Postnatal Left Ventricular Diastolic Function After Fetal Aortic Valvuloplasty

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Fetal aortic balloon valvuloplasty (FAV) has shown promise in altering in utero progression of aortic stenosis to hypoplastic left heart syndrome. In patients who achieve a biventricular circulation after FAV, left ventricular (LV) compliance may be impaired. Echocardiographic indexes of diastolic function were compared between patients with biventricular circulation after FAV, congenital aortic stenosis (AS), and age-matched controls. In the neonatal period, patients with FAV had similar LV, aortic, and mitral valve dimensions but more evidence of endocardial fibroelastosis than patients with AS. Patients with FAV underwent more postnatal cardiac interventions than patients with AS ($p = 0.007$). Mitral annular early diastolic tissue velocity (E′) was lower in patients with FAV and those with AS and controls in the neonatal period and over follow-up ($p < 0.001$). Septal E′ was similar among all 3 groups in the neonatal period. In follow-up patients, with FAV had lower septal E′ than patients with AS or controls ($p < 0.001$). Early mitral inflow velocity/E′ was higher in patients with FAV as neonates and at follow-up ($p < 0.001$). Mitral inflow pulse-wave Doppler-derived indexes of diastolic function were similar between groups. In conclusion, echocardiographic evidence of LV diastolic dysfunction is common in patients with biventricular circulation after FAV and persists in short-term follow-up. LV diastolic dysfunction in this unique population may have important implications on long-term risk of left atrial and subsequent pulmonary hypertension. **© 2011 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2011;108:556–560)**

Fetal aortic balloon valvuloplasty (FAV) has shown promise in altering in utero progression of aortic stenosis (AS) to hypoplastic left heart syndrome.[1–4] The postnatal course including size of the left-sided heart structures, left ventricular (LV) systolic function, and surgical management is variable in patients who have undergone FAV.[2] Recent studies have reported promising results, with 35% to 40% of patients achieving a biventricular circulation.[2,4] In children with other left heart obstructive lesions including congenital AS and aortic coarctation, LV diastolic dysfunction is common.[5–8] However, LV diastolic function in patients who have undergone FAV has not been evaluated. This report describes echocardiographic indexes of LV diastolic function in patients with a biventricular circulation after FAV and compares them to patients with isolated congenital AS and to normal controls.

Methods

Records of all patients at our institution who underwent technically successful FAV for evolving hypoplastic left heart syndrome from January 2005 through July 2009 were reviewed. The technique for FAV and short-term clinical outcomes have been previously reported.[1,9,10] Technically successful FAV was defined as FAV in which the aortic valve was crossed and a balloon inflated with clear evidence of increased flow across the valve by color Doppler. Only patients with a biventricular circulation at latest follow-up were included to minimize the effects of variable loading conditions. A biventricular circulation was defined as circulation in which the left ventricle was the sole source of systemic output with no intracardiac shunting except for an atrial septal defect or patent foramen ovale. To construct the infant AS cohort, we included patients diagnosed postnatally with congenital AS and who underwent balloon aortic valvuloplasty within the first 2 months of life from January 2005 through July 2009. Patients were excluded from the AS cohort if they had associated congenital heart disease except for aortic coarctation or if the LV was not apex forming. In the FAV and AS groups we included only patients who had complete assessment of diastolic function as defined later. Echocardiograms from age-matched patients (matched to FAV patients) with no structural or functional heart disease were used as controls. Separate control groups were selected for the neonatal period and follow-up age period (median age 23 months). Baseline patient characteristics, echocardiographic variables, and clinical course including cardiac interventions were collected and analyzed for each group. The committee for clinical investigation at Children's Hospital Boston approved the use of patient medical records for this retrospective review.

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The first complete postnatal echocardiogram for each patient with FAV or AS was included in analysis of neonatal anatomic variables. All patients underwent complete echocardiography with 2-dimensional, spectral Doppler, and color flow Doppler analyses before the first postnatal intervention. LV variables and z scores for these variables (end-diastolic volume, long-axis dimension, mass, mass/volume, ejection fraction) and aortic and mitral valve dimensions and z scores were collected and compared. The first postnatal echocardiogram for each patient with FAV and with AS was reviewed and presence of endocardial fibroelastosis was qualitatively assessed.

Indexes of diastolic function from the first postnatal echocardiogram that included tissue Doppler imaging and from the most recent follow-up echocardiogram with tissue Doppler imaging were collected and included in the analysis. Some patients in the 2 groups had tissue Doppler imaging data only in the neonatal period or at a follow-up visit and were included in the analysis of that age group only. Conventional pulse-wave Doppler indexes of diastolic function including peak early (E) and late (A) diastolic transmitral velocities, E/A ratio, A-wave duration, and E-wave deceleration time were measured from the spectral Doppler signal of the mitral valve inflow. Pulse-wave tissue Doppler imaging velocities were obtained from the lateral mitral annulus and the interventricular septum from the apical 4-chamber view. Tissue Doppler imaging measurements for each of the myocardial segments included peak early diastolic velocity (E′) and peak late diastolic velocity (A′). Only tracings that demonstrated a clear E′ were used. All measurements of diastolic variables were retrospectively remeasured by a single echocardiographer (K.F.) from images obtained at the time of the study. Each tissue Doppler imaging velocity was measured on 3 consecutive cardiac cycles and the average of these values was used for analysis. All examinations were performed using commercially available ultrasound equipment (Philips iE33, Koninklijke Philips Electronics, Netherlands).

Baseline anatomic variables for the AS and FAV groups are reported as median (range) and count for continuous and categorical variables, respectively. These 2 groups were compared using Wilcoxon rank-sum test and Fisher's exact test, as appropriate. Mean ± SD was used to describe mitral inflow and tissue Doppler imaging values because they were normally distributed. One-way analysis of variance was used to compare mean diastolic function parameters among the 3 groups during the neonatal and follow-up periods separately. Post hoc pairwise comparisons were performed with Bonferroni correction and Tamhane test to control for multiple comparisons and heterogeneity in variances across groups. Because tissue Doppler imaging values normally vary with age, we modeled the relation between tissue Doppler imaging values and age using linear regression with generalized estimating equation models to account for correlation between longitudinal measurements for each patient. In each generalized estimating equation model, 2 data points, the tissue Doppler imaging value from the initial neonatal echocardiogram and the value from the most recent echocardiogram, were included. All statistical analysis were 2-sided and type I error was controlled at a level of 0.05. Analyses were performed with SPSS 16.0 (SPSS, Inc., Chicago, Illinois) and STATA 10.1 (STATA Corporation, College Station, Texas).

Table 1
Neonatal echocardiographic variables

Variable	FAV (n = 18)	AS (n = 19)	p Value
Aortic valve (cm)	0.56 (0.35–0.83)	0.59 (0.42–0.76)	0.35
Aortic valve z score	−2.4 (−4.8 to 0.1)	−1.8 (−2.5 to 0.8)	0.25
Mitral valve lateral dimension	0.8 (0.7–1.3)	0.9 (0.8–1.3)	0.14
Mitral valve lateral dimension z score	−1.6 (−3.0 to −2.6)	−1.2 (−2.5 to 1.9)	0.34
Left ventricular diastolic volume z score	−0.8 (−2.6 to 6.6)	−1.6 (−2.5 to 2.8)	0.63
Left ventricular long axis dimension z score	−0.7 (−2.7 to 1.8)	0.2 (−4.6 to 3.2)	0.06
Left ventricular mass (g)	8.6 (4.1–14.6)	9.0 (4.3–24.4)	0.91
Left ventricular mass z score	0.2 (−2.0 to 1.5)	1.1 (−2.7 to 4.9)	0.19
Left ventricular mass/volume	1.1 (0.8–1.8)	1.2 (0.6–4.6)	0.15
Left ventricular mass/volume z score	1.1 (−0.8 to 6.0)	2.0 (−1.6 to 5.2)	0.19
Left ventricular ejection fraction (%)	40 (18–71)	56 (10–70)	0.03
Peak aortic stenosis gradient (mm Hg)	30 (0–93)	57 (42–111)	0.04
Aortic regurgitation grade	0 (0–3+)	0 (0–2+)	0.78
Endocardial fibroelastosis	17 (94%)	5 (26%)	<0.01

Values are expressed as median (range) or number of patients (percentage).

Table 2
Postnatal interventions

Variable	FAV (n = 18)	AS (n = 19)
Number of postnatal interventions*	3 (1–8)	1 (1–3)
Neonatal aortic valvuloplasty	17 (95%)	19 (100%)
Repeat aortic valvuloplasty	14 (78%)	6 (32%)
Endocardial fibroelastosis resection	13 (72%)	0 (0%)
Mitral valvuloplasty or replacement	9 (50%)	1 (5%)
Aortic valve replacement or Ross	7 (35%)	2 (11%)

* Surgical or percutaneous.

Results

From January 2005 through July 2009 43 patients underwent FAV at our institution. Nineteen of these had a biventricular circulation at most recent follow-up. Eighteen of the 19 patients had adequate echocardiographic data to be included in analysis. Median age at FAV was 23 weeks of gestation (range 21 to 29). For the congenital AS cohort, 33 patients were identified, 19 of whom had sufficient echocardiographic data to be included in the analysis. Median age at aortic valvuloplasty in the AS cohort was 5 days (range 0 to 60), with 8 patients having critical AS.

Comparison of neonatal (preintervention) anatomic variables between patients with FAV and those with AS is presented in Table 1. Median sizes of left heart structures were similar and generally within normal range in the 2 groups except for smaller aortic valve dimension in patients with

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