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**<Original Article>**

# Evaluation of echocardiographic markers in dogs with patent ductus arteriosus after ductal closure

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**Abstract:** This study evaluated several known echocardiographic markers related to the assessment of severity in dogs with patent ductus arteriosus (PDA) after the closure of ductus arteriosus (DA). Forty-two dogs with patent ductus arteriosus were enrolled in this study. Evaluated echocardiographic markers were left atrial to aortic root ratio, left ventricular end-diastolic dimension to aortic root ratio, indexed left ventricular end-diastolic and end-systolic dimensions, end-diastolic and end systolic volume index, pulmonic flow to systemic flow (Qp/Qs) ratio, velocities of pulmonary regurgitant and systolic jets, pulmonary flow profiles and the presence of mitral regurgitation. Those markers were evaluated before, 1 day, and 30 days after the closure of DA. Statistically significant changes in some echocardiographic markers (*i.e.*, Qp/Qs) were observed. Although several studies in human and dogs have evaluated the clinical outcome of PDA occlusion using several echocardiographic markers, this study has firstly evaluated all echocardiographic markers known to be useful for assessing the clinical outcome of PDA occlusion in human, and has demonstrated that those markers including the Qp/Qs and pulmonary flow profiles were useful in evaluating of clinical outcome of PDA in dogs and the reduction of LA and LV preload after ductal closure could dramatically reduce after successful ductal occlusion of PDA in dogs.

**Keywords:** Qp/Qs ratio, congenital heart defect, dogs, ductal closure, patent ductus arteriosus

## Introduction

Patent ductus arteriosus (PDA) is the most common congenital heart defect in small breed dogs. Left-to-right shunting PDA causes pulmonary over-circulation subsequent with left atrial (LA) and ventricular (LV) volume overload resulting in left-sided congestive heart failure [1, 10]. The key pathophysiology of PDA is the LA and LV volume overload from pulmonary overcirculation due to the recirculation circuit of ductal flow from pulmonic shunting flow [1, 6]. The LA volume overload results in subsequent LV volume overload due to increased transmitral flow, causing LA and LV enlargements. The LV volume overload subsequently leads to increase end-diastolic volume, indicating LV enlargement and reduced systolic function [1]. Therefore the successful ductal closure of PDA can dramatically reduce the blood volume entering the pulmonary circulation connected to the LA [4, 7, 19]. The reduction of LA volume can further reduce the blood volume entering the LV.

Surgical ligation and interventional closure with embolic coils or Amplatz canine ductal occluder are the most common method for treating PDA in dogs [9, 10, 16]. Although successful closure of PDA can be determined by loss of heart murmur by auscultation or echocardiographic evaluation on the shunt flow at pulmonary artery (PA), long-term outcome after the ductal closure can be more accurately assessed by echocardiography and cardiac biomarker assay [7, 8, 17-19].

The echocardiography is the best tool for characterizing and assessing PDA in human and small animals [4, 7, 8, 18, 19]. Several echocardiographic markers have evaluated for the surgical and interventional outcome after ductal closure in dogs [8, 19]. Known echocardiographic features indicating poor prognosis of PDA include increased left atrial to aortic root ratio (LA/Ao), left ventricular end-diastolic dimension to aortic root ratio (LVID/Ao), indexed left ventricular end-diastolic (iLVID) and end-systolic dimensions (iLVIS), end-diastolic (EDVI) and end systolic volume index (ESVI), and the presence of mitral regurgitation [8].

As the shunt flow from ductus arteriosus (DA) into the PA increases, the blood volume in pulmonary circulation increases relative to the blood volume in systemic circulation. By quantifying the ratio of pulmonary to systemic blood flow (Qp/Qs), the severity of shunt can be estimated [13]. If there is no other shunt in the heart, the increased Qp/Qs indicates

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the increased pulmonary blood flow. Since the shunt direction and volume rely on the relative resistance between pulmonary and systemic circulation, the Qp/Qs is a useful marker for evaluating prognosis of PDA [13]. The Qp/Qs ratio > 1 indicates that the shunt direction is left-to right. If the value is higher, the shunt flow into the PA is larger, suggesting large PDA in human. The velocities of pulmonary regurgitant and systolic jets indicate the RV pressure and the severity of pulmonary hypertension in human infants with PDA [17]. If infants with PDA have significantly elevated RV pressure by pulmonary hypertension, the regurgitant flow will be lower, while systolic flow will be higher. This pattern can be sub-categorized as pulmonary flow profiles, which is a useful prognostic marker in prenatal human patients [17]. Based on type of pulmonary profiles, the severity of PDA can be expected after birth. However, Qp/Qs ratio has never been investigated in dogs with PDA.

Because echocardiographic assessment after the ductal closure is important for determining clinical outcome of dog with PDA, the aim of this study was to evaluate echocardiographic markers related to severity of PDA in human after the ductal closure in dogs with PDA, particularly focusing on the Qp/Qs ratio.

## Materials and Methods

### Study population

Forty-two dogs with PDA were enrolled in this study. All dogs had a characteristic left basilar continuous murmur and echocardiographically confirmed left-to-right shunting at the DA. Any dogs with concurrent systemic disease, multiple congenital cardiac abnormalities, or receiving heart failure medications were excluded in this study. The PDA in all dogs was closed with either surgical ligation or interventional occlusion using either an embolization coils or Amplatz canine ductal occluder.

### Echocardiographic examination

To evaluate changes in echocardiographic markers, several echocardiographic indices indicating left ventricular performance were assessed before (D0), 1 day (D1) and 30 days (D30) after the ductal occlusion. Echocardiographic examinations were conducted in accordance with recommended standards for dogs by using an ultrasound machine (X-300; Siemens, Korea) with a 3 to 9 MHz phase array transducer. M-mode, Doppler, and 2-dimensional echocardiography were performed in left and right lateral recumbency [2]. M-mode echocardiography was used to measure the LVIS and LVID. Indexed LVIS and LVIS were calculated by the LVIS and LVID divided by body surface area of each dog [3, 15]. The 2D-echocardiography was used to measure the LA/Ao ratio and LVID/Ao ratio [11]. ESVI and EDVI were calculated by the following equation: $V = [(7 \times D^3) / (2.4 + D)]$ / body surface area ($m^2$) [12, 14]. Velocities of pulmonary regurgitant and systolic jets were measured at the pulmonary artery level of right parasternal short axis plane using continuous and pulse-

**Table 1.** Changes in echocardiographic variables after the closure of ductus arteriosus in this study population

| Variable | D0 | | D1 | | D30 | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD |
| Age (yr) | 2.51 | 2.48 | – | – | – | – |
| Sex | M(15) | F(27) | – | – | – | – |
| BW (kg) | 2.68 | 1.22 | 2.65 | 1.13 | 2.87 | 1.45 |
| BSA | 0.19 | 0.06 | 0.19 | 0.06 | 0.20 | 0.13 |
| ISACHC | I (22), II (16), III (2) | | – | | I (37), II (5), III (0) | |
| LA/Ao | 1.76 | 0.49 | 1.54* | 0.56 | 1.34* | 0.45 |
| LVID/Ao | 2.60 | 0.57 | 2.34* | 0.67 | 1.87* | 0.51 |
| iLVID | 14.90 | 3.85 | 13.40* | 2.56 | 11.00* | 4,25 |
| iLVIS | 9.13 | 2.61 | 9.12 | 2.72 | 8.79 | 2.87 |
| ESVI ($mL/m^2$) | 19.66 | 16.22 | 19.70 | 17.32 | 17.80 | 11.34 |
| EDVI ($mL/m^2$) | 51.44 | 29.97 | 45.30* | 25.43 | 37.21* | 15,25 |
| MR (n) | 21/42 | | 19/42 | | 10/42 | |
| PA (m/s) | 1.79 | 0.60 | 1.23* | 0.45 | 1.21* | 0.34 |
| PR (m/s) | 3.89 | 1.02 | 0.56* | 0.65 | 0.45* | 0.55 |
| Qp/Qs | 2.30 | 0.74 | – | – | – | – |
| Flow profile | A (39) | B (5) | – | – | – | – |

BW, body weight; BSA, body surface area; ISACHC, International Small Animal Cardiac Health Council; LA/Ao, left atrium to aorta ratio; LVID/Ao, left ventricular diastolic dimension to aorta ratio; iLVID, indexed left ventricular diastolic dimension; iLVIS, indexed left ventricular systolic dimension; ESVI, end systolic volume; EDVI, end diastolic volume index; MR, mitral regurgitation; PA, transpulmonic peak velocity; PR, pulmonic regurgitant flow velocity; A, growing pattern; B, pulsatile pattern. *Statistically significance sets at $p < 0.05$.

wave Doppler echocardiography. The presence of mitral regurgitation (MR) was assessed using color Doppler echocardiography at left apical two chamber plane [5]. To obtain pulmonary flow profiles, the PA flow was recorded using pulse Doppler echocardiography, after the DA was visualized at right parasternal short axis view [17]. To obtain the Qp/Qs, the PA velocity time integral (VTI) and length of right ventricular outflow tract (RVOT) was measured at right parasternal short axis view using pulse Doppler echocardiography, whereas the systemic VTI and length of left ventricular outflow tract (LVOT) was measured at left apical long axis [13]. The Qp/Qs was then calculated by the following equation: [RVOT VTI-cm × π × (RVOT-mm/2)$^2$] / [LVOT VTI-cm × π × (LVOT-mm/2)$^2$].

### Statistical analysis

Data are shown as the means ± SD. Statistical significance was defined as $p < 0.05$. A one-way repeated measure ANOVA in conjunction with a Bonferroni's multiple comparison test was used to compare each parameters before and after the ductal occlusion. The Spearman method was used to test for correlations between physiological variables and echocardiographic variables. SPSS 15.0 for Windows (SPSS, USA) was used for all statistical analysis.

## Results

### Study population

The study population consisted of 42 small breed dogs with PDA including Maltese (29/42), Pomeranian (5/42), Toy Poodle (3/42), Cocker Spaniel (2/42), mixed (2/42), and Yorkshire Terrier (1/42). Surgical ligation with thoracostomy was done in 1/42 dogs while interventional occlusion either with embolization coils or Amplatz canine ductal occluder was done in 24/42 and 17/42 dogs, respectively. Minimal diameter of the ductus was 2.2 ± 1.7 mm in this study population. Age was 2.5 ± 2.5 years (range, 6 months to 8 years old), while body weight was 2.7 ± 1.2 kg (range, 1.3–5.8 kg). Female was predominant (27/42). Heart failure stage grouped by International Small Animal Cardiac Health Council (ISACHC) in this study group was 24/42 in ISACHC I, 16/42 in ISACHC II and 2/42 in ISACHC III. After successful closure of PDA, the heart failure stage was decreased to 37/42 in ISACHC I and 5/42 in ISACHC II (Table 1).

### Echocardiographic changes after the ductal occlusion

On analysis of pulmonary flow pattern in this study population before ductal occlusion, 37/42 dogs showed growing pattern and 5/42 dogs showed pulsatile type (Fig. 1). The Qp/Qs ratio was > 1 in all dogs. The Qp/Qs ratio in 20/42 dogs was ranged 1–2, while 22/42 dogs were 2-4.

The LA/Ao, LVID/Ao, iLVID and EDVI were significantly reduced at D1 after the ductal occlusion ($p < 0.05$), while the iLVIS and ESVI were not significantly changed at D1 after the ductal occlusion ($p > 0.05$; Table 1). The LA/Ao, LVID/Ao, iLVID and EDVI kept to reduce at D30 after the ductal occlusion ($p < 0.05$; Table 1). Degree of residual shunt was graded by echocardiographic examination. Complete occlusion was identified in 32/42 dogs, while minimal and modest residual shunts were identified 8/42 and 2/42 dogs at D30 after the ductal occlusion, respectively. Significant correlation of the LVID/Ao was identified in the iLVID ($r = 0.889$, $p = 0.0001$) and EDVI ($r = 0.812$, $p = 0.001$). However, the Qp/Qs was not correlated to age (r = -0.32, p = 0.43), size of PDA ($r = 0.37$, $p = 0.31$) and echocardiographic

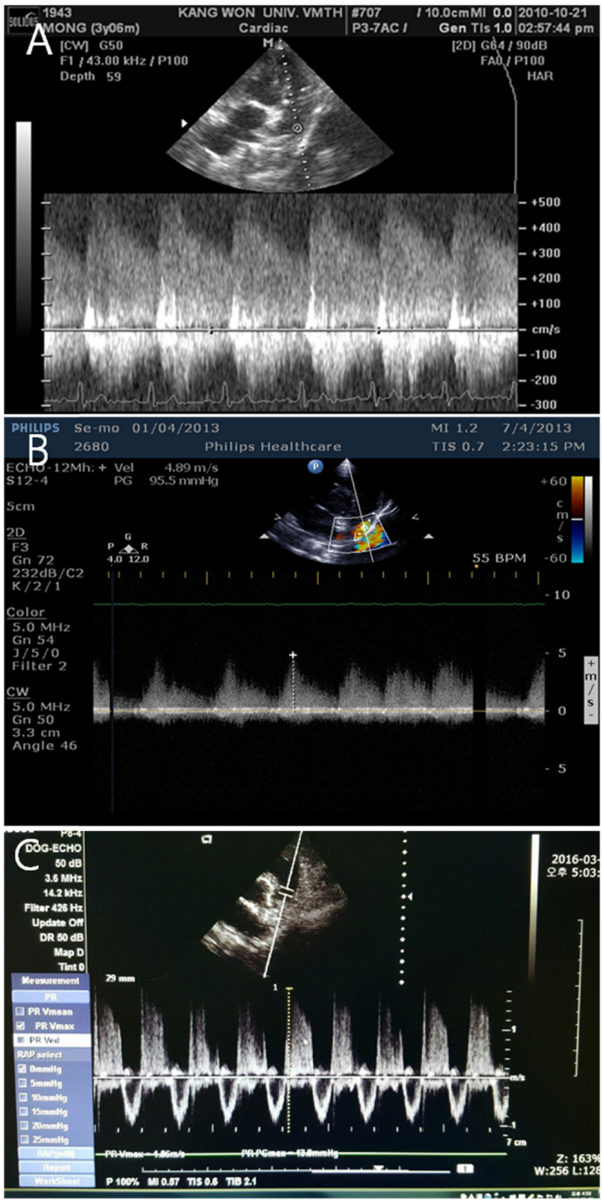


**Fig. 1.** Pulmonary flow profile taken at right parasternal short axis view in dogs with patent ductus arteriosus. (A) Growing pattern (continuous left to right high velocity flow pattern indicates lower pulmonary artery pressure than aortic pressure). (B) Pulsatile pattern. (C) Pulmonary hypertension pattern (bidirectional flow pattern indicates higher pulmonary artery pressure than aortic pressure.

markers ($r < 0.3$, $p > 0.05$). In addition, the MR was found in 19/42 dogs. Of these dogs, 17 dogs had > 40 mL/m$^2$ EDVI and > 2.5 LVID/Ao ratio. Number of dogs with MR was decreased with time (Table 1).

## Discussion

Earliest favorable echocardiographic signs for successful ductal closure in dogs with PDA are the reduction in LVID/Ao, iLVID and EDVI, which indicates LV volume reductions at diastole [8]. In this study, significant reductions in the LVID/Ao, iLVID and EDVI were observed from D1 after ductal closure. Those echocardiographic markers were persistently reduced at the end of test period (D30). Similar finding have also been reported in dogs [8, 19]. Interestingly, the iLVIS and ESVI indicating LV myocardial contractibility were not significantly changed after ductal closure. Furthermore, those markers were not significantly reduced even after D30 of ductal closure. This finding suggested the improvement of cardiac performance in dogs with PDA after successful ductal closure might be due to changes of loading condition in the left cardiac chambers, rather than due to improvement of myocardial contractility, as pointed out previously [4, 7, 18].

Since the shunt direction and volume rely on the relative resistance between pulmonary and systemic circulation, we expected that smaller shunts and younger dogs might have lower Qp/Qs, while larger shunts and older dogs might have higher Qp/Qs. However, there was no correlation of Qp/Qs to either age or ductal size, suggesting the amount of shunt flow into pulmonary circulation might be influenced by many factors (*e.g.*, loading condition, arrhythmias, and concurrent congenital heart defect) including relative ratio between pulmonary and systemic circulation and the size of PDA. The Qp/Qs was only worthy for predicting the shunt direction, but there was no correlation to any echocardiographic prognostic markers in this study.

In dogs with PDA, the mitral annulus gets larger as the LV enlarges, causing MR, even though the mitral valves are intact. Therefore the presence of MR indicates the enlarged LV, suggesting the advanced stage of PDA. Several studies found that the presence of MR were closely correlated to the severity of PDA [8, 10, 19]. In this study, the MR was observed in dogs having echocardiographic evidence of marked LV dilation (*e.g.*, > 40 mL/m$^2$ EDVI and > 2.5 LVID/Ao), indicating this finding was well agreed to others [8, 10, 19].

There are several study limitations in this study. Firstly, the LV volume at diastole and systole was calculated by the Teichholz equation, which might mislead the actual LV volume. Secondly, the PA velocity measured at right parasternal short axis plane often misleads the actual velocity due to large angle between the PA flow and ultrasound beam. Thus it is necessary to confirm the PA velocity at different echocardiographic view (*e.g.*, left apical view). Unfortunately, we have never attempted to measure the PA velocity at left apical view in earlier cases. Furthermore, it is recommended to use right parasternal short axis view to measure the QP/QS. Therefore we only used the data of PA velocity measured at right parasternal short axis view in this study. Lastly, the follow-up period was not long enough to evaluate the changes in regaining LV function, although the earlier markers were all returned to normal range within 30 days after ductal closure.

In conclusion, although several studies in human and dogs have evaluated the clinical outcome of PDA occlusion using several echocardiographic markers [4, 7, 8, 18, 19], this study has firstly evaluated human echocardiographic markers (*i.e.*, the Qp/Qs, pulmonary flow profiles) known to be useful for assessing the clinical outcome of PDA occlusion in human. In addition, this study has demonstrated that those markers were useful in evaluating of clinical outcome of PDA in dogs and the reduction of LA and LV preload after ductal closure could dramatically reduce after successful ductal occlusion of PDA in dogs.

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