Brief Communication
J Vet Intern Med 2012;26:183–185

Prevalence of Patent Foramen Ovale with Right-to-Left Shunting in Dogs with Pulmonic Stenosis

Y. Fujii, Y. Nishimoto, H. Sunahara, H. Takano, and T. Aoki

Background: Right-to-left (R-L) shunt caused by patent foramen ovale (PFO) concurrent with pulmonic stenosis (PS) is considered common, although there is a lack of published evidence.

Objectives: To investigate the prevalence of R-L shunt caused by a PFO in dogs with PS.

Animals: Thirty-one client-owned dogs with PS, without obvious extracardiac disease detected on the clinical examinations.

Methods: Case control study: R-L shunt probably caused by PFO was diagnosed when IV injected microbubbles appeared at the left atrial level with an intact atrial septum on echocardiography (bubble-positive dogs). The severity of PS concurrent tricuspid regurgitation (TR), relative thickness of the right ventricle, and relative right atrial area were compared between bubble-positive and bubble-negative dogs.

Results: The prevalence of R-L shunts caused by PFO was 39% (12 of 31 cases). The instantaneous pressure gradient (PG) across the pulmonic valve and relative thickness of the right ventricle were significantly increased in bubble-positive compared with those in bubble-negative dogs. None of the dogs with mild or moderate PS (pressure gradient < 80 mm Hg, n = 2) demonstrated R-L shunt. The prevalence of TR in bubble-positive dogs was significantly higher than that in bubble-negative dogs.

Discussion and Clinical Relevance: Patent foramen ovale PFO with R-L shunt was more common in dogs with very severe PS and absent in dogs with mild PS.

Key words: Anatomy and pathology; Cardiology; Cardiovascular; Congenital heart defects.

Pulmonic stenosis (PS) is one of the most common congenital heart diseases in dogs. It has been noted commonly that there was a patent foramen ovale (PFO) with right-to-left (R-L) shunting in human patients with critical PS.[1] R-L shunts could cause paradoxical embolism as well as systemic arterial oxygen desaturation in human patients,[2] although the incidence has not been reported in veterinary medicine.

The right atrium (RA) is enlarged in many cases of PS, probably because of increased right atrial pressure.[3] Atrial pressure could be influenced by the following factors: atrioventricular valve regurgitation, arterial valve insufficiency, and ventricular concentric hypertrophy. A hypertrophied ventricle leads to increased ventricular filling pressure because of diastolic dysfunction. During a diastole, the right atrium is directly exposed to right ventricular pressure via the open tricuspid valve. Thus, the right atrium dilates with increased filling pressure. We hypothesized that R-L shunt caused by PFO was common in dogs with PS, particularly in severe cases. Although mild to moderate R-L shunt caused by PFO concurrent with PS has been described in dogs,[4] the exact prevalence has not been reported. The purposes of this study were to investigate the prevalence of R-L shunts caused by PFO in dogs with PS and whether or not R-L shunts were related to the severity of PS.

Abbreviations:

PCV	packed cell volume
PFO	patent foramen ovale
PG	instantaneous pressure gradient
PS	pulmonic stenosis
RA	right atrium
RA/LA	right atrial area divided by left atrial area
R-L	right-to-left
RVWd/LVWd	right ventricular wall thickness divided by left ventricular wall thickness at end-diastole
TR	tricuspid regurgitation

Materials and Methods

Client-owned dogs with PS that presented to Azabu University from 2006 to 2009 were used for this study. A diagnosis of PS was established by physical examination, electrocardiography, thoracic radiography, and 2-D and Doppler echocardiography. Clinical signs noted on the medical records by the owner, clinicians, or both were reviewed. Inclusion in the study required a diagnosis of PS without obvious extracardiac disease detected on the clinical examinations listed above. The dogs with tetralogy of Fallot and PS with tricuspid valve dysplasia, atrial septal defect, or both suspected on 2-D echocardiogram were excluded from the study. Packed cell volume (PCV) was also measured to detect polycythemia.

Contrast echocardiography was performed in all dogs with PS because this technique was considered a sensitive method to detect R-L shunt across PFO, as previously described.[5] The echocardiographic contrast medium was obtained by connecting syringes with 5 mL of saline solution and 0.5 mL of air via a 3-way stopcock to combine the air and saline, and achieve an appropriate dilution. Boluses of agitated saline without large bubbles were rapidly injected into a peripheral vein. A PFO with R-L shunt was diagnosed when echogenic microbubbles were

School of Veterinary Medicine, Azabu University, Kanagawa, Japan.

Corresponding author: Y. Fujii, 1-17-71 Fuchinobe, Chuo-ku, Sagamihara-shi, Kanagawa 252-5201, Japan; e-mail: fujiiy@azabu-u.ac.jp

Submitted January 25, 2011; Revised August 24, 2011; Accepted October 12, 2011.

10.1111/j.1939-1676.2011.00839.x

imaged early (after 2 cycles) in the left atrium on the left apical 4-chamber view. The atrial septum was also assessed on 2-D echocardiography in the right parasternal long-axis view. The peak blood flow velocity across the pulmonic valve was measured with the best alignment to the turbulent flow in the main pulmonary artery by either the right parasternal short-axis view or the left cranial parasternal view of the heart base. The peak instantaneous pressure gradient (PG) across the pulmonic valve was calculated by the modified Bernoulli equation. The severity of PS was determined on the basis of PG as follows: mild, <50 mmHg; moderate, 50–80 mmHg; and severe, >80 mmHg.[3] The severe PS cases were further divided into 2 groups: PG, 80–150 mmHg and >150 mmHg. The relative thickness of the right ventricle was calculated as the right ventricular wall thickness divided by the left ventricular wall thickness at end-diastole (RVWd/LVPWd), by an acquired 2-D cine-loop at the chordae tendineae level in the right parasternal short-axis view. The right atrial area was assessed to estimate the right ventricular filling pressure.[6] The right and left atria were traced to obtain the areas by the left apical 4-chamber view at end-systole. Then, the right atrial area was divided by the left atrial area (RA/LA ratio) to calculate the relative size of the RA. The occurrence of tricuspid regurgitation (TR) was assessed by color Doppler echocardiography on the right parasternal long-axis and left apical 4-chamber views. When TR was observed, tricuspid anatomy was evaluated by 2-D echocardiography. Dogs with tricuspid valve dysplasia and suspected vegetative endocarditis were excluded.[7]

Dogs were divided into 2 groups (bubble-positive and bubble-negative) on the basis of the results of the contrast echocardiograms. PG across the pulmonic valve, concurrent TR, and RVWd/LVPWd, and RA/LA ratios were compared between bubble-positive and bubble-negative dogs.

A statistical analysis between the 2 groups was performed by Student's *t*-test when data showed a normal distribution. When the normality test failed, the Mann–Whitney *U*-test was used. Tricuspid regurgitation was evaluated by Fischer's exact test. A P value less than .05 was considered significant.

Results

This study included 31 dogs diagnosed with PS. There were 16 breeds, including mixed, Miniature Pinscher, West Highland White Terrier, French Bulldog, English Bulldog, Miniature Dachshund, American Pit Bull Terrier, Pomeranian, English Cocker Spaniel, Toy Poodle, Maltese, Beagle, Cavalier King Charles Spaniel, Yorkshire Terrier, Italian Greyhound, and Chihuahua, which was the most common breed (Table 1). Their ages at presentation ranged from 4 months to 7 years (median, 8 months; interquartile range, 5–18 months), and 18 dogs were males (58%). Concurrent heart disease was noted in 2 dogs—one with a restricted ventricular septal defect and the other with degenerative mitral valve disease. Clinical signs were present in 42% of dogs (13 out of 31, Table 1). Cyanosis, exercise intolerance, coughing upon exercise with excitement, and syncope were observed in 6 (19%), 5 (16%), 3 (10%), and 2 (6%) dogs, respectively, whereas ascites because of right-sided heart failure was present in 1 (3%). Cyanosis, observed in 1 bulldog from the bubble-negative group was diagnosed as brachycephalic airway obstruction syndrome. The 3 dogs with coughing were all Chihuahuas, and the cause was suspected to be airway disease.

Twenty-nine dogs (94%) were diagnosed with severe PS. Twelve dogs were found to be bubble positive (39%) on contrast echocardiography. The 2-D echocardiography did not reveal any obvious atrial septal defect in any dog. All dogs in the bubble-positive group were diagnosed with severe PS. Sixty-nine percent of dogs (9 out of 13 dogs) with PG over 150 mmHg were bubble-positive. Nineteen percent of dogs (3 out of 16 dogs) whose PG was between 80 and 150 mmHg were bubble-positive. None of the dogs whose PG was less than 80 mmHg was bubble-positive. The prevalence of R-L shunt was increased in dogs with high PGs. The mean peak-systolic PG in bubble-positive (n = 12) and bubble-negative dogs (n = 19) were 173 ± 60 and 126 ± 52 mmHg, respectively (P = .010). The mean peak-systolic PG in bubble-positive dogs was significantly increased, compared with that in bubble-negative dogs. The relative thickness of the right ventricle (RVWd/LVPWd) in bubble-positive and bubble-negative dogs was 1.86 ± 0.49 and 1.42 ± 0.42, respectively (P = .005). These 2 parameters were significantly different between the 2 groups. TR was observed in 10 (83%) of the bubble-positive and 9 (47%) of the bubble-negative dogs and was significantly over represented among the former (P = .05). No obvious morphological abnormality of the tricuspid valve was observed in any of the dogs with TR, leading to the suspicion that TR was most likely a secondary occurrence. The RA/LA ratio in bubble-positive (n = 19) and bubble-negative dogs (n = 11) was not significantly different between groups (1.32 ± 0.59 and 1.27 ± 0.50, respectively; P = .14).

Table 1. Case characteristics.

	Bubble (+)	Bubble (−)
No. of dogs	12	19
Age (months)	12.3 ± 18.1	21.4 ± 22.7
Range	(4–68 months)	(4–93 months)
Sex (f/m)	5/7	8/11
Breed (dog no.)		
Chihuahua	5	4
French Bulldog	1	3
English Bulldog	0	2
Other	6[a]	10[b]
Clinical signs		
Asymptomatic	4 (33%)	14 (74%)
Ex intolerance	4 (33%)	1 (5%)
Cyanosis	5 (42%)	1 (5%)
Cough	1 (8%)	2 (11%)
Syncope	1 (8%)	1 (5%)
Ascites	0	1 (5%)
Severity of PS		
Severe	12 (100%)	17 (89%)
Moderate	0	1 (5%)
Mild	0	1 (5%)

Ex intolerance, exercise intolerance; PS, pulmonic stenosis. Value for age is expressed as average ± SD.

[a]Includes miniature Dachshund, Beagle, Cavalier King Charles Spaniel, mixed breed, Italian Greyhound, and Yorkshire Terrier.

[b]Includes mixed breed, Miniature Pinscher, West Highland White Terrier, Miniature Dachshund, American Pit Bull Terrier, Pomeranian, English Cocker Spaniel, Toy Poodle, Maltese, and Yorkshire Terrier.

The mean PCV in bubble-positive (51 ± 12%) and bubble-negative dogs (47 ± 7%) were not significantly different; 2 bubble-positive dogs showed polycythemia (PCV > 65%).

Discussion

In the normal fetus, the valve of the ovale foramen allows blood to pass from the right to the left atrial cavities. After birth, when lung circulation begins and left atrial pressure increases and right atrial pressure decreases, the valve of the ovale foramen is pressed against the septum secundum, closing the ovale foramen and separating the right and left atria. Although fusion of the septum primum and septum secundum is incomplete in approximately 30% of the human cases,[8] it does not allow intracardiac shunting of blood. In patients with pulmonic stenosis, increased left atrial pressure after birth may not exceed right atrial pressure, which facilitates patency of the ovale foramen, resulting in continued shunting from the right to the left atrium. Our present results indicated that PFO with R-L shunt was more common in dogs with very severe PS and absent in dogs with mild PS. Although the natural prevalence of PFO has not been reported in clinically healthy dogs, the prevalence of PFO in 54 healthy laboratory Beagles was 0% on the basis of postmortem examination (Fujii Y et al, unpublished data). The prevalence of PFO in dogs with PS in this study could be high compared to that in normal subjects, although further study is needed to compare the prevalence of PFO within various breed populations.

It was reported that the presence of PFO in human patients whose right atrial pressure was high because of underlying cardiac or respiratory disease and could lead to systemic arterial desaturation and paradoxical systemic embolization.[9] To the best of our knowledge, these findings have not been reported in dogs, but the same incidence could occur in the veterinary field.

The presence of PFO with R-L shunt in dogs with severe PS could be attributed to elevated right atrial pressure. Our results revealed that the severity of right ventricular hypertrophy and prevalence of TR in bubble-positive dogs were higher than those in bubble-negative dogs. Diastolic dysfunction because of concentric right ventricular hypertrophy might contribute to this condition.

The prevalence of R-L shunts caused by PFO in severe PS dogs was reported to be 7.9% in a separate study, which was lower than that in our result (39%).[10] This discrepancy could be because of the different methods used to detect the presence of this condition. Angiography was used in the previous report, which might be unable to detect a mild shunting flow, although the techniques and equipment used might also affect the diagnosis. Other possible reasons are the disparate population of dogs with PS and the genetic differences among breeds. Although our group might have involved more severe PS, PS in the previous study may have also been severe, given the indication for balloon valvuloplasty.

This study had several limitations. First, the gold standard to diagnose PFO is the postmortem examination. Necropsy was not available in all dogs to confirm whether or not PFO was actually present. It is possible that no R-L shunt was observed in bubble-negative dogs with PFO if the right atrial pressure did not exceed the left. The contrast echocardiogram at rest used in this study may underestimate the true prevalence of PFO. Second, other types of R-L shunts such as those with an abnormal pulmonary arteriovenous connection might possibly induce the appearance of microbubbles at the level of the left atrium. Third, 2-D echocardiographic findings cannot completely rule out mild tricuspid valve dysplasia and small atrial septal defect as contributing factors in R-L shunts. Finally, the severity of pulmonary insufficiency, which could have affected right atrial pressure, was not evaluated in our study.

Acknowledgments

This study was performed at Azabu University and was presented in part at the 2010 ACVIM Forum, Denver, Colorado.

This research was partly supported by a Grant-in-Aid for Matching Fund Subsidy for Private Universities from the Promotion and Mutual Aid Corporation for Private Schools of Japan.

References

1. Kirklin J, Barratt-Boyes BG. Pulmonary stenosis and intact ventricular septum. In: Kirklin J, Barratt-Boyes BG, ed., Cardiac Surgery, 2nd ed. New York: Churchill Livingstone; 1993:1018.

2. Natanzon A, Goldman ME. Patent foramen ovale: Anatomy versus pathophysiology–which determines stroke risk? J Am Soc Echocardiogr 2003;16:71–76.

3. Kienle RD. Congenital pulmonic stenosis. In: Kittleson MD, Kienle RD, ed., Small Animal Cardiovascular Medicine, St. Louis, MO: Mosby; 1998:251–259.

4. Lombard CW, Ackerman N, Berry CR, et al. Pulmonic stenosis and right-to-left atrial shunt in three dogs. J Am Vet Med Assoc 1989;194:71–75.

5. Gonzalez-Alujas T, Evangelista A, Santamarina E, et al. Diagnosis and quantification of patent foramen ovale. Which is the reference technique? Simultaneous study with transcranial Doppler, transthoracic and transesophageal echocardiography. Rev Esp Cardiol 2011;64:133–139.

6. Do DH, Therrien J, Marelli A, et al. Right atrial size relates to right ventricular end-diastolic pressure in an adult population with congenital heart disease. Echocardiography 2011;28:109–116.

7. Adin D. Tricuspid valve dysplasia. In: Bonagura J, Twedt DC, ed. Kirk's Current Veterinary Therapy XIV, St. Louis, MO: Saunders; 2009:762–763.

8. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: An autopsy study of 965 normal hearts. Mayo Clin Proc 1984;59:17–20.

9. Soliman A, Shanoudy H, Liu J, et al. Increased prevalence of patent foramen ovale in patients with severe chronic obstructive pulmonary disease. J Am Soc Echocardiogr 1999;12:99–105.

10. Johnson MS, Martin M, Edwards D, et al. Pulmonic stenosis in dogs: Balloon dilation improves clinical outcome. J Vet Intern Med 2004;18:656–662.