Using Transthoracic Doppler Echocardiography to Diagnose Reduced Coronary Flow Velocity Reserve in the Posterior Descending Coronary Artery in Children With Elevated Right Ventricular Pressure

Shunsuke Shimada, MD; Kenji Harada, MD; Manatomo Toyono, MD; Masamichi Tamura, MD; Goro Takada, MD

Background
Advances in transthoracic Doppler echocardiography enable noninvasive measurements of coronary flow velocity and coronary flow velocity reserve (CFVR) in the posterior descending coronary artery (PD).

Methods and Results
To evaluate CFVR in the PD of children with elevated right ventricular (RV) pressure, 19 children with RV pressure overload and 13 age-matched controls with normal RV pressure were studied using transthoracic Doppler echocardiography. Average peak flow velocity (APV) was measured at rest and in hyperemic conditions (intravenous administration of adenosine of 0.16 mg·kg⁻¹·min⁻¹). Compared with controls, the PD CFVR was significantly reduced in the patients with elevated RV pressure (1.87±0.42 vs 2.49±0.55, p<0.01) because their mean baseline APV was significantly greater (27±6 vs 19±4 cm/s, p<0.01), although hyperemic APV was not significantly different (49±10 vs 48±14 cm/s, p=NS).

Conclusions
PD CFVR is limited in patients with elevated RV pressure because of elevation of the baseline resting flow velocity. (Circ J 2007; 71: 1912–1917)

Key Words: Coronary flow velocity reserve; Posterior descending coronary artery; Transthoracic Doppler echocardiography

Prolonged exposure of the right ventricle (RV) to a high resistance results in RV hypertrophy as a compensatory mechanism. On the other hand, the coronary circulation can accommodate marked changes in blood flow in response to increased oxygen demand. RV pressure overload has been reported to alter RV myocardial oxygen demand and, consequently, coronary flow reserve (CFR). The mismatch between myocardial blood supply and ventricular work demand has been proposed as a potential mechanism for RV or left ventricular (LV) dysfunction. Therefore, an understanding of the coronary circulation in such clinical conditions is important for appropriate hemodynamic management during long-term follow-up. Although monitoring of coronary flow and flow velocity reserve has been used as a measure of myocardial blood perfusion, these parameters usually have to be assessed by invasive or semi-invasive techniques that are highly expensive and not widely used.

Recent advances in Doppler and color echocardiography techniques have enabled estimation of the coronary flow dynamics in the posterior descending (PD) coronary artery. In addition, noninvasive measurement of coronary flow velocity using transthoracic Doppler echocardiography has shown equivalence with invasive measurement of coronary flow velocity by Doppler guide wire method. This study assessed the PD flow velocity and flow velocity reserve in children with elevated RV pressure.

Study Subjects
The study group comprised 32 patients: 19 children, aged 3 months to 12 years (2.7±3.7 years) with elevated RV pressure because of ventricular septal defect (n=7), tetralogy of Fallot (n=7), pulmonary valve stenosis (n=3) or double outlet RV (DORV) (n=2); 13 age-matched children aged 5 months to 12 years with normal RV systolic pressure (the control group) who had a small patent ductus arteriosus (n=6), a subpulmonary ventricular septal defect with a small left-to-right shunt (n=5), or mild coarctation of the aorta (n=2). All patients underwent cardiac catheterization or catheter intervention for diagnostic purposes. Studies were performed while the children were in a quiet resting state. Echocardiographic examination of the patients was performed in the cardiac catheterization laboratory before routine heart catheterization. Premedication consisted of pethidine hydrochloride administered subcutaneously 1 h before catheterization. Sedation with thiopental sodium (3 mg/kg iv) was administered when necessary. The nature of the study was discussed with each patient’s parents, and informed consent for the research protocol was obtained.

Echocardiography
Transthoracic Doppler echocardiographic examination was performed using an Aloka SSD-ProSound-5500 (Aloka Inc, Tokyo, Japan) with a 5.0MHz transducer. From the apical 2-chamber view with the transducer rotated counter-
clockwise and angulated posteriorly, PD flow signals could be seen in the interventricular sulcus in association with the middle cardiac vein. Occasionally, the transducer was aimed posteriorly from the subcostal view, allowing the PD flow signals to be seen along the diaphragmatic surface of the heart. The velocity scale was decreased to the minimum range and then gradually increased until color signals were optimized within the vessel lumen. The color gain was also adjusted to minimize color-flow scatter, and the Doppler filter was set at 200–400 Hz. After demonstration of the coronary flow signals, the pulsed Doppler sample volume was placed at the PD, and decreased to 0.5–1.0 mm. Visualization of the PD color flow signals was achieved from the standard short-axis view of the great vessels, as we reported previously. Measurements of maximum peak coronary flow velocity (MPV) and average peak coronary flow velocity (APV) were performed using the internal analysis package of the ultrasound unit. Measurements were calculated in consideration of the angle between the Doppler beam and the coronary flow direction as determined by the 2-dimensional (2D) echocardiogram. Absolute velocity was defined as the product of the measured velocity and cosine of the angle between the Doppler beam and the direction of blood flow.

**Coronary Flow Velocity Reserve (CFVR) Measurement**

After baseline recordings, adenosine triphosphate (ATP) was infused in the right antecubital vein at a dose of 0.16 mg·kg⁻¹·min⁻¹ for 6 min. Data were obtained at rest and during ATP infusion. The ratio of the APV during hyperemia to baseline APV was calculated as an index of flow velocity reserve.

**Cardiac Catheterization**

The RV systolic pressure was measured using a fluid-filled pressure manometer system and recorded with a Cath Lab System (Siemens Cathcor, Germany). The rate–RV systolic pressure product was calculated.

**Statistical Analysis**

Data are expressed as mean ± SD. For comparison data, the paired t-test was used. Statistical comparison between patients with normal RV pressure and patients with elevated RV pressure was performed using the unpaired t-test. To evaluate the effects of observational variability on the measurements of the PD flow velocities, 2 independent observers analyzed 10 randomly selected Doppler recordings. Intraobserver variability was assessed in 10 children who underwent the measurements by Doppler echocardiography. Analysis of the difference in the measurements was performed according to the technique of Bland and Altman. A p-value <0.05 was considered statistically significant.

**Results**

Clear envelopes of basal and hyperemic flow velocities in the PD were obtained in 17 of 19 (89%) patients with elevated RV pressure and in 12 of 13 (92%) controls, respectively, by transthoracic Doppler echocardiography. The success rate for the PD flow velocity recordings did not differ between the 2 groups. Three subjects (1 each with tetralogy of Fallot, DORV and a small patent ductus arteriosus), were completely excluded from the study because we were unable to determine the entire spectral velocity envelope or overlapping wall noise. Therefore, a total of 29 subjects were analyzed. Examples of PD flow velocity changes during hyperemia are shown in Fig 1 (normal RV pressure) and in Fig 2 (elevated RV pressure). Table 1 shows the echocardiographic data. The mean angle between the Doppler beam and the coronary flow direction as determined by the 2-dimensional (2D) echocardiogram. Absolute velocity was defined as the product of the measured velocity and cosine of the angle between the Doppler beam and the direction of blood flow.

**Fig 1.** An example of flow velocity changes in the posterior descending coronary artery during hyperemia in a patient with normal right ventricle pressure. ATP, adenosine triphosphate.
CFVR and basal APV, RV systolic pressure, rate–RV systolic pressure product were observed (r=–0.64, –0.57, and –0.55, respectively, p<0.01), as shown in Fig 3.

ATP infusion caused increases in heart rate (from 120±19 to 130±19 beats/min, p<0.01) and decreases in systolic (from 90±9 to 81±11 mmHg, p<0.01), diastolic (from 55±9 to 41±10 mmHg, p<0.01), and mean (from 68±7 to 55±8 mmHg, p<0.01) arterial pressures. Changes in heart rate and arterial blood pressures did not differ between the patients with elevated RV pressure and controls.

Good agreement was obtained between the 2 independent observers’ measurements of MPV, APV, and CFVR in the PD (r=0.97, 0.95, and 0.92, respectively). Mean differences for the peak diastolic flow velocity and the average peak velocity of diastolic flow in the PD were 0.19±2.53 cm/s, 0.17±2.26 cm/s, and 0.03±0.11, respectively. Excellent correlation was also observed in the intraobserver measurements of the peak diastolic flow velocity and the average peak velocity of diastolic flow in the PD (r=0.92, 0.98, and 0.94, respectively). Mean differences for the peak diastolic flow velocity and the average peak velocity of diastolic flow in the PD were 0.09±3.55 cm/s, 0.28±0.71 cm, and 0.02±0.09, respectively.

**Discussion**

Previous experimental studies in animals have shown an alteration of right coronary arterial blood flow as a result of elevated RV systolic pressure. CFVR has been reported as impaired in patients after atrial switch repair, suggesting
RV dysfunction in long-term survivors of the Mustard operation. Thus, CFVR measurement in the right coronary artery provides useful clinical and physiological information in patients with RV pressure overload; however, it usually requires invasive and expensive techniques with Doppler catheters or positron emission tomography. Transthoracic Doppler echocardiography has been proven to reliably assess coronary flow velocity noninvasively. Thus, PD flow velocity measurements by transthoracic Doppler echocardiography may be used in the clinical setting to assess coronary artery function. In the present study, flow signals in the PD, regardless of their origin from the right coronary artery or circumflex coronary artery, were able to be imaged in children with various heart diseases. The rate of success of measurement of the PD flow was sufficiently high for the clinical application. In the present study, CFVR was limited in the patients with elevated RV pressure, but the mechanism by which CFVR was reduced in the patients with elevated RV pressure could not be determined from our study. An increase in resting coronary flow has been demonstrated as a primary mechanism of restriction of CFR in patients with LV hypertrophy such as aortic regurgitation, mitral regurgitation, and hypertension. Thus, increased the resting APV can be proposed as a potential mechanism for reduced CFVR in patients with elevated RV pressure. Alternatively, abnormalities in regional blood flow may be the result of myocardial fibrosis secondary to prolonged RV hypertension. Prolonged RV pressure overload may result in decreased myocardial capillary density and, therefore, reduced flow reserve, although we have no data regarding this.

Study Limitations

First, in the current study, the PD flow velocities were calculated considering the angle between the Doppler beam and the coronary flow direction as determined by the 2D echocardiogram. When the angle of incidence to flow is excessive, measurements of velocities may be unreliable. However, the ratio of PD flow velocities during ATP infusion to those under control conditions should not be affected by the angle of incidence, because the cosine factors of the numerator and denominator would cancel out. Second, we measured flow velocity, not coronary flow volume, in the present study. The diameter of the PD is...
small, and accurate measurement of blood flow is particularly dependent on accurate measurement of vessel diameter. Flow-velocity measurements do not provide an absolute value but are linearly related to changes in absolute flow when vessel area remains unchanged. It is possible that the results seen in the present study may relate to changes in the lumen area of the coronary artery during hyperemia. Although the vasodilator is different, the change in CFVR had a strong correlation to lumen diameter change of the left anterior descending artery induced by nitroglycerin administration than by the change in basal coronary flow velocity.\textsuperscript{32} We cannot exclude the possibility that dilation of the PD may have led to augmented flow with less of an increase in velocity in the patients with elevated RV pressure. Third, we made no attempt to measure RV size, function or RV, any of which could influence PD CFVR. Accurate measurements of RV volume and mass require magnetic resonance imaging\textsuperscript{33} and this technique was not available in the present study. Fourth, control subjects examined in the present study were not entirely normal. We did not attempt to measure PD CFVR in normal children, for ethical reasons. The present study consisted of a small number of patients with elevated RV pressure because of various kinds of congenital heart disease. In future studies, larger numbers of patients with various cardiac diseases should be examined by the present method.

**Clinical Implications**

Prolonged systemic ventricular pressure overload impairs CFR, and coronary microcirculation abnormalities may contribute to impairment of ventricular function\textsuperscript{2–8} Therefore, an understanding of the coronary circulation under such clinical conditions is important for appropriate long-term hemodynamic management.

**Conclusions**

This study demonstrates that coronary flow velocity and CFVR in the PD of the patients with elevated RV pressure can be measured using transthoracic Doppler echocardiography. The PD CFVR is limited in patients with elevated RV pressure because of elevation of the baseline resting flow velocity.

**References**

478–486.


