

Evaluation of the influence of age on pulmonary arterial pressure by use of right ventricular catheterization, pulsed-wave Doppler echocardiography, and pulsed-wave tissue Doppler imaging in healthy Beagles

Elise Mercier, DVM; Myrielle Mathieu, DVM; Charlotte F. Sandersen, DVM, PhD; François H. Delvaux, Cécile M. Clercx, DVM, PhD; Kathleen Mc Entee, DVM, PhD

Objective—To assess the influence of age on pulmonary hemodynamics and hemorheological properties in healthy dogs.

Animals—14 healthy Beagles.

Procedures—Dogs were placed in 2 age groups as follows: young dogs (≤ 5 years old; $n = 8$) and old dogs (≥ 8 years old; 6). Hematologic characteristics, plasma total protein and fibrinogen concentrations, and blood viscosity were measured. Systolic time intervals of pulmonary blood flow were recorded by pulsed-wave Doppler echocardiography. Early (E') and late (A') diastolic myocardial velocities, isovolumic contraction velocity, and systolic myocardial velocity of the free tricuspid annulus were recorded by pulsed-wave tissue Doppler imaging (TDI). Dogs were anesthetized and pulmonary arterial pressures (PAP) and cardiac output were recorded with a pediatric thermodilution Swan-Ganz catheter.

Results—Hemorheological measurements were not different between the 2 groups. Systolic, mean, and diastolic PAP were higher in old dogs, compared with values in young dogs; this difference was attributed to a high pulmonary vascular resistance and low arterial compliance in old dogs. Systolic time intervals of pulmonary blood flow stayed unchanged. The A' wave of the free tricuspid annulus was increased in old, compared with that young dogs, and the E':A' ratio was decreased. Pulmonary vascular resistance was inversely correlated with compliance.

Conclusions and Clinical Relevance—The age of dogs should be taken into account when interpreting pulmonary hemodynamic results and TDI variables of right ventricular diastolic function. (*Am J Vet Res* 2010;71:891–897)

In humans, PAP increases with aging,^{1–4} and this increase is associated with changes in diastolic myocardial velocities of the tricuspid annulus.^{5–8} No data on age-related differences in PAP exist for dogs. The assessment of pulmonary hemodynamics and right ventricular systolic and diastolic properties by conventional and tissue Doppler echocardiography is now widely accepted and routinely used in veterinary clinical practice.⁹ However, a possible influence of age on hemodynamic variables has not yet been studied in dogs and could interfere with interpretation of these values. The

ABBREVIATIONS

A'	Late diastolic myocardial velocity
AT	Acceleration time of pulmonary blood flow
AT:ET ratio	Ratio of ejection time to acceleration time of pulmonary blood flow
C	Pulmonary arterial compliance
dPAP	Diastolic pulmonary arterial pressure
E	Pulmonary arterial elastance
E'	Early diastolic myocardial velocity
E':A' ratio	Ratio of early to late diastolic myocardial velocity
ET	Ejection time of pulmonary blood flow
mPAP	Mean pulmonary arterial pressure
oPAP	Occluded pulmonary arterial pressure
PAP	Pulmonary arterial pressure
PP	Pulmonary pulse pressure
PVR	Pulmonary vascular resistance
RAP	Right atrial pressure
S'	Systolic myocardial velocity
sPAP	Systolic pulmonary arterial pressure
TDI	Tissue Doppler imaging

Received January 15, 2009.

Accepted July 23, 2009.

From the Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Liège, 4000 Liège, Belgium (Mercier, Sandersen, Delvaux, Clercx, Mc Entee); and Laboratory of Physiology, Faculty of Medicine, Free University of Brussels, 1050 Brussels, Belgium (Mathieu, Mc Entee).

Presented in abstract form at the 18th Congress of the European College of Veterinary Internal Medicine, Ghent, Belgium, September 2008.

Address correspondence to Dr. Mercier (emercier@ulg.ac.be).

objectives of the study reported here were to assess the influence of aging on pulmonary hemodynamics and hemorheological characteristics by comparing 2 age groups of healthy Beagles, evaluate the relationship between systolic time intervals of pulmonary blood flow measured by conventional Doppler echocardiography and PAP measurements in both age groups, and evaluate the relationship between systolic and diastolic myocardial velocities of the free tricuspid annulus measured by TDI and PAP in both age groups.

Materials and Methods

The investigation was approved by the Institutional Animal Care and Use Ethics Committee of the University of Liège, Belgium, and was conducted in accordance with the National Institutes of Health *Guide for the Care and Use of Laboratory Animals*.

Animals and inclusion criteria—Fourteen healthy Beagles belonging to the Beagle colony of the Liège University Veterinary Small Animal Teaching Hospital were included. Dogs were placed in 2 age groups as follows: young dogs (≤ 5 years old; $n = 8$) and old dogs (≥ 8 years old; 6). Dogs were housed in small groups of 2 or 3 dogs in the same facility in adjoining rooms (on shaving litter), with identical feeding, vaccinations, and handling procedures. Some dogs were siblings. Anthelmintic treatments had been administered to all dogs within 3 months before the onset of the study.

Inclusion criteria included the following: absence of clinical signs consistent with respiratory or cardiac disease or any other disease with systemic consequences in the preceding 3 months; normal findings on physical examination, hematologic analysis, and serum biochemical analysis; findings on an ECG; a systolic arterial blood pressure measurement as determined by Doppler sphygmomanometry^a within the reference range (< 160 mm Hg)¹⁰; and absence of any observable structural or functional abnormality with hemodynamic consequences on Doppler echocardiographic examination.^b

Hemorheological measurements—Blood samples were obtained from the jugular vein for hematologic analysis and measurements of plasma total protein concentration, plasma fibrinogen concentration, and blood viscosity and elasticity. Blood viscosity was measured by a rheometer^c at 3 shear rates (2.5, 12.5, and 62.8 seconds⁻¹) at room temperature ($20 \pm 1^\circ\text{C}$).¹¹ Plasma fibrinogen concentration was measured according to the method of Clauss.¹²

Doppler echocardiography—Doppler echocardiography was performed under continuous ECG monitoring with a 5-MHz electronic probe with the dog in lateral recumbency and scanning through the dependent chest wall. A right parasternal window was used to record pulmonary blood flow by spectral pulsed-wave Doppler. Maximal velocity of pulmonary blood flow, ET, and AT were measured, and the AT:ET ratio was calculated. A left apical 4-chamber view was used for spectral pulsed-wave tissue Doppler recordings of the tricuspid free annulus longitudinal displacement. Early and late diastolic myocardial velocity, isovolumic con-

traction velocity, and S' were measured, and the E':A' ratio was calculated. All images were recorded and then analyzed off line according to specific guidelines^{13,14} by 2 investigators (EM and KMCE) who were blind to dog group (ie, young or old). Five consecutive measurements were averaged for each variable, regardless of respiratory phase. Echocardiographic values from 1 old dog were discarded because of behavior problems of the dog that prevented adequate measurement.

Right-sided cardiac catheterization—Anesthesia was induced and maintained with midazolam (1 mg/kg, IV, followed by 1 mg/kg/h, IV) and sufentanil (3 $\mu\text{g/kg}$, IV, followed by 3 $\mu\text{g/kg/h}$, IV). Dogs were mechanically ventilated (fraction of inspired oxygen, 0.4), and care was taken to maintain end-expiratory CO_2 between 30 and 35 mm Hg and body temperature at $> 36^\circ\text{C}$. A 6F introducer^d was introduced transcutaneously in the left jugular vein by the Seldinger technique.¹⁵ A 5F Swan-Ganz thermodilution catheter^e was advanced under fluoroscopic guidance and positioned with the tip in the main pulmonary artery. The sPAP, mPAP, dPAP, oPAP, and RAP were measured by use of a disposable extravascular pressure transducer^f and a pressure monitoring oscilloscope.^g Cardiac output was determined in triplicate by the thermodilution technique.^h Five milliliters of iced 5% dextrose solution was used as thermal indicator and injected manually into the right atrium via the proximal port of the Swan-Ganz catheter. From these measurements, stroke volume, PVR, PP, C, and E were calculated as follows:

$$\text{SV (mL/beat)} = (\text{CO [L/min]}/\text{HR [beats/min]}) \times 1,000$$

$$\text{PVR (mm Hg}\cdot\text{min/L)} = (\text{mPAP [mm Hg]} - \text{oPAP [mm Hg]})/\text{CO (L/min)}$$

$$\text{PP (mm Hg)} = \text{sPAP (mm Hg)} - \text{dPAP (mm Hg)}$$

$$\text{C (mL/beat}\cdot\text{mm Hg)} = \text{SV (mL/beat)}/\text{PP (mm Hg)}$$

$$\text{E (mm Hg}\cdot\text{beat/mL)} = \text{PP (mm Hg)}/\text{SV (mL/beat)}$$

where SV is stroke volume, CO is cardiac output, and HR is heart rate.

Statistical analysis—Hemorheological and hemodynamic data were tested for normality, and differences between the 2 groups of dogs were assessed by use of

Table 1—Mean $\pm$ SEM values of group characteristics of dogs in 2 age groups.

Variables	Young dogs (n = 8)	Old dogs (n = 6)	P value
Age (y)	2.7 $\pm$ 0.7	12.1 $\pm$ 1.0	< 0.001
Body weight (kg)	16.0 $\pm$ 1.3	16.1 $\pm$ 1.2	NS
Heart rate (beats/min)	145 $\pm$ 4.9	130 $\pm$ 8.5	NS
Respiratory rate (breaths/min)	21 $\pm$ 0.7	20.6 $\pm$ 0.9	NS
Systolic arterial blood pressure (mm Hg)	145.4 $\pm$ 7.1	157.4 $\pm$ 10.5	NS
NS = Not significant. Young dogs were those ≤ 5 years of age. Old dogs were those ≥ 8 years of age.			

Table 2—Mean $\pm$ SEM hematologic values and fibrinogen and total protein concentrations of dogs in 2 age groups.

Variables	Young dogs (n = 8)	Old dogs (n = 6)	P value
PCV (%)	36.1 $\pm$ 2.5	39.3 $\pm$ 3.74	NS
Mean corpuscular volume (fL)	67.9 $\pm$ 0.7	68.7 $\pm$ 1.0	NS
Mean corpuscular hemoglobin (pg)	22.9 $\pm$ 0.4	23.0 $\pm$ 0.4	NS
Mean corpuscular hemoglobin concentration (g/dL)	33.7 $\pm$ 0.3	33.7 $\pm$ 0.2	NS
Leukocytes			
Total (cells/ μ L)	7,308 $\pm$ 1,200	9,766 $\pm$ 1,642	NS
Neutrophils (cells/ μ L)	5,792 $\pm$ 487	7,890 $\pm$ 1,636	NS
Eosinophils (cells/ μ L)	329 $\pm$ 88	448 $\pm$ 147	NS
Lymphocytes (cells/ μ L)	1,597 $\pm$ 268	1,094 $\pm$ 255	NS
Monocytes (cells/ μ L)	455 $\pm$ 88	459 $\pm$ 77	NS
Fibrinogen (g/L)	1.7 $\pm$ 0.1	2.3 $\pm$ 0.2	0.003
Total protein (g/L)	55.5 $\pm$ 3.4	57.3 $\pm$ 2.7	NS
See Table 1 for key.			

Table 3—Mean $\pm$ SEM blood viscosity (in millipascal seconds) measured at 3 shear rates of dogs in 2 age groups.

Shear rates	Young dogs (n = 8)	Old dogs (n = 6)	P value
2.5 s ⁻¹	8.150 $\pm$ 2.105	7.870 $\pm$ 1.467	NS
12.5 s ⁻¹	6.752 $\pm$ 1.640	7.256 $\pm$ 1.216	NS
62.8 s ⁻¹	5.888 $\pm$ 1.283	6.529 $\pm$ 0.853	NS
See Table 1 for key.			

Table 4—Mean $\pm$ SEM standard Doppler echocardiography and TDI values of dogs in 2 age groups.

Variables	Young dogs (n = 8)	Old dogs* (n = 5)	P value
Indices of pulmonary blood flow			
PFV (m/s)	0.864 $\pm$ 0.042	0.817 $\pm$ 0.079	NS
AT (s)	0.093 $\pm$ 0.003	0.097 $\pm$ 0.003	NS
ET (s)	0.194 $\pm$ 0.004	0.207 $\pm$ 0.008	NS
AT:ET ratio	0.478 $\pm$ 0.013	0.469 $\pm$ 0.014	NS
TDI indices			
A' (m/s)	0.109 $\pm$ 0.009	0.147 $\pm$ 0.003	0.02
E' (m/s)	0.122 $\pm$ 0.011	0.130 $\pm$ 0.047	NS
E':A' ratio	1.13 $\pm$ 0.06	0.88 $\pm$ 0.04	0.01
ICV (m/s)	0.151 $\pm$ 0.010	0.180 $\pm$ 0.010	NS
S' (m/s)	0.158 $\pm$ 0.020	0.168 $\pm$ 0.013	NS
*Echocardiographic values from 1 old dog were discarded because behavior problems of the dog prevented adequate measurement			
ICV = Isovolumic contraction velocity. NS = Not significant. PFV = Maximal velocity of pulmonary blood flow.			
See Table 1 for remainder key.			

2-sided unpaired Student *t* test or a Mann-Whitney test. Coefficients of determination and associated probabilities were determined to examine the relationship between invasive and echocardiographic indices. All values were reported as mean $\pm$ SEM. Values of *P* < 0.05 were considered significant.

Results

Group characteristics—Young dogs (n = 8) ranged from 10 months to 5 years of age (5 males and 3 females; median age, 3 years old), and old dogs (6) ranged from 8 to 14.5 years of age (4 males and 2 females; median age, 13 years old). Body weight, heart rate, respiratory rate, and systolic arterial blood pressure were comparable in the 2 groups (Table 1).

Hemorheological measurements—Hematologic values and plasma total protein concentration were similar in the 2 groups, whereas plasma fibrinogen concentration was higher in old dogs than in young

dogs (Table 2). Blood viscosities were similar in the 2 groups at the 3 shear rates tested (Table 3).

Standard Doppler echocardiography and TDI—As indices of pulmonary blood flow, there was no difference between groups in maximal velocity of pulmonary blood flow, AT, ET, and AT:ET ratio. Compared with young dogs, old dogs had a higher A' at the level of the free tricuspid annulus and a lower E':A' ratio. Measurements of E', isovolumic contraction velocity, and S' were comparable in the 2 groups (Table 4).

Right-sided cardiac catheterization—Values of sPAP, mPAP, dPAP, PVR, PP, and E were higher in old dogs than in young dogs. Pulmonary arterial compliance was lower in old dogs than in young dogs, whereas oPAP, heart rate, cardiac output, and stroke volume were not significantly different between groups (Table 5).

Correlation between PAP and echocardiographic indices—Values of PVR and C were inversely related

Table 5—Mean $\pm$ SEM values for hemodynamic variables calculated or measured by cardiac catheterization of dogs in 2 age groups.

Mean $\pm$ SEM	Young dogs (n = 8)	Old dogs (n = 6)	P value
Heart rate (beats/min)	68.4 $\pm$ 2.3	65.1 $\pm$ 2.0	NS
Cardiac output (L/min)	1.89 $\pm$ 0.18	1.52 $\pm$ 0.12	NS
sPAP (mm Hg)	21.4 $\pm$ 1.5	30.6 $\pm$ 2.1	0.003
dPAP (mm Hg)	9.5 $\pm$ 1.1	13.4 $\pm$ 1.4	0.046
mPAP (mm Hg)	13.7 $\pm$ 1.2	19.3 $\pm$ 1.8	0.022
oPAP (mm Hg)	9.5 $\pm$ 1.4	10.7 $\pm$ 1.7	NS
RAP (mm Hg)	6.1 $\pm$ 1.1	8.0 $\pm$ 1.8	NS
Stroke volume (mL/beat)	28.0 $\pm$ 0.2	23.0 $\pm$ 0.1	NS
PVR (mm Hg/L·min ⁻¹)	2.3 $\pm$ 0.5	5.9 $\pm$ 0.5	< 0.001
PP (mm Hg)	11.9 $\pm$ 0.7	17.2 $\pm$ 0.9	< 0.001
C (mL·beat ⁻¹ /mm Hg)	2.37 $\pm$ 0.20	1.36 $\pm$ 0.12	0.002
E (mm Hg·beat/mL)	0.44 $\pm$ 0.03	0.76 $\pm$ 0.07	< 0.001

See Table 1 for key.

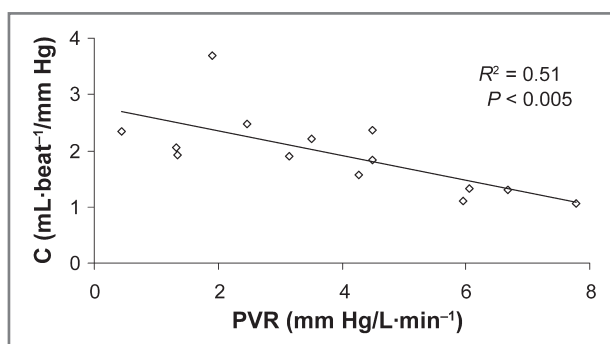


Figure 1—Correlation between PVR and C in 14 healthy Beagles.

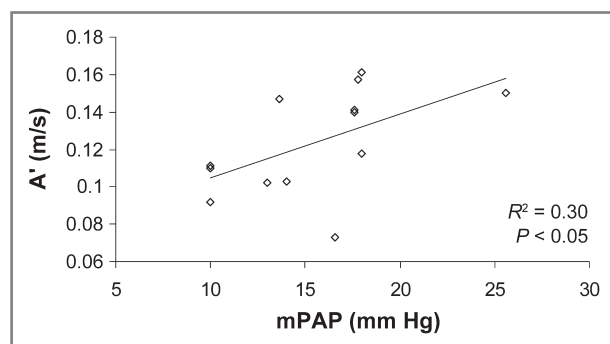


Figure 2—Correlation between A' and mPAP in 14 healthy Beagles.

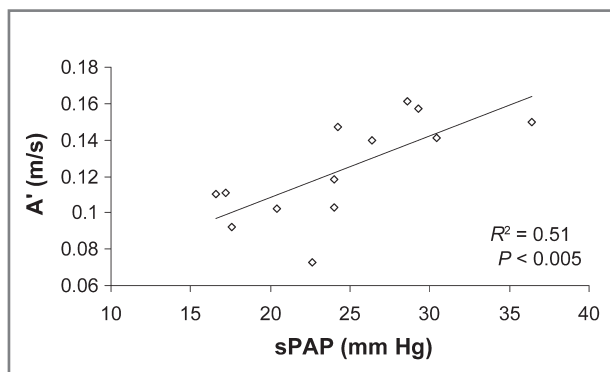


Figure 3—Correlation between A' and sPAP in 14 healthy Beagles.

(Figure 1). Systolic time intervals of pulmonary blood flow were not correlated with PAP. High mPAP (Figure 2) and sPAP values (Figure 3) were associated with a high A' maximal velocity.

Discussion

Results of the present study indicated that in old healthy Beagles, compared with young healthy Beagles, PAP and PVR were increased whereas C was decreased, and the A' wave of the free tricuspid annulus was increased and correlated with PAP. In humans, PAP increases with aging. This finding has been demonstrated by both cardiac catheterization^{1,16} and measurement of tricuspid regurgitation velocity.^{2-4,16-19} Moreover, Davidson and Fee¹ showed that the increase of PAP with age in humans was linear. Results of our study indicated that PAP also increased with age in dogs. In our study, values of sPAP (30.6 $\pm$ 2.1 mm Hg), dPAP (13.4 $\pm$ 1.4 mm Hg), and mPAP (19.3 $\pm$ 1.8 mm Hg) in old dogs that were anesthetized were higher than reference range values for sPAP (15 to 25 mm Hg), dPAP (5 to 10 mm Hg), and mPAP (10 to 15 mm Hg) in clinically normal awake dogs at sea level.²⁰ However, if pulmonary arterial hypertension is defined as a sustained increase in mPAP to > 25 mm Hg at rest,^{21,22} values obtained in our study were not diagnostic of pulmonary arterial hypertension. In humans, obesity⁴ and systemic arterial pressure² are other known factors affecting PAP in those individuals that are otherwise healthy. Because results for body weight and arterial pressure were similar in young and old dogs in our study, these 2 variables were not considered as confounding factors.

An increase in PAP may result from a high pulmonary blood flow, a chronic increase in left atrial pressure, a high PVR, or a low C.²³ Davidson and Fee¹ showed that, in humans, the increase in PAP is attributable to an increase in PVR and that the relation between these 2 variables is linear. The high PVR in old dogs of our study is in accordance with findings in humans. Our study showed that, in dogs, C is a second factor involved in the increase in PAP that occurs with age. Moreover, pulmonary blood flow and left atrial pressure (estimated by the oPAP) did not appear to be entailed in this process, which is in accordance with what has been shown in humans.¹

Pulmonary vascular resistance is directly influenced by blood viscosity and inversely correlated with the fourth power of the vascular radius. Blood viscosity is determined by PCV, RBC characteristics (including size, deformability, and aggregation), leukocyte number and type, and plasma viscosity.²⁴ As the relationship between PCV and blood viscosity is logarithmic, this has a greater effect on blood viscosity than all other factors combined.²⁵ However, its effect decreases when shear rates (the velocity gradient between flowing layers of blood) increase.²⁶ Deformability of RBCs is determined by viscoelastic properties of their membrane; cell geometry including cell size, shape, and surface area-to-volume ratio; and cytoplasmic viscosity, primarily determined by hemoglobin concentration.²⁷ Aggregation can be estimated by RBC sedimentation rate corrected for PCV.²⁸ Aggregation correlates with fibrinogen con-

centration and plasma viscosity. Total plasma protein concentration is the major determinant of plasma viscosity. However, increases in plasma concentration of high-molecular-weight proteins, such as fibrinogen and immunoglobulins, have a relatively greater effect on plasma viscosity than an increase in concentrations of proteins with a low molecular weight.²⁷ In our study, blood viscosities measured at 3 shear rates, as well as the main components of the blood, were similar in the 2 groups of dogs with the exception of plasma fibrinogen concentration, which was higher in old dogs than young dogs. High fibrinogen concentrations have been reported for aged humans.^{29–32} However, the influence of age on hemorheological characteristics in healthy humans remains controversial.³³ Some studies^{34,35} have shown an increase in blood viscosity with age, while others^{36–38} have not. In our study, an increase in blood viscosity with age could not explain the increase in PVR in old dogs, compared with that in young dogs, and arteriolar narrowing was considered as the main factor responsible for this increase with age.

Changes in right ventricular afterload are most often described in terms of changes in PVR. However, the most complete description of the pulmonary circulation is obtained from pulmonary vascular impedance that is computed by spectral analysis of pulmonary pressure and flow waves.³⁹ This method requires simultaneous recordings of instantaneous pressure and flow but allows for separation of right ventricular afterload into the 3 main components of resistance, E, and wave reflection. A second method to assess right ventricular afterload is to calculate effective arterial E, which is the ratio between end-systolic pressure and stroke volume. Effective arterial E integrates the effects of resistance, E, and wave reflections into a single number, but this method requires simultaneous recordings of instantaneous ventricular pressure and volume to determine the end-systolic point.⁴⁰ In our study, distal resistance was described by PVR, and proximal E was described by the compliance, computed as the ratio of stroke volume to PP. This ratio overestimates true compliance, but is highly correlated with it.⁴¹ Wave reflection was not investigated because it requires complex measurements and adds little information when proximal E is already taken into account. In humans, changes in both resistance and compliance have been shown to play a prominent role in the development of primary pulmonary arterial hypertension,⁴² with compliance being a strong predictor of death in these patients.⁴³ In our study, not only PVR but also C contributed to the increase in PAP in old dogs, and as already described in healthy humans and humans with pulmonary hypertension,^{42,44} these 2 variables were inversely related.

Uehara⁴⁵ reported a negative correlation between systolic time intervals and PAP as directly measured by right cardiac catheterization in dogs with heartworm disease. In a study⁴⁶ on the use of Doppler echocardiography in West Highland Terriers with interstitial pulmonary disease, the AT and AT:ET ratio were inversely correlated with sPAP. In dogs with pulmonary hypertension of various origins, Serres et al⁴⁷ found a correlation between AT, AT:ET ratio, and sPAP. On the other hand, Glaus et al⁴⁸ demonstrated that AT and AT:ET ra-

tios were shorter in dogs at high altitude but not in dogs at moderate altitude, living at 2,300 m above sea level with mean tricuspid peak pressure gradient of 29.5 ± 10.4 mm Hg. To our knowledge, no study has evaluated the effect of aging in dogs on systolic time intervals of pulmonary blood flow. In our study, the AT and AT:ET ratio were in accordance with reference range values reported for dogs,^{46,48,49} and no difference was found between young and old dogs. Therefore, these variables (AT and AT:ET ratio) were not useful in detecting high PAPs in old dogs of our study.

Chronic pulmonary hypertension causes alterations in right ventricular systolic and diastolic properties. Tricuspid annulus motion examined by TDI may reflect these changes. In humans, pulmonary hypertension is associated with decreases of tricuspid annulus S' and E':A' ratio.^{50–56} These changes have also been found in dogs.⁴⁷ In our study, tricuspid free annular myocardial velocities measured by pulsed-wave TDI were in accordance with reference range values reported for dogs.^{47,57} Late diastolic myocardial velocity was increased in old dogs, compared with that in young dogs, and the E':A' ratio was low. An inverse relationship between the E':A' ratio and age has been reported for the right^{5–8} and left ventricles⁵⁸ in humans and for the left ventricle in cats.⁵⁹ This suggests that there is an age-related limitation in early diastolic myocardial relaxation that requires an increase in atrial contraction force to maintain adequate ventricular filling. In our study, A' was correlated with mPAP and sPAP. Because there is no direct relationship between the right ventricle and pulmonary circulation in diastole, the PAP cannot directly explain the gradual increase in A'. Changes in the A' and E':A' ratio may rather be related to intrinsic myocardial changes during diastole (remodeling) as they are in normal aging of the left ventricle. In fact, a progressive decrease of peak early diastolic velocity in the human left ventricle with aging is believed to be a consequence of aged-related increases in cardiac mass and wall thickness³ and in extracellular matrix substance.⁶⁰ Nevertheless, a progressive increase in PAP might at least partially trigger right ventricular remodelling.

On the other hand, S' of the free tricuspid annulus was similar in the 2 groups of dogs in our study, indicating that right ventricular systolic function was maintained despite the high PAP in old dogs. The S' tricuspid wave is known to decrease in pulmonary hypertension,^{50–56} but to stay unchanged in aged clinically normal humans^{5–8} and in aged cats.^{61,62} Our study confirms the lack of influence of age on myocardial systolic velocity of the tricuspid annulus.

One limitation of the study reported here is the small number of dogs, limiting the power of the statistical tests. Although not significant changes, stroke volume and cardiac output decreased and RAP and systolic arterial blood pressure increased with age in the dogs of our study. As the influence of age on stroke volume, cardiac output, RAP, and systolic blood pressure has been described,^{1,2} we cannot exclude that changes in those variables with age would have achieved significance had our study included a greater number of dogs.

The present study showed that PAP is increased in old versus young healthy Beagles. This increase was a result of a decrease in C and an increase in PVR with age. The increase in resistance with age was a consequence of pulmonary arteriolar narrowing. Systolic time intervals of pulmonary blood flow measured by pulsed-wave Doppler echocardiography did not allow for detection of the increase in PAP, whereas the A' wave and the E':A' ratio measured by pulsed-wave TDI at the level of the free tricuspid annulus did. Therefore, the age of dogs should be taken into account when pulmonary hemodynamic results and TDI indices of the right ventricular diastolic function are being interpreted.

- a. Model 811-BTS, Parks Medical Electronics Inc, Aloka, Ore.
- b. Vivid 5, General Electric, Brussels, Belgium.
- c. BioProfiler, Vilastic Scientific Inc, Austin, Tex.
- d. Catheter introducer kit F6, Argon, Athens, Tex.
- e. 93-132-5F, Baxter, Irvine, Calif.
- f. Pressure monitoring kit, Baxter, Uden, Holland.
- g. Cardiopac 2, Datex, Helsinki, Finland.
- h. Cardiac Output 9520A, Edwards, Santa Ana, Calif.

References

1. Davidson WR Jr, Fee EC. Influence of aging on pulmonary hemodynamics in a population free of coronary artery disease. *Am J Cardiol* 1990;65:1454-1458.
2. Abergel E, Chatellier G, Toussaint P, et al. Doppler-derived pulmonary arterial systolic pressure in patients with known systemic arterial pressures. *Am J Cardiol* 1996;77:767-769.
3. Dib JC, Abergel E, Rovani C, et al. The age of the patient should be taken into account when interpreting Doppler assessed pulmonary artery pressures. *J Am Soc Echocardiogr* 1997;10:72-73.
4. McQuillan BM, Picard MH, Leavitt M, et al. Clinical correlates and reference intervals for pulmonary artery systolic pressure among echocardiographically normal subjects. *Circulation* 2001;104:2797-2802.
5. Alam M, Wardell J, Andersson E, et al. Characteristics of mitral and tricuspid annular velocities determined by pulsed wave Doppler tissue imaging in health subjects. *J Am Soc Echocardiogr* 1999;12:618-628.
6. Kukulski T, Hubbert L, Arnold M, et al. Normal regional right ventricular function and its change with age: a Doppler myocardial imaging study. *J Am Soc Echocardiogr* 2000;13:194-204.
7. Nikitin NP, Witte KK, Thackray SD, et al. Longitudinal ventricular function: normal values of atrioventricular annular and myocardial velocities measured with quantitative two-dimensional color Doppler tissue imaging. *J Am Soc Echocardiogr* 2003;16:906-921.
8. Lindqvist P, Waldenström A, Henein M, et al. Regional and global right ventricular function in healthy individuals aged 20-90 years: a pulsed Doppler tissue imaging study. *Echocardiography* 2005;22:305-314.
9. Chetboul V. Tissue Doppler imaging: a promising technique for quantifying regional myocardial function. *J Vet Cardiol* 2002;4:7-12.
10. Stepien RL, Rapoport GS, Henik RA, et al. Comparative diagnostic test characteristics of oscillometric and Doppler ultrasonographic methods in the detection of systolic hypertension in dogs. *J Vet Intern Med* 2003;17:65-72.
11. Thurston GB. Viscoelastic properties of blood and blood analogs. In: How TV, ed. *Advances in hemodynamics and hemorheology*. Greenwich, Conn: JAI Press Inc, 1996;1-30.
12. Clauss A. Gerinnung-physiologische schnell-method zur bestimmung des fibrinogens. *Acta Haematol* 1957;17:237-246.
13. Sahn DJ, Demaria A, Kisslo J, et al. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978;58:1072-1083.
14. Thomas WP, Gaber CE, Jacobs GJ, et al. Recommendations for standards in transthoracic two-dimensional echocardiography in the dog and cat. *J Vet Intern Med* 1993;7:247-252.
15. Henderson RA, Dillon AR, Brawner WR, et al. Technique for percutaneous pulmonary arterial catheterization in conscious dogs. *Am J Vet Res* 1985;46:1538-1539.
16. Berger M, Haimowitz A, Van Tosh A, et al. Quantitative assessment of pulmonary hypertension in patients with tricuspid regurgitation using continuous wave Doppler ultrasound. *J Am Coll Cardiol* 1985;6:359-365.
17. Kitabatake A, Inoue M, Asao M, et al. Non invasive evaluation of pulmonary hypertension by a pulsed Doppler technique. *Circulation* 1983;68:302-309.
18. Isobe M, Yazaki Y, Takaku F, et al. Prediction of pulmonary arterial pressure in adults by pulsed Doppler echocardiography. *Am J Cardiol* 1986;57:316-321.
19. Dabestani A, Mahan G, Gardin JM, et al. Evaluation of pulmonary artery pressure and resistance by pulsed Doppler echocardiography. *Am J Cardiol* 1987;59:662-668.
20. Gross DR. Normal cardiovascular parameters from intact, awake animals. In: Gross DR, ed. *Animals models in cardiovascular medicine*. 4th ed. Philadelphia: WB Saunders, 1994.
21. Gaine SP, Rubin LJ. Primary pulmonary hypertension (Erratum published in *Lancet* 1999;353:74). *Lancet* 1998;352:719-725.
22. Galie N, Torbicki A, Barst R. Guidelines on diagnosis and treatment of pulmonary arterial hypertension. *Eur Heart J* 2004;25:2243-2278.
23. Kienle RD, Kittleson MD. Pulmonary arterial and systemic arterial hypertension. In: Kittleson MD, Kienle RD, eds. *Small animal cardiovascular medicine*. St Louis: Elsevier, 1998;433-448.
24. Weiss DJ, Richwagen K, Evanson OA. Effects of hematocrit and erythrocyte deformability on pulmonary vascular pressures in perfused pony lungs. *Am J Vet Res* 1996;57:346-350.
25. Somer T, Meiselman HJ. Disorders of blood viscosity. *Ann Med* 1993;25:31-39.
26. Geor RJ, Weiss DJ, Smith CM II. Hemorheologic alterations induced by incremental treadmill exercise in Thoroughbreds. *Am J Vet Res* 1994;55:854-861.
27. Stuart J, Nash GB. Red cell deformability and haematological disorders. *Blood Rev* 1990;4:141-147.
28. Stuart J, Nash GB. Technological advances in blood rheology. *Crit Rev Clin Lab Sci* 1990;28:61-93.
29. Ishikawa S, Kario K, Nago N, et al. Factor VII and fibrinogen levels examined by age, sex, and other atherosclerotic risk factors in a Japanese population. The Jichi Medical School Cohort study. *Thromb Haemost* 1997;77:890-893.
30. Paramo JA, Belouqui O, Roncal C, et al. Validation of plasma fibrinogen as a marker of carotid atherosclerosis in subjects free of clinical cardiovascular disease. *Haematologica* 2004;89:1226-1231.
31. Drenos F, Miller GJ, Humphries SE. Increase of plasma fibrinogen levels and variability with age in a sample of middle aged healthy men. *Ann Hum Genet* 2007;71:43-53.
32. Paramo JA, Orbe J, Belouqui O, et al. Association of age, inflammatory markers and subclinical atherosclerosis in subjects free from cardiovascular disease [in Spanish]. *Med Clin (Barc)* 2008;131:361-366.
33. Feher G, Koltai K, Toth K. Are hemorheological parameters independent of aging? *Clin Hemorheol Microcirc* 2007;36:181-182.
34. Ajmani RS, Rifkind JM. Hemorheological changes during human aging. *Gerontology* 1998;44:111-120.
35. Seki K, Sumino H, Nara N, et al. Relationships between blood rheology and age, body mass index, blood cell count, fibrinogen, and lipids in healthy subjects. *Clin Hemorheol Microcirc* 2006;34:401-410.
36. Ponzetto M, Neirotti M, Romin R, et al. Hemorheological and photoplethysmographical modifications with aging. *Arch Gerontol Geriatr* 1996;22:207-211.
37. Feher G, Koltai K, Kesmarky G, et al. Hemorheological parameters and aging. *Clin Hemorheol Microcirc* 2006;35:89-98.
38. Manetta J, Aloulou I, Varlet-Marie E, et al. Partially opposite hemorheological effects of aging and training at middle age. *Clin Hemorheol Microcirc* 2006;35:239-244.
39. Brimioulle S, Maggiorini M, Stephanz J, et al. Effects of low

- flow on pulmonary vascular flow–pressure curves and pulmonary vascular impedance. *Cardiovasc Res* 1999;42:183–192.
40. Burkhoff D, Sagawa K. Ventricular efficiency predicted by an analytical model. *Am J Physiol* 1986;250:R1021–R1027.
 41. Segers P, Brimiouille S, Stergiopulos N, et al. Pulmonary arterial compliance in dogs and pigs: the three-element Windkessel model revisited. *Am J Physiol* 1999;277:H725–H731.
 42. Lankhaar JW, Westerhof N, Faes TJC, et al. Pulmonary vascular resistance and compliance stay inversely related during treatment of pulmonary hypertension. *Eur Heart J* 2008;29:1688–1695.
 43. Mahapatra S, Nishimura RA, Sorajja P, et al. Relationship of pulmonary arterial capacitance and mortality in idiopathic pulmonary arterial hypertension. *J Am Coll Cardiol* 2006;47:799–803.
 44. Lankhaar JW, Westerhof N, Faes TJC, et al. Quantification of right ventricular afterload in patients with and without pulmonary hypertension. *Am J Physiol Heart Circ Physiol* 2006;291:H1731–H1737.
 45. Uehara Y. An attempt to estimate the pulmonary artery pressure in dogs by means of pulsed Doppler echocardiography. *J Vet Med Sci* 1993;55:307–312.
 46. Schober KE, Baade H. Doppler echocardiographic prediction of pulmonary hypertension in West Highland white terriers with chronic pulmonary disease. *J Vet Intern Med* 2006;20:912–920.
 47. Serres F, Chetboul V, Gouni V, et al. Diagnostic value of echo-Doppler and tissue Doppler imaging in dogs with pulmonary arterial hypertension. *J Vet Intern Med* 2007;21:1280–1289.
 48. Glaus TM, Tomsa K, Hässig M, et al. Echocardiographic changes induced by moderate to marked hypobaric hypoxia in dogs. *Vet Radiol Ultrasound* 2004;45:233–237.
 49. Kirberger RM, Bland-van den Berg P, Grimbeek RJ. Doppler echocardiography in the normal dog: part II. Factors influencing blood flow velocities and a comparison between left and right heart blood flow. *Vet Radiol Ultrasound* 1992;33:380–386.
 50. Caso P, Galderisi M, Cicala S, et al. Association between myocardial right ventricular relaxation time and pulmonary arterial pressure in chronic obstructive lung disease: analysis by pulsed Doppler tissue imaging. *J Am Soc Echocardiogr* 2001;14:970–977.
 51. Moustapha A, Lim M, Saikia S, et al. Interrogation of the tricuspid annulus by Doppler tissue imaging in patients with chronic pulmonary hypertension: implications for the assessment of right-ventricular systolic and diastolic function. *Cardiology* 2001;95:101–104.
 52. Lindqvist P, Waldenström A, Wikström G, et al. Right ventricular myocardial isovolumic relaxation time and pulmonary pressure. *Clin Physiol Funct Imaging* 2006;26:1–8.
 53. Melek M, Esen O, Esen AM, et al. Tissue Doppler evaluation of tricuspid annulus for estimation of pulmonary artery pressure in patients with COPD. *Lung* 2006;184:121–131.
 54. McLean AS, Ting I, Huang SJ, et al. The use of right ventricular diameter and tricuspid annular tissue Doppler velocity parameter to predict the presence of pulmonary hypertension. *Eur J Echocardiogr* 2007;8:128–136.
 55. You XD, Pu ZX, Peng XJ, et al. Tissue Doppler imaging study of right ventricular myocardial systolic activation in subjects with pulmonary arterial hypertension. *Chin Med J (Engl)* 2007;120:1172–1175.
 56. Rajagopalan N, Simon MA, Mathier MA, et al. Identifying right ventricular dysfunction with tissue Doppler imaging in pulmonary hypertension. *Int J Cardiol* 2008;128:359–363.
 57. Chetboul V, Carlos Sampedrano C, Gouni V, et al. Quantitative assessment of regional right ventricular myocardial velocities in awake dogs by Doppler tissue imaging: repeatability, reproducibility, effect of body weight and breed, and comparison with left ventricular myocardial velocities. *J Vet Intern Med* 2005;19:837–844.
 58. Henein M, Lindqvist P, Francis D, et al. Tissue Doppler analysis of age-dependency in diastolic ventricular behaviour and filling. *Eur Heart J* 2002;23:162–171.
 59. Disatian S, Bright JM, Boon J. Association of age and heart rate with pulsed-wave Doppler measurements in healthy, nonsedated cats. *J Vet Intern Med* 2008;22:351–356.
 60. Gerstenblith G, Frederiksen J, Yin FC, et al. Echocardiographic assessment of a normal adult aging population. *Circulation* 1977;56:273–278.
 61. Koffas H, Dukes-McEwan J, Corcoran BM, et al. Pulsed Tissue Doppler imaging in normal cats and cats with hypertrophic cardiomyopathy. *J Vet Intern Med* 2006;20:65–77.
 62. Disatian S, Bright JM, Boon J. The effects of age and heart rate on tricuspid annular motion velocities in healthy nonsedated cats. *J Vet Intern Med* 2007;21:731–736.