The Relationship of Coronary Sinus Dilation with Pulmonary Artery Pressure in Pediatric Patients

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ABSTRACT

Background: Increased right atrial pressure due to pulmonary hypertension may impair venous drainage with resultant coronary sinus dilation. The aim of this study was to search for correlations between coronary sinus diameter and estimated pulmonary artery pressure in children.

Methods: In a prospective study, 100 children who were referred consecutively for transthoracic echocardiography were included in this study. Ratios of coronary sinus diameter to weight, body surface area and aortic annulus were calculated for each patient. Correlation between coronary sinus diameter and estimated pulmonary artery pressure was studied by person correlation. A tricuspid regurgitation peak gradient more than 36 mmHg or pulmonary regurgitation peak gradient more than 25 mmHg were considered as pulmonary hypertension.

Results: Sixty-eight of our participants had no pulmonary hypertension and 32 did. Mean age was 7.6 years in the patients without pulmonary hypertension and 8.0 years in the patients with pulmonary hypertension (P=0.11). Mean coronary sinus diameter to aortic annulus diameter ratio was 0.49 ± 0.13 in the patient with pulmonary hypertension versus 0.38 ± 0.12 in the patient without pulmonary hypertension (P<0.001). The coronary sinus diameter to body surface area ratio was 1.3 ± 0.59 versus 0.7 ± 0.28 (P<0.001), and coronary sinus diameter to weight ratio was 0.06 ± 0.03 versus 0.02 ± 0.01 (P<0.001).

Conclusion: coronary sinus dilation was documented in pediatric patients with pulmonary hypertension. The ratios of coronary sinus diameter to aortic annulus diameter, body surface area and weight correlated significantly with pulmonary hypertension.

►Implication for health policy/practice/research/medical education:
Implication is intended for estimation of pulmonary pressure in children.

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Introduction

Pulmonary hypertension is characterized by an elevation in mean pulmonary artery pressure greater than 25 mmHg at rest or greater than 30 mmHg with exercise (1). Multiple etiologies are implicated in pulmonary hypertension in children (2).

Noninvasive detection of pulmonary hypertension by a reliable, simple method can usually be done by estimating pulmonary artery systolic pressure with Doppler echocardiography, whereas increased pulmonary artery pressure is usually accompanied by changes in right atrial pressure and inferior vena cava collapse (3, 4). Some reports have noted differences between right atrial pressure (estimated either as the size of the right atrium or degree of inferior vena cava collapse) and right atrial pressure measured by right heart catheterization (5, 6).

The coronary sinus, which drains the myocardial veins, opens into the right atrium. The size of the coronary sinus can be used as an index of increased right atrial pressure. Dilation of the coronary sinus in adult patients with right-sided heart disease and pulmonary hypertension has been studied (7). Although the coronary sinus is easily visualized
in pediatric patients and may be dilated in right-sided heart diseases, to date the importance of this dilation in pediatric patients with pulmonary hypertension has not been studied in detail.

Because the size of the coronary sinus in children differs depending on age, weight and body surface area, the present study was designed to search for possible correlations between dimensions of the corrected coronary sinus and estimated pulmonary artery pressure.

Methods
We recruited 100 pediatric patients (with or without cardiac problem, less than 18 years) who had easily measurable and fine enveloped tricuspid or pulmonary insufficiency for transthoracic echocardiography to the hospitals affiliated with Shiraz University of Medical Sciences, Shiraz, southwestern IR Iran. Patients with atrial septal defect, persistent left superior vena cava as determined by contrast echocardiography, pulmonary stenosis, atrio-ventricular or ventriculo-arterial discordance were excluded. The research was approved by the ethics committee of the university, and written informed consent was obtained from the patients or their parents.

Echocardiographic Methods
Echocardiography was done with a General Electric-Vivid 3 echocardiographic system (General Electric-Vivid 3 Vingmed, Horten, Norway), using a 3 MHz or 7 MHz probe. Coronary sinus diameters were measured in subcostal view in infant and lower age in those with good subcostal view, in older children, four-chamber view with some posterior angulations of echocardiographic probe or long axis view was used (Fig. 1). Aortic annulus (in long-axis view), inferior vena cava (in inspiration and expiration), mean tricuspid regurgitation gradient, peak tricuspid regurgitation gradient, peak pulmonary regurgitation gradient and pulmonary regurgitation end diastolic gradient were recorded for each patient. The aortic annular diameter was measured at the time of maximal aortic leaflet excursion as the maximal distance separating the bases of the noncoronary and right coronary cusps. Inferior vena cava was measured in long axis view, 1 cm below the connection to right atrium by M-mode echocardiography. Weight and height were measured in each patient and body surface area was calculated by the Mosteller formula. Tricuspid regurgitation peak gradient more than 36 mmHg or pulmonary regurgitation peak gradient more than 25 mmHg were considered as indirect evidence for pulmonary hypertension. All measurements were carried out three times in each patient by the same pediatric cardiologist and the mean value was used for calculation of sizes.

Statistical Analysis
Quantitative variables were expressed as the mean ± standard deviation. Qualitative variables were determined by numbers and percentages. To establish the differences between independent groups, Student’s t-test was used to exhibit mean differences between normally distributed quantitative variables. Pearson’s correlation analysis was used to assess, correlations, and linear regression was utilized to examine the relationship between coronary sinus diameter and tricuspid or pulmonary regurgitation gradients. A receiver operating characteristic curve was generated for coronary sinus diameter, and the discrimination threshold of this parameter was varied to determine the ability of coronary sinus diameter to distinguish patients with and without pulmonary hypertension. Statistical analyses were done with MedCalc 8.0 software (Mariakerke, Belgium). The results were considered statistically significant when P value was less than 0.05.

Results
This analysis included 100 children of which 68 and 32 cases were with and without pulmonary hypertension respectively. Mean age was 7.6 years in the patients without and 8 years in those with pulmonary hypertension (P =0.11). In the patients with pulmonary hypertension 25 patients had left-to-right shunt (12 with ventricular septal defect and 13 with patent ductus arteriosus), 4 had cardiomyopathy, 4 had hematologic disorders (sickle cell or thalassemia major), 3 had lung disease, and 5 had idiopathic pulmonary hypertension.

The mean ratio of coronary sinus diameter to aortic...
Annulus diameter was 0.49 ± 0.13 in the patients with pulmonary hypertension versus 0.38 ± 0.12 in those without pulmonary hypertension (P = 0.0001). The mean ratio of coronary sinus diameter to body surface area was 1.3 ± 0.59 in the patients with pulmonary hypertension versus 0.7 ± 0.28 in the cases without pulmonary hypertension (P = 0.0001). The mean coronary sinus diameter to weight ratio was 0.06 ± 0.03 in the former group versus 0.02 ± 0.01 in the latter (P = 0.0001).

The ratios of coronary sinus diameter to aortic annulus diameter...
diameter ($P=0.001$, $r=0.51$), coronary sinus diameter to body surface area ($P=0.0001$, $r=0.62$) and coronary sinus diameter to weight ($P=0.000$, $r=0.62$) correlated significantly with pulmonary insufficiency peak gradient. The ratios of coronary sinus diameter to aortic annulus diameter ($P<0.001$, $r=0.54$), coronary sinus diameter to body surface area ($P<0.001$, $r=0.66$) and coronary sinus diameter to weight ($P<0.001$, $r=0.65$) correlated significantly with pulmonary insufficiency peak gradient, and pulmonary insufficiency end diastolic gradient.

The receiver operating characteristic curve generated for the ratio of coronary sinus to body surface area showed that a ratio 1.02 or higher could be regarded as a cutoff point to discriminate between patients with and without pulmonary hypertension. This threshold had a sensitivity of 68.7 percent (95 percent confidence interval: 50-83.9), a specificity of 92.6 percent (95 percent confidence interval: 83.7-97.5), a positive likelihood ratio of 9.35, and a negative likelihood ratio of 0.34 (Figure 2). For the ratio of coronary sinus diameter to weight, a threshold cutoff value of 0.05 or higher could be considered as the cutoff point, with a sensitivity of 62.5 percent (95 percent confidence interval: 43.7-78.9), a specificity of 97.1 percent (95 percent confidence interval: 89.8-99.6), a positive likelihood ratio of 21.25 and a negative likelihood ratio of 0.39 (Fig. 3).

The ratio of coronary sinus to aortic annulus diameter showed a threshold 0.381 with a sensitivity of 62.5 percent (95 percent confidence interval: 43.7-78.9), a specificity of 97.1 percent (95 percent confidence interval: 89.8-99.6), a positive likelihood ratio of 2.32, and a negative likelihood ratio of 0.29 (Fig. 4).

Inferior vena cava collapsibility during respiration correlated significantly with the ratios of coronary sinus diameter to aortic annulus ($r =0.34$, $P =0.004$), coronary sinus diameter to body surface area ($r =0.41$, $P<0.001$) and coronary sinus diameter to weight ($r =0.37$, $P<0.001$).

**Discussion**

This study found statistically significant differences between children with and without pulmonary hypertension in the ratios of coronary sinus to aortic annulus diameter, coronary sinus to body surface and coronary sinus to weight. The indexed coronary sinus also correlated significantly with pulmonary insufficiency peak gradient, pulmonary insufficiency end diastolic peak gradient and inferior vena cava collapsibility. Gunes et al. evaluated the size of the coronary sinus in adult patients and found significant associations with pulmonary artery systolic pressure, right atrial pressure, inferior vena cava size, and the size of right heart chambers (7).

Although it is invasive, catheterization is the gold standard technique for measuring pulmonary artery pressure. Noninvasive estimation of pulmonary artery pressure is often based on the peak velocity of the jet of tricuspid regurgitation or pulmonary regurgitation. The simplified Bernoulli equation describes the relationship of tricuspid regurgitation velocity and the peak pressure gradient of tricuspid regurgitation. To estimate pulmonary artery systolic pressure, right atrial pressure also needs to be taken into account. Right atrial pressure can be estimated based on the diameter and respiratory variation of the inferior vena cava in adults, although a fixed value of 5 or 10 mmHg is often assumed. Despite the good correlation between tricuspid regurgitation velocity and tricuspid regurgitation pressure gradient, Doppler-derived pressure estimates may
be inaccurate in some patients. For example, in patients with severe tricuspid regurgitation, the simplified form of the Bernoulli equation may underestimate pulmonary artery systolic pressure. Overestimations of about 10 mmHg for pulmonary artery systolic pressure is common (8). Therefore, pulmonary hypertension cannot reliably be defined by a cutoff value for Doppler-derived pulmonary artery systolic pressure (9).

The reliability of several cutoff values for tricuspid regurgitation velocity, with right-side cardiac catheterization as the reference, has been assessed in two screening studies in adult patients. One study evaluated the reliability of prospective screening of patients with scleroderma, based on a tricuspid regurgitation velocity 2.5 m/s in symptomatic patients or 3.0 m/s irrespective of symptoms. The results showed that 45 percent of the echocardiographic diagnoses of pulmonary hypertension were false positives (10). In symptomatic patients with human immunodeficiency virus infection, a tricuspid regurgitation velocity of 2.5 m/s or 2.8 m/s as a criterion for pulmonary hypertension were found to be false positive in 72 percent and 29 percent, respectively, of the sample (11). In another study, a tricuspid regurgitation pressure gradient of 40 mmHg (tricuspid regurgitation velocity 3.2 m/s) with an assumed right atrial pressure of 10 mmHg (corresponding to a systolic pulmonary artery pressure of 50 mmHg) was used as the cutoff value for a diagnosis of pulmonary hypertension. The Doppler diagnosis was confirmed in all 32 patients who underwent right heart catheterization (12). In our study we used the cutoff value of tricuspid regurgitation peak gradient of more than 36. For a right atrial pressure of at least 5 mmHg, the estimated systolic pulmonary pressure would thus be 41 mmHg. Theoretically, mean pulmonary artery pressure can be calculated as 0.61 by pulmonary artery systolic pressure + 2 mmHg) (8). The mean pulmonary pressure estimated in the present study was 26 mmHg.

Trivial pulmonary regurgitation, which was easily detectable by Doppler echocardiography, is normally present in a high percentage of healthy persons (13, 14). Masuyama et al. showed that the end diastolic pulmonary artery pressure can be estimated accurately by using the pulmonary regurgitation jet at end diastole, and also the peak pulmonary regurgitation flow velocity in early diastole correlated well with mean pulmonary artery pressure (15). In minor degrees of pulmonary insufficiency, the pulmonary regurgitation signal is useful for measuring end-diastolic pressure of the pulmonary artery (16).

Ehtisham et al. visualized coronary sinus in 81 percent of 43 patients who underwent right heart catheterization for the evaluation of pulmonary hypertension (17). Andrade et al. studied 400 patients aged from 5 to 80 years and defined coronary sinus diameter as 0.4–0.8 cm (18). In our study coronary sinus could be measured in all pediatric patients in apical or sub-costal views. Due to the course of the coronary sinus around the posterior aspect of the left atrioventricular groove in the parasternal long-axis view of the left ventricle, coronary sinus is seen in cross-section as a circular structure adjacent to the posterior mitral valve. Except in patients with a dilated coronary sinus, this echocardiographic view does not always provide a good definition of the coronary sinus. The apical view has been considered as the best choice to evaluate the coronary sinus in a normal heart (18). A dilated coronary sinus can result from increased blood flow due to abnormal venous drainage, as occurs in persistent left superior vena cava, total anomalous intracardiac pulmonary venous drainage, impaired right ventricular function, severe tricuspid regurgitation, coronary sinus diverticulum, or coronary artery-to- coronary sinus fistula (19, 20). Most of these conditions are easily detectable by echocardiography, and left hand contrast echocardiography is a useful method to rule out persistent left superior vena cava draining into the coronary sinus. Patients with decreased left ventricular systolic function show mild coronary sinus dilatation with attenuation of coronary sinus contraction in the presence of congestive heart failure and significant venous congestion. In our study all patients had normal left ventricular systolic function according to echocardiographic observation. The cardiac venous system drains into the coronary sinus, which opens into the right atrium. Thus coronary sinus dilation can be associated with increased right atrial pressure. The collapsibility of inferior vena cava in our study had good correlation with coronary sinus size which can be an index of right atrial pressure. Earlier studies also have documented coronary sinus dilation in adults with pulmonary hypertension and increased right atrial pressure (18, 20).

The coronary sinus is likely to be dilated in pediatric patients with pulmonary hypertension. The ratios of Coronary sinus diameter to aortic annulus diameter, body surface area and weight correlated significantly with tricuspid regurgitation gradient, pulmonary regurgitation gradient and inferior vena cava collapsibility. Thus, echocardiographic evaluation of the coronary sinus in children can be considered an integral component of the echocardiographic assessment of pulmonary hypertension or increased right atrial pressure.

Limitations
The gold standard for determining pulmonary pressure is right heart catheterization. This procedure was not performed in our pediatric patients because of ethical concerns.

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