Effects of Balloon Valvuloplasty on Coronary Blood Flow in Neonates With Critical Pulmonary Valve Stenosis Assessed With Transthoracic Doppler Echocardiography

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Background: Treating pulmonary valve stenosis with balloon valvuloplasty (BV) is a good model to study the effect of right ventricular (RV) pressures on coronary flow.

Methods: Transthoracic Doppler echocardiography was used to register coronary flow in 10 age-matched healthy controls and 7 neonates before and 1 day after BV.

Results: Left ventricular fractional shortening and cardiac output increased significantly after BV. Right coronary artery diameter decreased from 1.2 ± 0.2 to 1.1 ± 0.1 mm ($P < .02$). Posterior descending coronary artery flow parameters decreased significantly, with blood flow decreasing from 8.4 to 5.7 ± 1.9 mL/s ($P < .003$). RV end-diastolic pressure and RV systolic pressure explained almost totally the variation in coronary flow ($r^2 = 0.87$).

Conclusions: RV end-diastolic pressure and RV systolic pressure determined coronary flow in neonates with critical pulmonary valve stenosis. Cardiac output and left ventricular fractional shortening increased after pulmonary valve BV. (J Am Soc Echocardiogr 2009;22:165-169.)

Keywords: Coronary flow, Pulmonary valve stenosis, Transthoracic Doppler echocardiography

Severe neonatal pulmonary valve stenosis (PVS) is an acute pediatric cardiac problem. The assessment of its severity is based mostly on the registered Doppler gradient across the pulmonary valve.[1] Intracardiac pressure and flow conditions affect coronary flow in patients with congenital heart disease.[2,3] Stenosis increases myocardial work oxygen demand and consequently coronary flow. Increased flow leads to increased endothelial cell shear stress and nitric oxide secretion, which dilates the coronary arteries.[4] A mismatch between myocardial blood supply and ventricular work demand results in right ventricular (RV) dysfunction. Understanding the physiology of coronary flow is important for appropriate treatment.

Recent advances in Doppler and color echocardiography techniques have enabled the estimation of coronary flow dynamics in neonates,[5,6] children,[7-9] and adults.[10,11] Transthoracic Doppler echocardiography has been shown to be equivalent with the invasive measurement of coronary flow velocity by intracoronary Doppler guidewire.[10] This method has the potential to show the effects of acute changes in loading conditions on blood flow.[12]

We assessed coronary flow parameters in the posterior descending coronary artery (PDCA) and the left anterior descending (LAD) coronary artery with transthoracic pulsed-wave Doppler echocardiography before and after balloon valvuloplasty (BV) in neonates with severe PVS.

METHODS

Coronary flow parameters were determined by transthoracic Doppler echocardiography in 7 newborns with critical PVS at the age of 2 to 6 days (mean age, 3.8 ± 1.7 days). Pulmonary valve gradient and coronary flow measurements were performed on conscious patients before and 1 day after BV. Age-matched healthy neonates (n = 10) were included as controls.

The neonates were born at term after normal vaginal delivery and had high Apgar scores. They were in good clinical condition and had no signs of heart failure at presentation. Systolic murmur was heard at the left sternal edge. Ductus arteriosus was moderate in size and similarly patent both before and after BV and in controls. The exclusion criteria were clinical signs of infection or inflammation or C-reactive protein level > 0.8 mg/L prior to the procedures. Written consent was obtained from the guardians or parents of the neonates enrolled in the study. The study protocol conformed to the principles outlined in the Declaration of Helsinki.[13] The study was approved by the ethics committee for human research at Lund University.

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Transthoracic Doppler echocardiographic examinations were performed using a Sequoia C512 (Acuson, Mountain View, CA) with a 7-MHz to 10-MHz transducer. Standard M-mode, B-mode, and Doppler echocardiographic studies revealed the anatomy and function of the heart. Left ventricular mass was calculated from M-mode echocardiography in accordance with the recommendations of the American Society of Echocardiography.[14] Left ventricular fractional shortening was computed using the standard formula.[15]

Cardiac output was calculated from aortic ring diameter (measured from the long-axis view by M-mode echocardiography), heart rate, and velocity-time integral (VTI) measurements. Because the PDCA was almost parallel to the reflecting ultrasound, it was impossible to measure its diameter. Therefore, the internal dimension of the main right coronary artery (RCA) was measured and used in flow calculations instead. The internal dimension of the RCA was measured from the standard left parasternal short-axis view at the R wave with the calipers applied on the inner borders of the vascular lumen. The internal dimension of the LAD coronary artery was measured at 2 to 3 mm distal to the bifurcation of the left main coronary artery.

An apical 4-chamber view was obtained. The probe was angulated anteriorly and rotated anticlockwise until the disappearance of the right ventricle from the view. Flow in the proximal half of the PDCA locating in the posterior interventricular groove was registered after finding good coronary flow signals. The velocity scale was decreased to the minimum range and then gradually increased until color signals were optimized within the vessel lumen. The pulsed Doppler sample volume was placed within the proximal half of the PDCA, and the sample volume was adjusted to 0.5 to 1.0 mm. A sample volume that gave the best quality envelope and pure sound throughout the cardiac cycle was chosen. The internal dimension of the LAD coronary artery was measured from the standard parasternal short-axis view at the R wave. The calipers were applied to the internal borders 2 to 3 mm distal to the bifurcation of the left main coronary artery. The technique was otherwise similar to that used in the registration of the flow in the PDCA. We have described the methods earlier in detail.[16]

The studies were recorded on magneto-optical discs for later analysis. All M-mode, 2-dimensional, and Doppler echocardiographic measurements of PDCA and LAD coronary artery flow were analyzed blindly by one examiner (E.H.A.) many months after the actual studies. Coronary blood flow was calculated according to the following formula: coronary blood flow (mL/s) = $VTI_t \times$ heart rate $\times \pi$(coronary radius)^2, where VTI_t is the VTI in systole plus the VTI in diastole.

During heart catheterization, a 5Fr multipurpose catheter with two side holes (Cordis Corporation, Miami Lakes, FL) was advanced into the right ventricle. RV angiography was done for the measurement of pulmonary valve ring diameter and visualizing the RV outflow tract. Infundibular pulmonary stenoses, sinusoids, or fistulas were not noted on RV angiography. In all 7 neonates, the PDCA raised from the RCA, as shown on recirculation images. Because angiography was not done in controls, we do not know the precise anatomy and origins of their PDCAs. The catheter was advanced with the help of a straight-tip 0.025-in guidewire (Terumo, Tokyo, Japan) further up to the pulmonary artery and through patent ductus arteriosus to the descending aorta. A Tyshak (NuMED, Inc, Hopkinton, NY) or Meditech XXL (Boston Scientific Corporation, Natick, MA) balloon catheter 1.2 to 1.4 (mean, 1.25) times the pulmonary valve diameter was chosen for dilatation. The mean procedure time was 80 minutes (range, 60-120 minutes). RV angiography after balloon dilatation showed good flow through the pulmonary valve, with no significant insufficiency.

Statistical Analysis

Paired Student's *t* tests were used for comparison between the data before and after the procedure and with data from the controls. Simple and multiple regression analyses were used to find the correlation between pressure and flow data. Statistical analyses were performed using StatView version 5.0 (SAS Institute Inc, Cary, NC). A P value $< .05$ was considered statistically significant. Data are presented as mean ± SD. A reproducibility test was performed according to the British Standards Institution.[17]

Reproducibility Test

To test the reproducibility of the measurements of LAD coronary artery flow velocities and VTI, the 10 control children underwent two registrations 15 minutes apart. The paired data were analyzed regarding peak flow velocity in diastole (PFV_d), VTI_t, and blood flow. The analyses of the Doppler tracings were performed offline, separately and independently of each other.

RESULTS

Blood pressure and the rate-pressure product of the left ventricle did not change significantly after BV. Blood hemoglobin concentration was the same before and after the procedure (15.3 ± 0.7 vs 14.9 ± 0.9 g/100 mL; $P < .3$).

Electrocardiograms showed no signs of subendocardial ischemia. The mean diameter of the pulmonary valve ring was 8 mm (range, 6-10 mm). The maximal systolic gradient across the pulmonary valve according to Doppler velocity registration varied from 50 to 100 mm Hg (mean, 55 mm Hg) before and from 10 to 25 mm Hg (mean, 20 mm Hg) after BV ($P < .001$). Left ventricular fractional shortening increased after BV from 32.8 ± 3.4% to 37 ± 5.7% ($P < .01$), and left ventricular cardiac output increased from 100 ± 12 to 118 ± 13 mL/min/kg ($P < .004$). Demographic and echocardiographic data before and after BV and in controls are shown in Table 1.

RCA diameter decreased from 1.2 ± 0.2 to 1.1 ± 0.1 mm ($P < .02$). PFV_d, VTI_t, and blood flow decreased in the PDCA from 40 ± 4.5 cm/s, 15 ± 2.7 cm, and 8.4 ± 1.8 mL/s to 26.3 ± 4.1 cm/s ($P < .0001$), 8.2 ± 2.2 cm ($P < .0002$), and 5.7 ± 1.9 mL/s ($P < .003$), respectively.

The ratio of systolic coronary flow to diastolic coronary flow ratio increased in the PDCA from 47% before to 54% after BV ($P < .3$; Table 2). Simple regression analysis showed a correlation between the change in PDCA flow and RV end-diastolic pressure before and after BV ($r = 0.78$, $P < .008$; Figure 1). The average peak flow velocity and RV end-diastolic pressure ($r = 0.8$, $P < .0002$; Figure 2) and the average peak flow velocity and RV systolic pressure ($r = -0.85$, $P < .0002$; Figure 3) had very significant correlations. Multiple regression analysis showed that the average peak flow velocity was explained both by RV end-diastolic pressure and RV systolic pressure ($r = 0.93$, $r^2 = 0.87$, $P < .0002$).

LAD coronary artery PFV_d, VTI_t, and blood flow decreased from 60 ± 6 cm/s, 34 ± 3 cm, and 12.6 ± 2.2 mL/s to 40 ± 5 cm/s ($P < .0001$), 16.4 ± 3.4 cm ($P < .0001$), and 8.8 ± 1.9 mL/s ($P < .007$), respectively. LAD coronary artery diameter decreased from 1.4 ± 0.3 to 1.3 ± 0.2 mm ($P < .002$). RCA and LAD coronary artery diameters after BV remained significantly larger than in healthy controls (1.1 ± 0.1 vs 1.0 ± 0.11 mm, $P < .03$, and 1.3 ± 0.2 vs