The relationship between left ventricular dilation and right ventricular diastolic function in children with a patent ductus arteriosus

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ABSTRACT

The impact of a dilated left ventricular (LV) on right ventricular (RV) diastolic function has not been investigated. We hypothesized that in patients with a patent ductus arteriosus (PDA), LV dilation causes elevation of the RV end-diastolic pressure (RVEDP) through ventricular-ventricular interaction. We identified patients' ages 6 months to 18 years who underwent transcatheter PDA closure at our center from 2010 to 2019. One hundred and thirteen patients were included with a median age of 3 years (0.5–18). The median LV end-diastolic dimension (LVEDD) Z-score was 1.6 (−1.4–6.3). RVEDP was positively associated with RV systolic pressure (0.38, $P < 0.01$), ratio of pulmonary artery/aortic systolic pressure (0.4, $P < 0.01$), and pulmonary capillary wedge pressure (0.71, $P < 0.01$). RVEDP was not associated with LVEDD Z-score (0.03, $P = 0.74$). In children with a PDA, RVEDP was not associated with LV dilation, but was positively associated with RV systolic pressure.

Keywords: End-diastolic pressure, hemodynamics, patent ductus arteriosus, right ventricular function

INTRODUCTION

In patients with right ventricular (RV) dilation, the enlarged RV can negatively affect the left ventricular (LV) diastolic performance through negative interventricular interaction.[1] This negative interventricular interaction can occur in patients with repaired tetralogy of Fallot (TOF). In a prior series of patients with repaired TOF, RV end-diastolic volume by magnetic resonance imaging was positively associated with LV end-diastolic pressure (EDP) at catheterization.[1] The pericardium has a fixed volume with a limited compliance. As the RV enlarges, it impinges on the LV. Given the limited pericardial volume, the LV diastolic volume is compromised leading to increased EDP and diastolic dysfunction.

In contrast, the effect of LV dilation on RV diastolic function has not been previously studied. It is conceivable that LV dilation can negatively impact RV diastolic function due to negative interventricular interaction. A patent ductus arteriosus (PDA) can lead to LV dilation. In patients with a pressure-restrictive PDA, we hypothesized that LV dilation would be associated with an elevated RV end-diastolic pressure (RVEDP). To examine this hypothesis, we evaluated children who had undergone transcatheter PDA closure and determined if the degree or LV dilation on echocardiography was associated with the RVEDP measured at catheterization.

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METHODS

We retrospectively identified patients' aged 6 months to 18 years who underwent transcatheter PDA closure at Levine Children's Hospital from January 1, 2010 to September 30, 2019. Catheterization reports and angiograms and precatheterization echocardiograms were examined. For inclusion, patients were required to have had a precatheterization echocardiogram within 6 months of the catheterization, and the study had to include a measurement of the LV end-diastolic dimension (measured in mm) (LVEDD) and associated LVEDD Z-score. In addition, included patients had to have documentation of the RVEDP in the catheterization report. If a patient underwent several echocardiograms preceding the catheterization, the echocardiogram performed closest to the catheterization was included for measurement. We excluded patients if the pulmonary artery pressure was elevated (defined as a mean pulmonary artery pressure >25 mmHg or >1/2 systemic pulmonary artery systolic pressure). We also excluded patients with any other type of congenital heart disease (including a secundum atrial septal defect and ventricular septal defect), with moderate or greater tricuspid regurgitation, with moderate or greater pulmonary regurgitation, or with LV ejection fraction (LVEF) <45%. This retrospective cohort study was approved by the Atrium Health Institutional Review Board. For included patients, we reviewed the medical record and extracted demographic, clinical, echocardiographic, catheterization-derived, and angiographic variables. For the precatheterization echocardiogram, the following variables were extracted directly from the echocardiogram reports: LVEDD Z-score, indexed LV end-diastolic volume (indexed LVEDV), LVEF, peak instantaneous gradient across the PDA, and the size of the PDA (small, moderate, or large). For catheterization-based data, we extracted the following variables from the report: RVEDP, pulmonary artery systolic pressure, RV systolic pressure, pulmonary artery mean pressure, aortic systolic pressure, pulmonary capillary wedge pressure, and Qp/Qs. Patients' angiograms were reviewed for the extraction of PDA Type (A-F) and minimum diameter of the PDA.

Descriptive statistics were calculated, including means and standard deviations for continuous variables, and counts and percentages for categorical variables. Associations were assessed between RVEDP and patient variables using simple linear regression models with RVEDP as the dependent variable. The Student's *t*-test was used to compare RVEDP between patients with LVEDD Z-score >2 and those with Z-score ≤2. All statistical analyses were performed on SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC). A two-tailed $P < 0.05$ was considered statistically significant.

RESULTS

A total of 113 patients met the inclusion criteria. The baseline characteristics are listed in Table 1. The median age was 3 years (range: 0.5–18 years), and the median weight was 13.5 kg (range: 6.2–76.4). The median LVEDD Z-score was 1.6 (range: 1.4–6.3), and 48 (42%) patients had a Z-score ≥2. The median ratio between the pulmonary artery and aortic pressure was 0.3 (0.2–0.5). The median pulmonary artery mean pressure was 18 mmHg (range: 11–25). Most patients had a conical, Type A PDA.

Table 2 shows associations between RVEDP and patient variables. RVEDP was significantly associated with pulmonary capillary wedge pressure (coefficient: 0.71, $P < 0.01$), RV systolic pressure (coefficient: 0.38, $P < 0.01$), and the ratio of the pulmonary artery/aorta systolic pressure (coefficient: 0.41, $P < 0.01$). No association was found between RVEDP and markers of LV dilation, including LVEDD Z-score ($P = 0.74$) and indexed LVEDV ($P = 0.9$).

Figure 1 shows the RVEDP in patients with LVEDD Z-score ≥2 and in those with Z-score <2. RVEDP was not significantly different between these two groups ($P = 0.5$). Furthermore, RVEDP was not significantly different in patients with Qp/Qs ≥1.5 and those <1.5 (p = NS).

DISCUSSION

In a group of pediatric patients undergoing cardiac catheterization for transcatheter closure of a PDA, RVEDP was not significantly associated with markers of LV dilation, including LVEDD Z-score and indexed LVEDV. However, RVEDP was associated with RV systolic pressure, the ratio of the pulmonary artery/aorta systolic pressure, and pulmonary capillary wedge pressure.

Studies have shown that RV dilation can lead to LV diastolic dysfunction. Schwartz *et al.* found that in
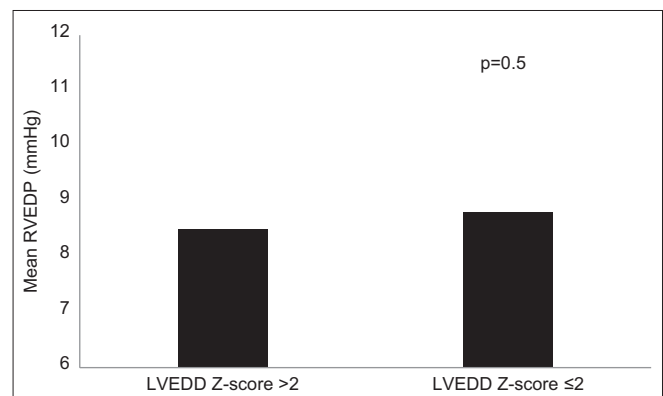
Figure 1: Comparison of RVEDP between patients with LVEDD Z-score >2 or ≤2. RVEDP: Right ventricular end-diastolic pressure, LVEDD: Left ventricular end-diastolic dimension

Table 1: Baseline characteristics of 113 patients who underwent catheterization for patent ductus arteriosus closure

Variable	Median (range) or *n* (%)
Demographic	
Age at catheterization (years)	3.0 (0.5-18.0)
Weight at catheterization (kg)	13.5 (6.2-76.4)
Male	30 (27)
Echocardiographic	
LVEDD Z-score	1.6 (−1.4-6.3)
LVEDD Z-score ≥2	48 (42)
Indexed LVEDV (mL/m²)	81.0 (18.0-173.0)
LVEF	65 (46.7-82.0)
Catheterization	
RVEDP (mmHg)	9.0 (4.0-15.0)
Pulmonary artery systolic pressure (mmHg)	23.0 (16.0-40.0)
RV systolic pressure (mmHg)	25.0 (19.0-40.0)
Pulmonary artery mean pressure (mmHg)	18.0 (11.0-25.0)
Aorta systolic pressure (mmHg)	75.5 (63.0-102.0)
Pulmonary artery/aorta systolic pressure	0.3 (0.2-0.5)
Qp/Qs	1.3 (1.0-4.6)
Pulmonary capillary wedge pressure (mmHg)	12.0 (6.0-22.0)
Angiographic	
Minimum diameter of patent ductus arteriosus (mm)	2.0 (0.5-4.5)
Patent ductus arteriosus type	
A	69 (61)
B	3 (3)
C	24 (21)
D	3 (3)
E	13 (11)
F	1 (1)

LV: Left ventricular, RV: Right ventricular, RVEDP: RV end-diastolic pressure, LVEDD: LV end-diastolic dimension, LVEF: LV ejection fraction, LVEDV: LV end-diastolic volume

Table 2: Univariate regression analysis of possible association between various patient variables and right ventricular end-diastolic pressure

Variable	Coefficient	*P*
Age	0.13	0.17
Sex	0.08	0.4
LVEDD Z-score	0.03	0.74
Indexed LVEDV	−0.01	0.9
RV systolic pressure	0.38	<0.01
Pulmonary artery/aorta systolic pressure	0.41	<0.01
Qp/Qs	0.1	0.3
Pulmonary capillary wedge pressure	0.71	<0.01

LV: Left ventricular, RV: Right ventricular, LVEDD: LV end-diastolic dimension, LVEDV: LV end-diastolic volume

patients with repaired TOF, LVEDP was positively associated with RV dilation.[1] In patients with repaired TOF and progressive RV dilation, LV diastolic volume is compromised as the pericardium limits the ability of the LV to expand in the setting of an enlarged RV. Pericardial constraint limits the total ventricular volume that can be achieved and mediates diastolic ventricular interaction.[1]

Based on these data and physiology, we conversely hypothesized that a dilated LV would negatively impact

RV diastolic function and would lead to elevated RVEDP. We chose to evaluate patients with a restrictive PDA because these patients will have varying degrees of LV dilation, but should have normal pulmonary artery pressure and normal or near normal LV systolic function. We excluded patients with elevated pulmonary artery pressure as increased pulmonary pressure could influence RVEDP by increasing RV afterload. To the best of our knowledge, the influence of LV dilation on RV diastolic pressure has not been previously examined.[2]

Our study did not find a significant association between markers of LV dilation by echocardiogram and RVEDP. When the cohort was divided in those with an LVEDD Z-score >2 or ≤2, the mean RVEDP was not significantly different between the two groups. There are several possible explanations for our results. First, we may have failed to identify an association between LV dilation and RVEDP, because severe LV dilation was uncommon in our cohort. In children and adolescents, the RVEDP is typically low and the RV end-diastolic volume is less than the LVEDV. Thus, increases in LV size may not impact the RV end-diastolic volume and pressure, especially if the LV dilation is only mild. In fact, the median LVEDD Z-score among our cohort was 1.6; thus, most patients had a normal or mildly dilated LV. Severe LV dilation was uncommon among our patients. In patients with mild LV dilation, the influence of the mildly dilated LV on the RV size and diastolic function is likely minimal.

Alternatively, it is also possible that LV size may not significantly affect RV diastolic function. Perhaps the geometry of the RV limits its vulnerability in the setting of a dilated LV. The RV cavity is typically crescentic shaped with thin walls. The chamber may be more compliant at the baseline, and thus, small-to-moderate changes in LV volume may not impact the RV's diastolic performance.

Furthermore, in our group of patients, RVEDP was associated with markers of RV afterload, including RV systolic pressure and the ratio of the pulmonary artery/ aorta systolic pressure. These data suggest that RV diastolic function is more influenced by RV afterload than by interventricular interaction. Animal models show that the RV is more sensitive to afterload than the LV; in these models, small increases in RV afterload can cause significant decreases in RV stroke volume.[2,3] In a patient group with minimal LV dilation, it is reasonable that markers of RV afterload influenced the RVEDP more so than LV size. It is also possible that the association between RVEDP and RV systolic pressure could be due to volume status and pulmonary vasodilation from anesthesia. We observed a relationship between RVEDP and the ratio of the pulmonary artery/aortic systolic pressure; however, this relationship may have been related to systemic and pulmonary vasodilation from

general anesthesia. Ultimately, firm conclusions about the influence of LV dilation on RV diastolic function cannot be drawn from our limited study. Additional study of patients with more severely dilated LVs would be useful.

RVEDP was also associated with pulmonary capillary wedge pressure which is a surrogate left atrial pressure. Intravascular volume status likely drives this relationship. All patients are given standard precatheterization instructions, but some may be without oral intake for longer than others.

Our study has a several important limitations to recognize. First, the values for LVEDD Z-score and indexed LVEDV were extracted directly from the echocardiogram reports and not from the echocardiographic images. Thus, any variability in how these values were obtained by the treating echocardiographers could affect the validity of our results. Similarly, we extracted the RVED*P* values from the catheterization reports, and variability could potentially exist in the manner in which the treating interventionalists recorded the RVEDP. Finally, we did include patients with mildly decreased LV systolic function which may have affected LV size and even RVEDP. However, the median LVEF was 65%, and only a very small number of patients had LVEF <55%. Thus, it is unlikely that the small number of patients with LVEF between 45% and 55% significantly affected our findings.

CONCLUSIONS

In our cohort of pediatric patients undergoing catheterization for PDA closure, RVEDP was not associated with markers of LV dilation, but, instead, was associated with markers of RV afterload such as RV systolic pressure and the pulmonary artery/aorta systolic pressure ratio. Further study is required; however, in a cohort of patients with mild LV dilation, LV size does not appear to have a significant effect on RVEDP.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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