P$ of 1.7). Therefore, our data provide a generalizable evaluation of LA:Ao in healthy dogs, which can be reasonably extrapolated to the canine population at large.

One of the breeds that commonly exceeded the historical $LA:Ao_{MAX(RPSA)}$ reference limit of 1.6 was the boxer. Previous studies have demonstrated that boxers have smaller aortae for their bodyweight than other breeds [25]. Our data support this observation, with all boxers in our study having wAo <1.0 and 13/16 having wAo <0.9. Examination of the data showed that, although wAo had no relationship with bodyweight, all but two boxers in our study fell below a wAo value of 0.9 in a plot of wAo vs bodyweight (**Supplementary Figure 2**). Similarly, the English setters and Beagles with large LA:Ao (>1.6) had wAo < 0.9, while English setters with normal LA:Ao had wAo > 0.9. This suggests that, rather than having large LA, some breeds, and some individuals within breeds have small aortae for their size. Indeed, all the dogs with LA:Ao >1.6 in our study, regardless of breed, had wAo <1.0 – in other words, their large LA:Ao was the result of a smaller-than-expected aorta, rather than a big left atrium. Therefore, clinicians might need to examine the aortic size for some dogs that appear to have mild or equivocal left atrial enlargement, based on LA:Ao calculations, before classifying such individuals as "abnormal", especially if no other abnormalities can be detected. If an individual has a wAo that is <1.0, clinicians should consider the possibility that the large LA:Ao is the result of a small aorta, rather than a big left atrium.

Somewhat surprisingly, 75% of our population had a wAo <1.0, and 62% had a wAo <0.95, regardless of their bodyweight or $LA:Ao_{MAX}$. This might suggest that our population was somewhat overweight (we did not estimate body condition scores for any dogs). However, boxers and setters are not commonly overweight – indeed, the English setters were mostly hunting dogs, imaged by two investigators, and the boxers were imaged by two investigators. Therefore, these dogs might represent populations that truly have small aortae (on occasion) for their body size. We cannot, with our study design, completely rule out the effect of investigator, or a breed-investigator interaction as a reason for our findings in English setters and boxers. However, our findings for boxers agree with previous observations of aortic size.

We did not examine relationships with age or sex. We did not record hydration status or blood pressure for any dogs. Neither age, nor sex have been shown to affect the variables of interest. We had no reason to suspect that our cohort of apparently healthy dogs should have hypertension, or be dehydrated.

In conclusion, we present more robust reference intervals for LA:Ao in dogs from two views and three distinct diastolic time points. We have shown that previously published upper reference limits for LA:Ao$_{MAX}$ might be slightly low and that LA:Ao obtained at different time-points or from different views are not interchangeable.

Conflicts of Interest

The authors have no conflict of interest to disclose.

Funding sources

This study was not funded by any agency.

Endnotes

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Table 1. Summary statistics for right parasternal short-axis LA:Ao_P measurements provided by 5 investigators

Investigator	n	Minimum	25th %	Median	75th %	Maximum
1	131	0.97	1.25	1.39	1.49	1.99
2	43	0.97	1.24	1.30	1.39	1.80
3	17	1.09	1.20	1.29	1.32	1.50
4	6	1.00	1.15	1.41	1.53	1.70
5	23	1.09	1.22	1.26	1.32	1.62
6	13	1.07	1.29	1.37	1.43	1.54

Investigator 1 differed from Investigators 2, 3 and 5 (P=0.02)

LA:Ao_P: Left-atrial-to-aortic ratio measured at the onset of atrial systole.

Table 2. Reference limits for LA:Ao measurements obtained from 2 views at different points in the cardiac cycle from 233 healthy adult dogs.

Variable (measurand)	Lower reference limit	90% Confidence interval of the lower reference limit	Upper reference limit	90% Confidence interval of the upper reference limit
$LA:Ao_{MAX\ (RPSA)}$	1.05	0.97-1.10	1.73	1.67-1.76
$LA:Ao_{P\ (RPSA)}$	1.04	0.97-1.08	1.70	1.62-1.83
$LA:Ao_{MIN\ (RPSA)}$	0.86	0.75-0.94	1.53	1.48-1.65
$LA:Ao_{MAX\ (RPLA)}$	1.40	1.33-1.49	2.11	2.07-2.17
wLA	0.97	0.92-1.07	1.57	1.54-1.62
$nLA_{MAX\ (RPSA)}$	0.72	0.7-0.8	1.17	1.15-1.2
$nLA_{MIN\ (RPSA)}$	0.53	0.47-0.55	0.89	0.85-0.92
$nLA_{P\ (RPSA)}$	0.65	0.58-0.7	1.07	1.05-1.09
$nLA_{MAX\ (RPLA)}$	1.15	1.09-1.17	1.73	1.64-1.79

LA:Ao: Left-atrial-to-aortic ratio; RPSA: Right parasternal short-axis view; RPLA: Right parasternal long-axis view; $LA:Ao_{MAX}$: Left-atrial-to-aortic ratio measured at the maximal left atrial diameter (early diastole); $LA:Ao_{MIN}$: Left-atrial-to-aortic ratio measured at the onset of ventricular systole; wLA: left atrial-to-weight-based aortic ratio; nLA_{MAX}: maximum left atrial diameter indexed to bodyweight; nLA_{MIN}: minimal left atrial diameter indexed to bodyweight; nLA_P: left atrial diameter at the onset of atrial systole indexed to bodyweight.

w

Table 3. Scaling exponents, proportionality constants and upper reference limits for canine left atrial measurements indexed to bodyweight obtained from 233 dogs.

Variable (measurand)	Scaling exponent (b)[a]	Proportionality constant (m)[a]	Upper reference limit	90% Confidence interval of the upper reference limit
$nLA_{MAX\ (RPSA)}$	0.355	0.989	1.17	1.15-1.2
$nLA_{P\ (RPSA)}$	0.346	0.937	1.07	1.05-1.09
$nLA_{MIN\ (RPSA)}$	0.387	0.845	0.89	0.85-0.92
$nLA_{MAX\ (RPLA)}$	0.31	1.14	1.73	1.64-1.79

[a] Scaling exponent and constant fit the regression equation $Y = mX^b$

RPSA: Right parasternal short-axis view; RPLA: Right parasternal long-axis view; nLA_{MAX}: maximum left atrial diameter indexed to bodyweight; nLA_{MIN}: minimal left atrial diameter indexed to bodyweight; nLA_P: left atrial diameter at the onset of atrial systole indexed to bodyweight.

Figure Legends

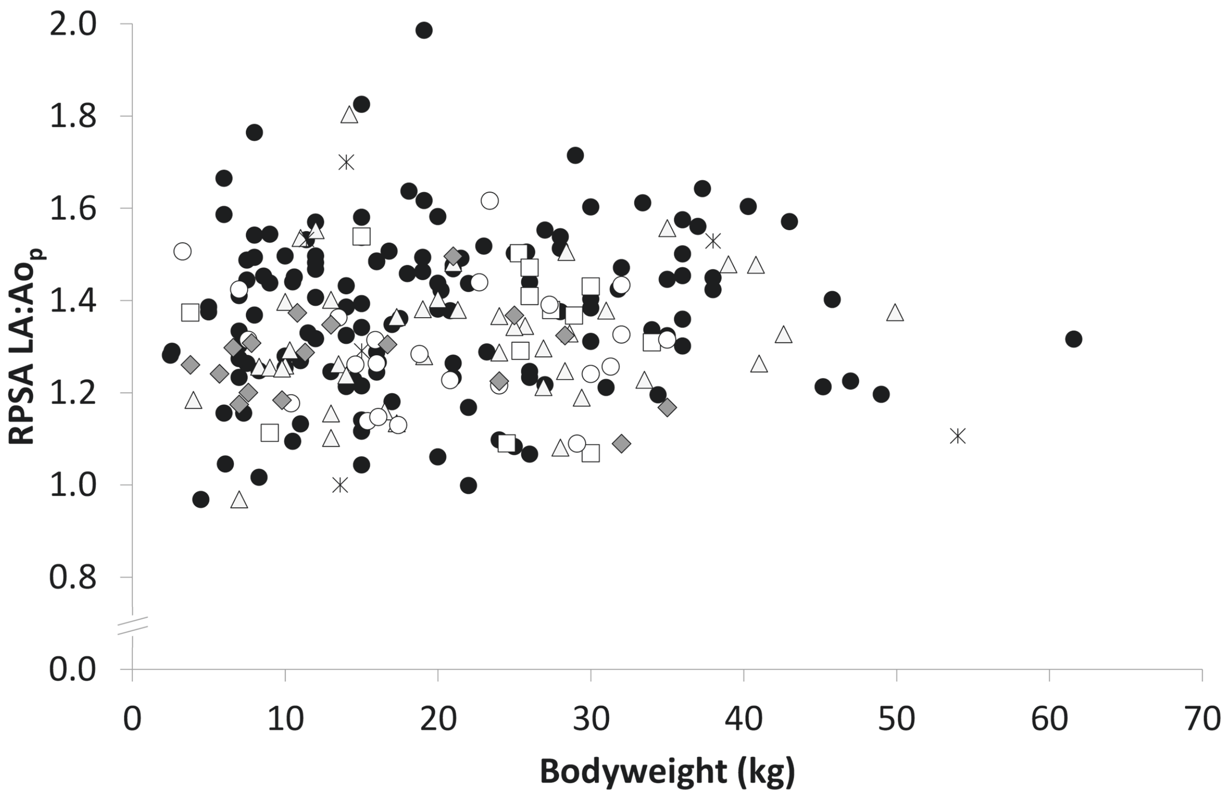
Figure 1. Left-atrial-to-aortic ratio measurements for six investigators, obtained at the P wave from the right parasternal short-axis view. Investigator 1 (black circles) had slightly higher left-atrial-to-aortic ratio (LA:Ao) measurements than investigators 2 (triangles) and 3 (diamonds) (P=0.02). RPSA – right parasternal short-axis, LA:Ao_{P} – LA:Ao obtained at the P wave of the ECG

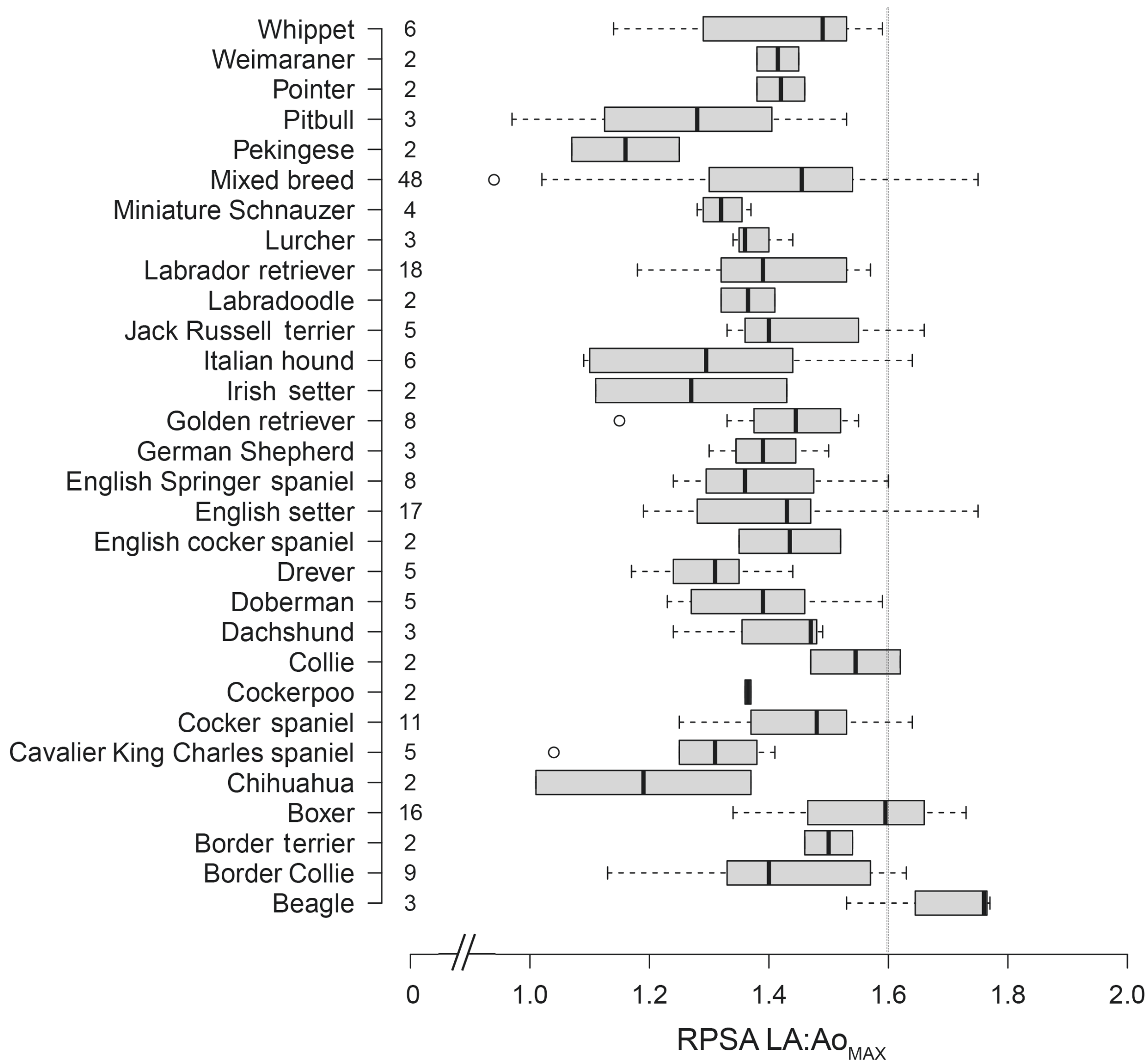
Figure 2. **(A)** Box and whisker plots of the left-atrial-to-aortic ratio measurements, obtained in early diastole (LA:Ao_{MAX}), for every breed (and mixed-breed dogs) included in the study represented by more than one individual. The boxes denote the quartiles, the line denotes the median, the whiskers extend to 1.5x the interquartile range and circles denote values falling outside of the whiskers. **(B)** Dot plots showing the distribution of LA:Ao_{MAX} for Beagles, Boxers and English setters.

Figure 3. Weight-based aortic (wAo) measurements plotted against left-atrial-to-aortic ratios obtained from the right parasternal short-axis view in early diastole (LA:Ao_{MAX}) display a modest negative relationship. Most dogs with LA:Ao_{MAX}>1.6 had a wAo <0.9 (lower right quadrant), especially English setters (open squares), Boxers (grey diamonds) and Beagles (open triangles).

Supplementary Figure 1. Left-atrial-to-aortic ratios, obtained from the right parasternal short axis view in early diastole (A, RPSA LA:Ao_{MAX}), at the P wave (B, RPSA LA:Ao_{P}), at the onset of systole (C, RPSA LA:Ao_{MIN}); Left-atrial-to-aortic ratio obtained from the right parasternal long-axis view in early diastole (D, RPLA LA:Ao_{MAX}); weight-based left atrial measurements, obtained from the right parasternal short-axis view in early diastole (E, RPSA wLA_{MAX}); and weight-based left ventricular measurements, obtained from the right parasternal short-axis view in diastole (E, RPSA wLV). No variables demonstrated any relationships with bodyweight.

Supplementary Figure 2. Weight-based aortic measurements (wAo) plotted against bodyweight. Boxers (grey diamonds) and Beagles (open triangles) consistently fell below a wAo of 0.95. English setters (open squares) were scattered above and below this value.


2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.0
RPSA LA:Ao$_p$
0
10
20
30
40
50
60
70
Bodyweight (kg)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Weimaraner 2
Pointer 2
Pitbull 3
Pekingese 2
Mixed breed 48
Miniature Schnauzer 4
Lurcher 3
Labrador retriever 18
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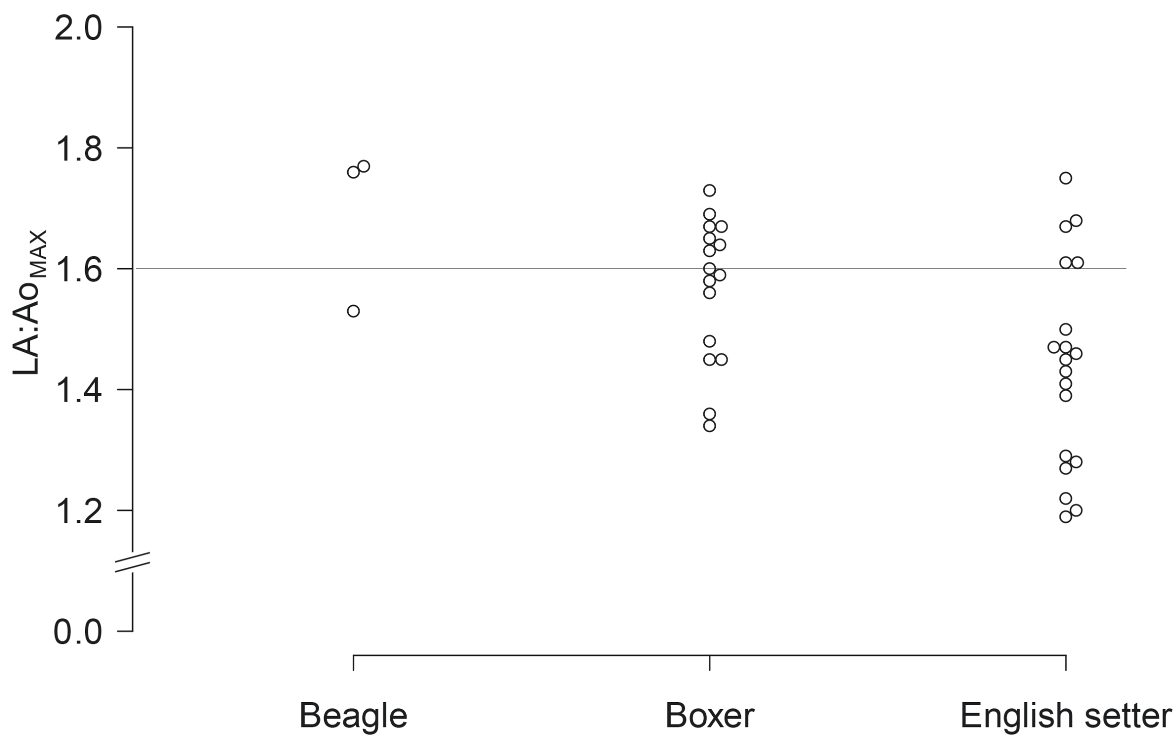
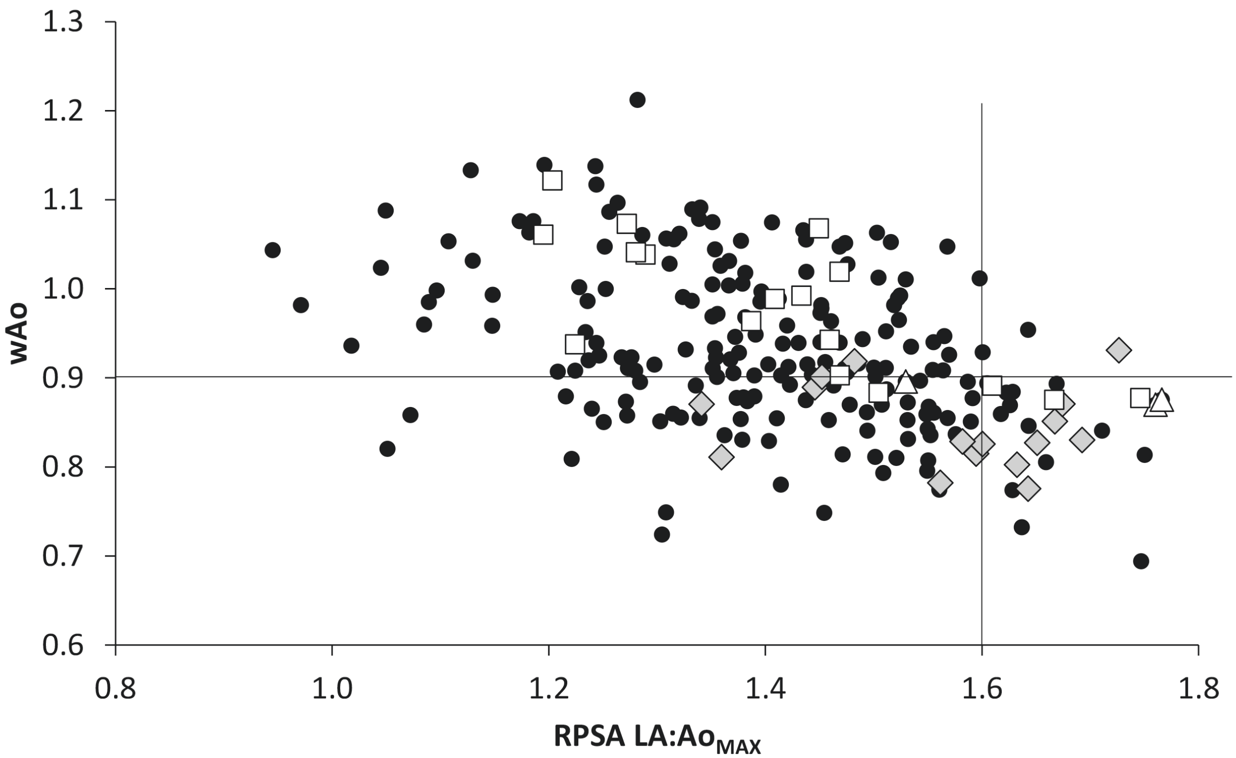
Jack Russell terrier 5
Italian hound 6
Irish setter 2
Golden retriever 8
German Shepherd 3
English Springer spaniel 8
English setter 17
English cocker spaniel 2
Drever 5
Doberman 5
Dachshund 3
Collie 2
Cockerpoo 2
Cocker spaniel 11
Cavalier King Charles spaniel 5
Chihuahua 2
Boxer 16
Border terrier 2
Border Collie 9
Beagle 3
0
1.0
1.2
1.4
1.6
1.8
2.0
RPSA LA:Ao$_{MAX}$



2.0
1.8
1.6
1.4
1.2
0.0
LA:Ao$_{MAX}$
Beagle
Boxer
English setter


1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
wAo
0.8
1.0
1.2
1.4
1.6
1.8
RPSA LA:Ao$_{MAX}$