Usefulness of the Indexed Effective Orifice Area in the Assessment of Subaortic Stenosis in the Dog

Marie Claude Bélanger, Rocky Di Fruscia, Jean G. Dumesnil, and Philippe Pibarot

To evaluate the usefulness of the Doppler-derived effective orifice area (EOA) in assessing the hemodynamic severity of subaortic stenosis (SAS) in dogs, 2-dimensional and Doppler echocardiographic examinations were performed in 16 dogs with SAS, 22 normal adult dogs, and 22 normal puppies. The EOA was calculated by the continuity equation using the stroke volume determined in the right ventricular outflow tract. The EOA was significantly lower ($P < .001$) in the SAS dogs (0.76 ± 0.45 cm$^2$) and in the normal puppies (1.58 ± 1.00 cm$^2$) than in the normal adult dogs (2.34 ± 0.78 cm$^2$). The EOA index for body surface area (IEOA) was significantly lower (0.89 ± 0.48 cm$^2$/m$^2$) in SAS dogs than in the normal puppies (2.42 ± 0.85 cm$^2$/m$^2$) or adults (2.22 ± 0.76 cm$^2$/m$^2$). The normal dogs (adults and puppies) had an IEOA of ≥1.25 cm$^2$/m$^2$. Among the demographic and echocardiographic parameters measured in this study, only the indexed EOA was significantly associated ($P = .03$) with the occurrence of adverse events (eg, syncope, episodic weakness, ventricular arrhythmias). This study demonstrates the usefulness and feasibility of the indexed EOA as measured by Doppler echocardiography for noninvasive assessment of SAS severity in dogs.

Key words: Doppler echocardiography; Heart valve disease; Hemodynamics.

Subaortic stenosis (SAS) is a common congenital malformation of the canine heart. It is characterized by a fibrous (nodule, band, or anulus) narrowing of the left ventricular outflow tract. SAS is seen most frequently in large breeds of dogs, and hereditary transmission has been identified in the Newfoundland dog.1,2 The condition usually is detected incidentally upon the first physical examination of a puppy.

Cardiac catheterization, although invasive and expensive, is the gold standard in the diagnosis of SAS. Unfortunately, this method requires general anesthesia in dogs, which can cause a reduction in the pressure gradient of up to 50% when compared with the gradient in the conscious dog.3 In veterinary cardiology, the severity of SAS is evaluated by measuring increased velocity (V) and turbulence of flow beyond the stenotic area. The pressure gradient ($\Delta P$) then is calculated using the modified Bernoulli equation: $\Delta P_{\text{m} \text{ax}} = 4V^2$. The peak transstenotic pressure gradient is used to estimate the severity of the condition and to establish a prognosis. SAS generally is considered mild, moderate, or severe when the peak gradient is <36 mm Hg, 36–80 mm Hg, and >80 mm Hg, respectively.3,4 However, because it is highly flow dependent, the pressure gradient is not an accurate indicator of stenosis severity in the presence of abnormally low or high transvalvular flow.5-7 In human medicine, there is a general consensus that it is preferable to assess the severity of aortic stenosis using the stenotic effective orifice area (EOA) because it is much less flow dependent than the gradient.8-11 The EOA represents the cross-sectional area occupied by the flow at the level of the aortic valve leaflets (ie, the narrowest section of the stenotic jet) and is therefore slightly smaller (by 15–20%) than the anatomic area of the stenotic lesion that can be measured by 2-dimensional echocardiographic planimetry.12-15 The EOA can be determined by Doppler echocardiography using the continuity equation or by catheter using the Gorlin equation, and the agreement between these 2 methods is very high.14-16

The main objective of this study was to apply the EOA concept for the assessment of SAS severity in dogs and to determine its clinical usefulness. For this purpose, we determined and compared the EOA in dogs with SAS, in normal adult dogs, and in normal puppies. Then, we evaluated the predictive value of the EOA with regard to the occurrence of adverse events in dogs with SAS.

Methods

Animals

Sixteen dogs with isolated SAS were included in this study. The diagnosis of SAS was based on the presence of a systolic ejection murmur at the aortic auscultation area and flow acceleration across the left ventricular outflow tract (LVOT) as measured by continuous-wave Doppler examination; maximal LVOT velocity of >2 m/s corresponds to a peak transvalvular gradient of >16 mm Hg. The LVOT also was scanned with pulsed-wave Doppler to ascertain that the acceleration was at the subvalvular level. Study animals also included 2 client-owned normal adult dogs (>1 year old) of various large and giant breeds and mixed breeds and 22 normal puppies (age range: 2–6 months). These dogs were defined as normal based on a normal history, physical examination, cardiac auscultation, and 2-dimensional, M-mode, and Doppler echocardiography.

Doppler Echocardiographic Measurements

All echocardiographic examinations were performed by the same cardiologist (RDF) with an Ultramark 9 ATL ultrasound system equipped with a 5-MHz or 2.5-MHz phased array transducer. The examinations were carried out without sedation.

Assessment of Stenosis Severity. The continuity equation is based on the theory of conservation of mass applied to fluids, which specifies that flow through a given area of a conduit must equal flow through an adjacent area over a given time. Accordingly, the stroke volume
Effective Orifice Area in SAS

(SV) ejected through the LVOT during systole is equal to the flow that passes through the EOA of the aortic valve as expressed by this equation:

\[ SV = A_{EOA} \times VT_{LVOT} = EOA \times VT_{AO} \]

where \( A_{EOA} \) is the cross-sectional area of the LVOT calculated from the LVOT diameter as measured by 2-dimensional echocardiography, \( VT_{LVOT} \) is the velocity-time integral (VTI) of the LVOT pulsed-Doppler signal, and \( VT_{AO} \) is the velocity-time integral of the aortic jet continuous-wave Doppler signal. This equation is used to calculate the valvular EOA in human patients with aortic valve stenosis, which is by far the most common cause of aortic stenosis in humans.\(^{19,20}\) In dogs, however, the stenosis is located at the subvalvular level in 90% of cases.\(^{18}\) It is possible to adapt the continuity equation for the determination of EOA in subaortic stenosis. Stenosis is located within the LVOT, and thus stroke volume cannot be determined in the LVOT because it would be markedly overestimated. Alternatively, others have proposed and validated the use of stroke volume measured at the level of the mitral valve annulus or at the level of the right ventricular outflow tract (RVOT) in the continuity equation.\(^{14,15} \) In the present study, the EOA of the subaortic stenosis was calculated using stroke volume determined in the RVOT as follows:

\[ EOA = \frac{SV}{VT_{AO}} = \frac{A_{EOA} \times VT_{LVOT}}{VT_{AO}} \]

\( A_{EOA} \) is the cross-sectional area of the RVOT calculated from the RVOT diameter (\( D_{RVOT} \)) measured from the right parasternal short-axis view at the base of the pulmonary valve leaflets from inner edge to inner edge during early systole using the following equation:

\[ A_{EOA} = \pi D_{RVOT}^2 / 4 \]

RVOT velocity was obtained from the same view using pulsed-wave Doppler with the sample volume positioned just beneath the pulmonic valve. The maximal velocities of the spectral envelope were traced for measurement of the RVOT velocity time integral (VTI\(_{RVOT}\)). A minimum of 5 consecutive cardiac cycles were measured and averaged to minimize the variation of VT\(_{LVOT}\) due to the respiratory cycle. The continuous-wave Doppler velocity signal of the subaortic stenotic jet was recorded from the left apical 4-chamber view. Care was taken to align the Doppler beam with the jet (intercept angle <20°). Five cardiac cycles with the highest velocity and most well-defined outer velocity envelope were selected for measurement and averaging of peak and mean jet velocities and VTI. The peak and mean transstenotic pressure gradients were calculated by the modified Bernoulli equation (\( \Delta P = 4V^2 \)) as previously described and validated in dogs with SAS.\(^{18} \)

Cardiac output was calculated from the product of heart rate and stroke volume measured by Doppler in the RVOT and was indexed for body surface area (BSA) to take into account body size variation among dogs. BSA was calculated from body weight using the formula BSA = (10.1 × \( w^{0.42} \)) × 10⁻⁴, where \( w \) is body weight in grams.\(^{21} \)

Aortic regurgitation was assessed using the width of the regurgitant jet at its origin relative to the dimension of the LVOT. Mild regurgitation corresponded to a very narrow jet, which only extended a short distance below the aortic valve. Moderate regurgitation corresponded to a longer and larger jet that remained narrow (<20% of the LVOT diameter) at the level of the aortic annulus and did not extend beyond the tip of the mitral valve leaflets. Severe aortic regurgitation corresponded to a jet larger than 20% of the LVOT diameter.\(^{22} \) Mitral regurgitation was examined by color Doppler in the right parasternal, apical 4-chamber, and apical 2-chamber views and was assessed by a semiquantitative method, which compares the maximal jet area of the regurgitant mitral flow to the left atrial size.\(^{23,24} \) Jet areas of less than 20% of the left atrial area corresponded to mild regurgitation. Values of 20–40% corresponded to moderate regurgitation, and values larger than 40% were considered severe.

**Assessment of Left Ventricular Geometry.** A major consequence of aortic stenosis is the development of concentric left ventricular hypertrophy, which is an important risk factor for cardiovascular morbidity and mortality.\(^{25} \) M-mode echocardiographic measurements were performed in each dog in accordance with the recommendations of the American Society of Echocardiography (ASE).\(^{26,27} \) From a parasternal left ventricular long-axis view, standard recordings of left ventricular M-mode echocardiograms were obtained. Left ventricular minor axis internal dimension and posterior wall and septal thickness were measured from leading edge to leading edge at end diastole. The M-mode cursor was positioned at the tip of the mitral valve leaflets orthogonal to the long axis of the left ventricle. Left ventricular mass was calculated using the corrected formula of the American Society of Echocardiography and was indexed for BSA.\(^{28,29} \)

\[ \text{LV mass} = 0.8 \times [1.04 \times ((\text{LVPWT} + \text{IVST} + \text{LVID})^3 - (\text{LVID})^3)] + 0.6 \]

where LVPWT, IVST, and LVID are the end-diastolic left ventricular (LV) posterior wall thickness, interventricular septum thickness, and LV internal dimension, respectively. Some controversy exists about which method should be used to estimate LV mass in dogs. Wyatt et al.\(^{30} \) showed that 2-dimensional formulae are superior to M-mode formulae. However, Chen\(^{31} \) demonstrated that the corrected ASE formula using M-mode measurements provides an accurate estimate of LV mass in dogs. We selected the M-mode method for the purpose of this study because in our laboratory the interobserver variability appeared to be lower than that of the 2-dimensional method. The relative wall thickness (RWT) was calculated to estimate the degree of concentric hypertrophy:

\[ \text{RWT} = \frac{\text{LVPWT}}{\text{(LVPWT} + \text{LVID)/2}} \]

**Assessment of Adverse Events.** Adverse events associated with SAS (episodic weakness, syncope, ventricular arrhythmias) were recorded as reported by the owners or observed on physical examination, ECG, or both. Ventricular arrhythmias were assessed by ECG on each animal for a period of 30 minutes. More than 3 ventricular premature complexes per minute, couplets, or triplets were considered abnormal.

**Statistical Analysis**

A 1-way analysis of variance was used to compare the echocardiographic data among the 3 groups: normal adults, normal puppies, and SAS dogs. If normality or equality of variance tests failed, analysis of variance was performed on the log transform of the data. Statistical analysis of the association of variables was performed with the Pearson correlation coefficient or the determination coefficient adjusted for degrees of freedom when the relationship was linear or nonlinear, respectively. Graphs were constructed with the best-fit regression equation using curve-fitting software.\(^4 \) P-values of <.05 were considered significant.

**Results**

**Comparison of Demographic Data**

Table 1 shows the demographic characteristics for the 3 groups of dogs. The puppies were younger and therefore had significantly lower weight and BSA when compared with the normal adult and SAS dogs. In addition, the mean values of age, weight, and BSA were significantly lower in the SAS group than in the normal adult group.
study had moderate or severe aortic, mitral, or pulmonic valve regurgitation.

The peak and mean transstenotic gradients were markedly higher in the SAS dogs than in the normal adults or puppies. There was no significant difference in gradients between the normal adults and the normal puppies. The Doppler echocardiographic measurement of EOA was feasible for all dogs in the study. The SAS dogs had significantly lower EOA when compared with the normal dogs. The normal puppies also had lower EOA than did the normal adults. However, when indexed for BSA, the EOA was similar in normal adults and normal puppies but markedly lower in the SAS dogs.

**Dependence of Gradients on the Indexed EOA**

There was a strong inverse exponential relationship between peak or mean gradients and EOA (Fig 1). Moreover, this relationship was stronger when the EOA was indexed for BSA (Fig 2). These relationships indicate that pressure gradients increase dramatically when EOA is <1.00 cm² or when indexed EOA is <0.80–0.90 cm²/m². Most normal or SAS dogs are distributed on the same curve (Fig 2). However, their localization on the curve is different. All normal adult dogs and puppies have an indexed EOA of ≥1.25 cm²/m² and therefore have low gradients regardless of their indexed EOA. However, most SAS dogs have an indexed EOA of <1.00 cm²/m² and therefore are on the steep portion of the exponent curve where the gradients are very high and can increase dramatically with further decreases in the indexed EOA. These relationships and the data presented in Table 1 indicate the importance of indexing EOA for BSA. Several of the normal puppies would have been classified as having aortic stenosis based on EOA (Fig 1).

This potential misclassification is prevented by indexing EOA for BSA (Fig 2).

**Assessment of Adverse Events**

Of the 16 dogs with SAS, 6 (38%) had adverse events: 3 dogs had a history of syncope, 4 had episodic weakness, and 4 had occasional multifocal premature ventricular beats during ECG. One dog died suddenly 4 weeks after presentation. Table 3 includes a comparison of Doppler echocardiographic data in the SAS dogs depending on the presence or absence of adverse events. Indexed EOA was not different between the two groups. Of the 16 dogs with SAS, 1 dog had frequent syncope and died suddenly 4 weeks after echocardiographic examination. This dog had a peak gradient of 53 mm Hg, which is not considered severe based on the criteria currently used in veterinary medicine (peak gradient >80 mm Hg).

However, this dog's indexed EOA was 0.38 cm²/m², which is considered severe in human patients with aortic stenosis on the basis of generally accepted criteria (indexed EOA <0.60 cm²/m²). Apparently, the gradient underestimated the severity of the stenosis in this dog because of abnormally low left ventricular output (cardiac index: 2.03 L/min/m²). None of the normal dogs in this study had a cardiac index of <2.5 L/min/m², and the normal range of cardiac index reported for normal conscious dogs is 3.1–4.7 L/min/m².

**Comparison of Doppler Echocardiographic Data**

Table 2 shows the echocardiographic data for the 3 groups. As expected, normal puppies had significantly lower LV mass than did normal adults. However, this difference did not persist when LV mass was indexed for BSA. SAS dogs had significantly greater LV mass and LV mass index when compared with normal adults or puppies. SAS dogs also had a higher degree of concentric LV hypertrophy, as indicated by the significantly higher relative wall thickness ratio, when compared with normal adults or puppies.

The normal puppies had significantly higher heart rate, lower stroke volume, and lower cardiac output when compared with normal adults and SAS dogs. The cardiac index, however, was similar in normal puppies and adult dogs. The SAS dogs had similar heart rate, stroke volume, and cardiac output but higher cardiac index when compared with the normal adult dogs.

Based on color Doppler echocardiography, 14 of the 44 normal dogs (32%) and 13 of the 16 SAS dogs (81%) had mild aortic regurgitation. None of the dogs included in the
Table 1. Demographic characteristics of the normal adult dogs (n = 22), normal puppies (n = 22), and dogs with subaortic stenosis (SAS) (n = 16).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Adult Dogs</th>
<th>Normal Puppies</th>
<th>SAS Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>14 (64%)</td>
<td>9 (41%)</td>
<td>7 (44%)</td>
</tr>
<tr>
<td>Male</td>
<td>8 (36%)</td>
<td>13 (59%)</td>
<td>9 (56%)</td>
</tr>
<tr>
<td>Age (months)*</td>
<td>52 ± 39, 48 (24–60)</td>
<td>4 ± 2, 4 (2–6)</td>
<td>16 ± 8* 8 (3–31)</td>
</tr>
<tr>
<td>Weight (kg)*</td>
<td>34 ± 7, 33 (30–38)</td>
<td>16 ± 8* 18 (7–22)</td>
<td>26 ± 8* 28 (20–33)</td>
</tr>
<tr>
<td>Body surface area (m²)*</td>
<td>1.05 ± 0.13, 1.04 (0.95–1.12)</td>
<td>0.61 ± 0.23* 0.69 (0.35–0.78)</td>
<td>0.87 ± 0.20* 0.92 (0.74–1.02)</td>
</tr>
</tbody>
</table>

* Data are expressed as mean value ± SD and median (25–75% quantiles).

Discussion

Assessment of Stenosis Severity

Assessment of the severity of SAS in dogs is challenging. The condition usually is subclinical, even in severe cases, and physical findings other than a cardiac murmur can be misleading. In veterinary medicine, assessment of the severity of SAS has been made largely on the basis of the Doppler- or catheter-derived transstenotic pressure gradients, which are inaccurate in many situations in humans.14,33–35 As stated by Judge and Otto,36 "The importance of valve area in clinical evaluation is highlighted by the observation that, depending upon transaortic volume flow, a maximum gradient of 50 mm Hg can be seen with mild, moderate or severe reduction in valve area." Physiologically, pressure gradients are determined by 2 factors: the EOA of the stenosis and the transstenotic flow. In turn, transstenotic flow is related to cardiac output, which at rest is largely determined by BSA. Hence, it is logical that indexed EOA (ie, EOA divided by BSA) correlates best with the pressure gradient. The relationship we found between pressure gradients and indexed EOA in dogs with SAS is very similar to that found in human patients with aortic valve stenosis.37–40

Peak and mean pressure gradients largely are dependent on quantitative transstenotic flow. Accordingly, the gradients would overestimate the severity of the stenosis in presence of abnormally high cardiac output and underestimate the severity in presence of abnormally low cardiac output. Cardiac output and thus transstenotic flow may be abnormally high under several conditions, including hyperthermia, pain, stress, and fear. The environmental setting required for echocardiographic examination likely represents a stressful event for most dogs examined. This stress probably increases cardiac output above the normal resting value and thus may increase the pressure gradient in SAS dogs, which in turn may cause an overestimation of the stenosis. Although some of the normal dogs likely experienced stress related to the procedure and had high cardiac index, none of these dogs had a substantial gradient across the LVOT. In the absence of LVOT obstruction, a marked increase in flow due to stress or exercise will only result in a minimal increase in pressure gradient.41–45 In contrast, a

Table 2. Doppler echocardiographic data* in normal adult dogs (n = 22), normal puppies (n = 22), and dogs with subaortic stenosis (SAS) (n = 16).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Adult Dogs</th>
<th>Normal Puppies</th>
<th>SAS Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass (g)</td>
<td>133 ± 30, 133 (116–150)</td>
<td>49 ± 27* 54 (22–72)</td>
<td>160 ± 62* 173 (126–201)</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>127 ± 29, 123 (104–155)</td>
<td>75 ± 18* 77 (61–88)</td>
<td>181 ± 58* 185 (132–225)</td>
</tr>
<tr>
<td>Relative wall thickness ratio</td>
<td>0.43 ± 0.05, 0.43 (0.40–0.47)</td>
<td>0.40 ± 0.06, 0.40 (0.34–0.43)</td>
<td>0.51 ± 0.11*, 0.50 (0.42–0.60)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>99 ± 24, 98 (84–112)</td>
<td>139 ± 29*, 141 (120–163)</td>
<td>109 ± 20* 111 (97–123)</td>
</tr>
<tr>
<td>Pulmonary VTI (cm)</td>
<td>11 ± 3, 11 (9–12)</td>
<td>10 ± 3, 11 (8–12)</td>
<td>13 ± 4*, 13 (11–15)</td>
</tr>
<tr>
<td>Stroke volume (mL)</td>
<td>37 ± 11, 35 (28–43)</td>
<td>19 ± 12, 19 (8–30)</td>
<td>35 ± 15* 32 (22–44)</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>3.62 ± 1.16, 3.56 (2.59–3.99)</td>
<td>2.44 ± 1.38*, 2.28 (1.25–3.51)</td>
<td>3.63 ± 1.30*, 3.67 (2.69–5.10)</td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>3.47 ± 1.24, 3.13 (2.60–4.25)</td>
<td>3.81 ± 1.06, 3.71 (3.10–4.62)</td>
<td>4.24 ± 1.17, 4.39 (3.23–5.02)</td>
</tr>
<tr>
<td>Peak aortic velocity (m/s)</td>
<td>1.24 ± 0.21, 1.23 (1.12–1.41)</td>
<td>1.05 ± 0.14, 1.06 (1.00–1.12)</td>
<td>4.08 ± 1.30*, 4.20 (3.01–4.84)</td>
</tr>
<tr>
<td>Aortic VTI (cm)</td>
<td>16 ± 3, 16 (15–17)</td>
<td>12 ± 2.2, 12 (10–13)</td>
<td>58 ± 25* 61 (38–72)</td>
</tr>
<tr>
<td>Peak gradient (mm Hg)</td>
<td>6 ± 2, 6 (5–8)</td>
<td>5 ± 1.4, 4 (4–5)</td>
<td>73 ± 43*, 71 (37–94)</td>
</tr>
<tr>
<td>Mean gradient (mm Hg)</td>
<td>3 ± 1, 3 (3–4)</td>
<td>2 ± 1.2 (2–3)</td>
<td>42 ± 21* 45 (28–55)</td>
</tr>
<tr>
<td>EOA (cm²)</td>
<td>2.34 ± 0.78, 2.01 (1.74–3.09)</td>
<td>1.58 ± 0.10, 1.41 (0.71–2.16)</td>
<td>0.76 ± 0.45*, 0.63 (0.43–0.96)</td>
</tr>
<tr>
<td>Indexed EOA (cm²/m²)</td>
<td>2.22 ± 0.76, 2.03 (1.61–3.67)</td>
<td>2.42 ± 0.85, 2.23 (1.80–2.93)</td>
<td>0.89 ± 0.48*, 0.74 (0.51–1.27)</td>
</tr>
</tbody>
</table>

* Data are expressed as mean value ± SD and median (25–75% quantiles).

LV, left ventricular; VTI, velocity-time integral; EOA, effective orifice area.

Significant difference between normal puppies and normal adult dogs.

Significant difference between SAS dogs and normal adult dogs.

Significant difference between SAS dogs and normal puppies.
Table 3. Doppler echocardiographic data in dogs with subaortic stenosis with regard to the presence (n = 6) or absence (n = 10) of adverse events.

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>No Adverse Events</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LV mass (g)</strong></td>
<td>152 ± 62, 166 (142–190)</td>
<td>174 ± 63, 173 (109–236)</td>
</tr>
<tr>
<td><strong>LV mass index (g/m²)</strong></td>
<td>175 ± 57, 182 (144–206)</td>
<td>190 ± 64, 192 (120–249)</td>
</tr>
<tr>
<td>Relative wall thickness ratio</td>
<td>0.49 ± 0.08, 0.49 (0.42–0.57)</td>
<td>0.53 ± 0.14, 0.56 (0.43–0.65)</td>
</tr>
<tr>
<td>Heart rate (bpm/min)</td>
<td>106 ± 22, 102 (93–120)</td>
<td>113 ± 17, 113 (98–123)</td>
</tr>
<tr>
<td>Stroke volume (mL)</td>
<td>32 ± 16, 30 (21–44)</td>
<td>38 ± 12, 37 (31–44)</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>3.14 ± 1.09, 2.97 (2.57–3.70)</td>
<td>4.28 ± 1.36, 4.59 (3.84–5.40)</td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>3.89 ± 0.77, 3.87 (3.18–4.56)</td>
<td>4.71 ± 1.50, 5.02 (4.33–5.75)</td>
</tr>
<tr>
<td>Peak gradient (mm Hg)</td>
<td>59 ± 46, 50 (25–72)</td>
<td>96 ± 30, 90 (80–127)</td>
</tr>
<tr>
<td>Mean gradient (mm Hg)</td>
<td>37 ± 24, 34 (17–52)</td>
<td>51 ± 12, 53 (50–57)</td>
</tr>
<tr>
<td>EOA (cm²)</td>
<td>0.90 ± 0.51, 0.81 (0.60–1.15)</td>
<td>0.51 ± 0.15, 0.52 (0.35–0.61)</td>
</tr>
<tr>
<td>Indexed EOA (cm²/m²)</td>
<td>1.08 ± 0.51, 1.19 (0.57–1.38)</td>
<td>0.57 ± 0.18, 0.57 (0.38–0.73)</td>
</tr>
</tbody>
</table>

* Data are expressed as mean value ± SD and median (25–75% quartiles).

**LV, left ventricular; EOA, effective orifice area.**

A small increase in flow across a stenotic orifice will cause a dramatic increase in the pressure gradient.

Longstanding severe SAS can cause a decrease in LV systolic function because of the chronic afterload excess. Dogs with severe SAS, depressed LV function, and low cardiac output will exhibit only mildly or moderately increased pressure gradients. Human patients with severe aortic stenosis, as determined by an indexed EOA of <0.60 cm²/m² and concomitant low ejection fraction (<50%) and low pressure gradient (mean gradient <30 mm Hg), have a markedly higher risk of morbidity and mortality. Hence, when the peak pressure gradient alone was used to classify patients with severe versus mild to moderate stenosis, 19% of the patients with severe stenosis were erroneously considered to have clinically insignificant disease. In these situations of abnormally low or high cardiac output, the EOA provides a more accurate estimate of the severity of the stenosis than does the pressure gradient because EOA is much less flow dependent. Therefore, measurement of indexed EOA is recommended in dogs with SAS with abnormally high or low cardiac index, especially in moderate to severe cases.

In human medicine, EOA should be indexed for BSA to take into account the cardiac output requirements of the patient. Hence, a stenosis with an EOA of 1.0 cm² can be relatively well tolerated in a sedentary patient with a BSA of ≤1.5 m², whereas stenosis could cause severe symptoms in a patient with a BSA of >2.0 m². The indexing of EOA for BSA is even more important in veterinary medicine because of the major variations in body size that occur depending on age and breed. An indexed EOA of 1.25 cm²/m² can be considered normal. The stenosis becomes important from a hemodynamic standpoint when the indexed EOA is <1.0 cm²/m². Below this threshold, the gradient and thus the systolic wall stress increases markedly.

**Assessment of Adverse Events**

In human patients with aortic valve stenosis, several factors are associated with the occurrence of symptoms or adverse clinical outcome, including the patient's age, concomitantly...
itant coronary artery disease, transvalvular peak velocity, EOA, indexed EOA, ejection fraction, and relative wall thickness ratio. In this study of dogs with SAS, only indexed EOA was significantly associated with the occurrence of adverse events. Based on the results of previous studies in humans and of the present study, dogs with SAS that have an indexed EOA of <0.60 cm²/m² should be monitored more closely and eventually should be considered for therapeutic intervention, especially if clinical signs or ventricular arrhythmias are present. However, because of the relatively small number of dogs with SAS included in the present study, additional studies with larger numbers of dogs will be necessary to further evaluate the predictive value of indexed EOA and to confirm the critical threshold below which SAS should be considered severe.

Study Limitations

Lchmkulh and Bonagura showed that the subcostal view was optimal for assessment of maximal aortic velocity in 83% of dogs with SAS. Gew chose to use the left apical view because it was better tolerated by sedated dogs. The subcostal view sometimes is difficult to obtain in large, anxious, conscious dogs with tense abdomens. Doppler echocardiographic measurements were performed with the left apical window, and we cannot be certain that true maximal velocities were always recorded. However, the close correlation (r = 0.87) obtained between the gradient and indexed EOA supports the validity of this method.

The main limitation of this study is the absence of a "gold standard" to validate the Doppler echocardiographic measurement of EOA. Nonetheless, measurement of EOA using the continuity equation method has been extensively validated in humans with aortic valve stenosis as well as in dogs with experimentally induced valvular or supravalvular aortic stenosis. The high reproducibility of the EOA measurement has also been demonstrated in dogs with supravalvular stenosis by Kitabatake et al, who reported intraobserver and interobserver variability coefficients of 3.8% and 4.0%, respectively. These results are similar to those reported for humans with valvular aortic stenosis (ie, intra- and interobserver variability of <5% in experienced laboratories). In the present study, this method was applied to dogs with SAS. For this purpose, we used right ventricular (RV) stroke volume in the continuity equation instead of stroke volume determined in the LVOT as suggested in previous studies in humans. In the absence of aortic or pulmonary regurgitation, RV stroke volume averaged over several cycles is identical to LV stroke volume. In an experimental study performed in dogs, Stewart et al found a very high correlation and agreement between stroke volume determined by Doppler echocardiography in the RVOT (r = 0.93) or LVOT (r = 0.98) and that determined invasively with a flow meter. Brown et al also found high correlation between RVOT stroke volume and LVOT stroke volume, as determined by Doppler echocardiography in dogs. However, RVOT stroke volume tended to underestimate LVOT stroke volume. This overestimation may be due to errors in the measurement of RVOT diameter, averaging over a small number of cycles when measuring the RVOT velocity-time integral, pulmonic regurgitation, or other unknown factors. Most errors in the estimation of RVOT stroke volume probably are due to errors in the measurement of RVOT diameter. Newer ultrasound systems provide better 2-dimensional image resolution and are capable of zooming in on the region of interest. This ability will limit potential errors in RVOT diameter measurement.

Moderate or severe aortic regurgitation can cause an increase in flow and thus in the pressure gradient across the aortic valve, and this effect results in an overestimation of the aortic stenosis. The same limitation exists for SAS when EOA is calculated using RV stroke volume. In the presence of moderate or severe aortic regurgitation, RV stroke volume is lower than LV stroke volume, and thus EOA is underestimated (ie, the stenosis is overestimated). However, in the presence of moderate or severe pulmonic regurgitation, RV stroke volume is higher than LV stroke volume and EOA is overestimated, thus resulting in underestimation of SAS. Calculation of EOA using stroke volume determined in the RVOT therefore should not be used to estimate the severity of SAS when moderate or severe aortic or pulmonic regurgitation is present.

In this study, we demonstrated the feasibility and usefulness of EOA measured by Doppler echocardiography using the continuity equation for the noninvasive assessment of the severity of SAS in dogs. This parameter may be particularly useful in conditions where the transstenotic pressure gradients are unreliable, such as in the presence of abnormal low or high cardiac output. To compensate for variation in body size, it is important to index EOA for BSA. Indexed EOA was superior in predicting the occurrence of adverse events in the SAS dogs when compared with currently used echocardiographic parameters, including the peak and mean transstenotic gradients. Pending further data, an indexed EOA of <0.60 cm²/m² should be considered as an indicator of severe SAS.

Footnote

× Table Curve, Jandel Scientific, San Rafael, CA

Acknowledgment

The study was supported by a grant from Le Fonds du Centenaire of the School of Veterinary Medicine, University of Montreal.

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