Systolic and Diastolic Function of the Fetal Single Left Ventricle

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Background: The functionally single fetal right ventricle demonstrates reduced longitudinal relative to circumferential contraction velocities and deformation, a pattern similar to the normal fetal left ventricle. Altered diastolic properties are also present, with greater reliance on atrial contraction for right ventricular filling. It is unknown whether the functionally single left ventricle (SLV) demonstrates similar altered deformation patterns and diastolic properties.

Methods: Echocardiograms from 29 fetuses with SLVs were retrospectively compared with those from 48 controls with appropriately grown left ventricles. Ventricular function was assessed using Velocity Vector Imaging velocity, tissue deformation, two-dimensional, and Doppler flow parameters.

Results: Fetuses with functionally SLVs showed no difference in peak global left ventricular longitudinal velocity or displacement or strain, while global radial displacement was increased ($P < .001$). The ratio of longitudinal to circumferential deformation was also no different from that in controls. The SLVs showed increased diameters ($P < .001$) with normal lengths. Mitral inflow peak E-wave ($P < .05$) and A-wave ($P < .0001$) velocities were increased, with a reduced E/A ratio ($P < .001$). A-wave inflow fraction was also increased ($P < .05$), with no change in A duration. Although ejection time was no different, inflow duration was increased ($P < .01$) and there was a trend toward reduction of the Tei index ($P = .07$).

Conclusions: The functionally single fetal left ventricle shows comparable changes to the single right ventricle, with a more spherical morphology and greater reliance on atrial contraction for ventricular filling than in controls. However, in contrast to the single right ventricle, the SLV had a normal longitudinal to circumferential deformation ratio with enhanced early diastolic filling. (J Am Soc Echocardiogr 2014;27:972-7.)

Keywords: Fetal development, Fetal echocardiography, Functionally single ventricle, Myocardial contraction, Speckle-tracking

The systemic right ventricle in long-term palliated congenital heart disease has relatively reduced longitudinal compared with circumferential contraction velocities and deformation.[1] This altered pattern of right ventricular (RV) contraction is similar to that of the normal left ventricle and has been demonstrated in hypoplastic left heart syndrome (HLHS) during infancy.[2,3] Our recent finding of similar changes in fetal HLHS pattern of contraction and an increased reliance on atrial contraction for filling[4] suggests that the observed alterations begin in utero and may be a consequence of the abnormal loading conditions rather than an effect of postnatal surgical palliation strategies. However, it is unknown whether the fetal left ventricle also demonstrates similar altered deformation patterns and diastolic properties when destined to function in a univentricular circulation.

Using speckle- and feature-tracking techniques, fetal myocardial velocity and deformation have been assessed in normal fetal hearts,[5-10] patients with structural congenital heart disease,[4,9-13] and patients with functional pathology.[14] Significant advantages of these techniques are that they allow retrospective assessment of relatively rare lesions from two-dimensional images in archived data.

We hypothesized that the functionally single left ventricle (SLV) in the fetus would not undergo the same changes in myocardial velocity and deformation patterns as the single right ventricle, given that it already exhibits a relative dominance of circumferential deformation. The aim of this study therefore was to assess whether there are any differences in left ventricular (LV) function between normal fetuses and those with functionally SLVs using speckle- and feature-tracking Velocity Vector Imaging (VVI; Siemens Medical Solutions, Malvern, PA).

METHODS

A retrospective review of fetal echocardiograms obtained between February 2003 and March 2011 of pregnancies encountered in our

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0894-7317/$36.00

http://dx.doi.org/10.1016/j.echo.2014.06.012

Abbreviations

DICOM = Digital Imaging and Communications in Medicine

HLHS = Hypoplastic left heart syndrome

IVC = Inferior vena cava

LV = Left ventricular

RV = Right ventricular

SLV = Single left ventricle

VTI = Velocity-time integral

VVI = Velocity Vector Imaging

program with fetal SLV secondary to hypoplasia of the right ventricle was performed. Fetuses were excluded if they had SLVs associated with double-outlet ventriculoarterial connections, common atrioventricular valves, or Ebstein's anomaly. Four-chamber images were analyzed in 29 eligible fetuses with SLVs. The earliest gestation fetal echocardiogram for those with more than one study was analyzed. A further 48 previously reported appropriately grown gestation-matched controls from normal pregnancies were also assessed.[4] These fetuses had structurally and functionally normal hearts, with fetal echocardiography performed to evaluate for potential recruitment as research controls or for clinical indications including suspected congenital heart disease on routine screening or family history. The study was approved by the Health Research Ethics Board of the University of Alberta.

The fetal echocardiograms were obtained on Phillips iE33 (Philips Medical Systems, Bothell, WA), GE Voluson E8 (GE Medical Systems, Milwaukie, WI), or Siemens Acuson S2000 (Siemens Medical Solutions) cardiac ultrasound machines. The Digital Imaging and Communications in Medicine (DICOM) images from the selected fetal echocardiograms were imported into Syngo US Workplace version 3.5 (Siemens Medical Solutions) for offline analysis. The VVI analysis frame rate of archived DICOM data was 30 frames/sec.

A single operator (P.A.B.) used VVI version 2.0 software to assess LV global peak systolic longitudinal velocity, displacement, and strain, as well as peak global radial velocity and displacement for both the SLV and control fetuses. The onset of each cardiac cycle was determined using anatomic M-mode assessment of the earliest inward motion of the ventricular free wall. The ventricular endocardial border was traced from the lateral atrioventricular valve annulus to the apex and back to the septal atrioventricular valve annulus for each of the ventricles examined. Manual adjustments were made as required to ensure that all segments appropriately tracked myocardial motion after processing by the software algorithm.

Because this was a retrospective study, specific images to allow direct measurement of circumferential deformation were not available. As previously described,[4] we have used a surrogate marker of circumferential deformation, the global radial shortening index, which is based on the fractional change in end-diastolic diameter. This radial shortening index is proportional to circumferential deformation through the relationship diameter = circumference/π. The global radial shortening index was then used in the calculation of a ratio of longitudinal to circumferential deformation (deformation ratio = peak global longitudinal strain/global radial shortening index).

Ventricular length (plane of atrioventricular valve annulus to ventricular apex) and diameter (perpendicular to the midpoint of length) at end-diastole were measured from the DICOM loops used for the VVI analysis (Figure 1). Sphericity index was calculated by dividing end-diastolic diameter by length (sphericity index = end-diastolic diameter/end-diastolic length). Ventricular fractional area change was expressed as a percentage calculated by the VVI software algorithm from the manual endocardial border traces.

A single operator (P.A.B.) performed all Doppler measurements and calculations. Heart rate was calculated from Doppler flow assessment of atrioventricular valve inflow. Pulmonary venous, inferior vena cava (IVC), umbilical artery, and venous Doppler flow patterns were also assessed. The percentage reversal of IVC and pulmonary venous Doppler flow during atrial systole were calculated by measuring the forward and backward velocity-time integrals (VTIs) (respective Doppler A-wave VTI $\times$ 100/Doppler forward flow VTI). Umbilical arterial pulsatility index was calculated using the formula [(peak systolic velocity − end-diastolic velocity)/mean velocity].[15]

Doppler mitral valve inflow and aortic valve ejection were assessed for the SLV and control fetuses. Ejection and inflow times were corrected for cardiac cycle duration by dividing the measured interval by the corresponding RR interval to obtain a proportion. LV systolic-to-diastolic duration ratios for the SLV and control fetuses were calculated (systolic to diastolic duration ratio = [cardiac cycle duration − mitral inflow duration]/mitral inflow duration). LV filling was assessed by measurement of peak E- and A-wave inflow velocities, A-wave duration, and the E/A ratio. A-wave inflow fraction (A-wave inflow fraction = mitral inflow A-wave VTI/mitral inflow total VTI) was calculated, as was the LV Tei or myocardial performance index using the standard technique.[16] All Doppler measures were averaged over three cardiac cycles.

Statistical analyses were performed using Prism version 5.3 (GraphPad Software, La Jolla, CA). Data are reported as mean $\pm$ SD. Individual comparisons were performed using unpaired *t* tests. Comparisons between the SLVs and normal control left ventricles with advancing gestation were performed by analysis of covariance. Intraobserver (P.A.B.) and interobserver (N.S.K.) variability was assessed for LV VVI velocity, displacement, and strain. The relative mean difference (absolute difference between reviewers divided by the arithmetic mean of measures) was calculated in a randomly selected group of 10 fetuses with SLVs. The systematic bias of repeated measures was also calculated using Bland-Altman analysis.

RESULTS

The 77 fetal echocardiograms (29 functionally SLVs, 48 controls) reviewed for this study were performed between 19 and 39 weeks gestation. There were no differences in gestational age between the SLV and control groups (26.0 $\pm$ 5.0 vs 28.1 $\pm$ 6.4 weeks, $P = .15$). Of the SLV fetuses, 15 had tricuspid atresia, eight had pulmonary atresia with intact ventricular septum, and six had double-inlet left ventricles. Most of the pregnancies complicated by fetal SLV ($n = 28$) were referred for fetal echocardiography because of the finding of a structural heart defect on routine obstetrical screening. In one fetus with SLV, a family history of nonsyndromic pulmonary stenosis was the reason for referral. One mother had factor V Leiden deficiency. All other mothers were healthy at the time of the pregnancy. No major extracardiac pathology was identified in any of the SLV fetuses, either before or after birth. One fetus had vertebral anomalies and mild facial dysmorphism and was mildly symmetrically growth restricted at birth. Karyotype was normal, and the growth restriction was considered part of a nonspecific syndrome on the basis of a full genetic assessment. Two SLV pregnancies had single umbilical arteries with normal growth throughout the pregnancy. One mother with a history of substance abuse before the pregnancy delivered the infant prematurely at 31 weeks. There were 23 live births and six terminations of pregnancy. At last follow-up