Persistent Reduction in Left Ventricular Strain Using Two-Dimensional Speckle-Tracking Echocardiography after Balloon Valvuloplasty in Children with Congenital Valvular Aortic Stenosis

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Background: The aim of this study was to investige serial changes of myocardial deformation using two-dimensional speckle-tracking echocardiographic (2DSTE) imaging in children undergoing balloon valvuloplasty for congenital valvular aortic stenosis (VAS).

Methods: Thirty-seven children with isolated congenital VAS were enrolled in this study prospectively. Patients underwent echocardiographic evaluation at three instances: before balloon valvuloplasty, 6 months after intervention, and 3 years after intervention. Longitudinal, circumferential, and radial peak systolic strain values were determined, as well as systolic strain rate and the time to peak global systolic strain. Linear mixed statistical models were used to assess changes in 2DSTE parameters after balloon intervention. Using one-way analysis of variance, 2DSTE results at 3-year follow-up were compared with 2DSTE measurements in 74 healthy age-matched children and 76 children with uncorrected VAS whose severity of stenosis corresponded to residual stenosis of study subjects at 3-year follow-up.

Results: Global peak strain and strain rate measurements in all three directions were decreased before intervention compared with healthy children. Global peak strain and strain rate measurements increased significantly ($P < .001$) several months after balloon valvuloplasty and continued to increase at 3-year follow-up. However, at 3-year follow-up, global peak strain and strain rate in the longitudinal and circumferential directions were significantly lower ($P < .001$) compared with both control groups. Measurements of time to peak global systolic strain were significantly shorter at early follow-up compared with measurements before intervention ($P < .05$).

Conclusions: Shortly after balloon valvuloplasty for severe congenital VAS, there is an improvement in systolic myocardial deformation. However, 2DSTE parameters do not return to normal at 3-year follow-up. These abnormalities in systolic deformation cannot be fully attributed to residual stenosis or aortic regurgitation. (J Am Soc Echocardiogr 2012;25:473-85.)

Keywords: Balloon valvuloplasty, Child, Congenital heart disease, Echocardiography, Long-term follow-up, Speckle tracking, Two-dimensional strain echocardiography, Ultrasound, Valvular aortic stenosis

Patients with congenital valvular aortic stenosis (VAS) are subjected to long-standing pressure overload of the left ventricle, leading to alterations in left ventricular (LV) architecture and myocardial dysfunction.[1] Previous studies in both children and adults have indicated that abnormal LV systolic function starts at an early stage of the disease, with progressive reduction of regional and global deformation.[2,3] However, those early alterations in myocardial function have proven to be difficult to detect in congenital VAS with conventional (echocardiographic) imaging modalities. Two-dimensional (2D) strain echocardiographic or 2D speckle-tracking echocardiographic (2DSTE) imaging has emerged as a relatively new index of regional and global myocardial function. The spectrum of potential clinical applications is very wide. Because of its ability to differentiate between active and passive deformation of myocardial segments, to quantify intraventricular dyssynchrony, and to evaluate individual components of myocardial function such as longitudinal myocardial shortening, 2DSTE imaging can detect myocardial dysfunction at an early stage.[4-7] Previous studies have indicated that 2DSTE imaging is more sensitive than conventional echocardiography in detecting early myocardial dysfunction in

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Abbreviations
AVR = Aortic valve replacement
LV = Left ventricular
2D = Two-dimensional
2DSTE = Two-dimensional speckle-tracking echocardiographic
VAS = Valvular aortic stenosis

VAS.[8-11] Two-dimensional strain parameters have been shown to be abnormal even in children with asymptomatic, mild congenital aortic stenosis.[3] In adults with degenerative VAS, these abnormal alterations in (regional) deformation appear to be only partially reversible after aortic valve replacement (AVR).[10-13] In children with congenital isolated VAS, the treatment of choice is valvulotomy, either surgical or balloon valvuloplasty. The reversibility of systolic myocardial dysfunction after valvulotomy in children with congenital VAS has not been established by means of 2DSTE imaging.

The aim of the present study was twofold: first, to assess the effects of balloon valvuloplasty on myocardial deformation assessed with 2DSTE imaging in all three directions of deformation (longitudinal, circumferential, and radial) in children with isolated congenital VAS, and second, in case of persistent abnormal 2DSTE findings at 3-year follow-up to determine whether these abnormalities could be attributed to a residual valvar stenosis.

METHODS

Study Population

All asymptomatic children with severe isolated congenital VAS visiting the outpatient clinic at the Children's Heart Centre Nijmegen between May 2005 and May 2009, who were scheduled for balloon valvuloplasty, were prospectively analyzed for their eligibility for inclusion in the present study. Inclusion criteria consisted of isolated congenital VAS (e.g., thickening of the valve or functional bicuspid aortic valve), accompanied by a repeated Doppler-derived peak systolic instantaneous aortic flow velocity ≥ 4.0 m/sec (which corresponds to a transvalvular pressure gradient of >64 mm Hg) at subsequent visits. Peak LV–to–peak aortic pressure gradient assessed during catheterization under general anesthesia had to be confirmative of aortic stenosis (according to the American College of Cardiology and American Heart Association 2006 guidelines for the management of patients with valvular heart disease[14]). Previous studies have indicated that general anesthesia results in a decreased stroke volume and lower pressure gradient estimations.[15] Exclusion criteria were (1) moderate or severe aortic regurgitation (i.e., grade > 1), (2) (a history of repeated) abnormal cardiac rhythm such as (supra)ventricular tachycardia, (3) previous balloon and/or surgical valvulotomy, (4) acute or chronic illness at the time of echocardiographic evaluation, and (5) metabolic and/or genetic syndrome.[16,17] Demographic and anthropometric characteristics, including age and gender, were collected at the same time the echocardiographic study was performed. A complete history, a physical examination, electrocardiography, and echocardiographic or 2DSTE examinations were performed three times: (1) <1 month before balloon valvuloplasty, (2) at intermediate follow-up (6 months) after balloon intervention, and (3) at 3-year follow-up.

Control Groups

Subjects who were routinely referred for echocardiographic evaluation of asymptomatic, innocent heart murmurs or for screening purposes between May 2005 and November 2009 were retrospectively analyzed for their eligibility for inclusion in the study to serve as a control group. Patients with structural (congenital) heart disease, abnormal cardiac rhythm, and/or (histories of) chronic or acute illness were excluded. A group of 74 healthy, age-matched children was included and examined to provide normal reference values for conventional echocardiographic and 2DSTE parameters.

A total of 76 children, consisting of a cohort of 45 children with mild, isolated congenital VAS (peak systolic flow velocity, 2.5–3.0 m/sec) and a cohort of 31 children with moderate, isolated congenital VAS (peak systolic flow velocity, 3.0–4.0 m/sec) without prior surgical or balloon intervention were previously analyzed and described by our research group.[3] In the present study, their 2DSTE results were compared with 2DSTE findings in children with residual aortic stenosis at 3-year follow-up after balloon intervention.

This study was approved by the local ethics committee and conformed with the Declaration of Helsinki. Consent was given by each participant and/or his or her parents.

Conventional Echocardiographic Parameters

All subjects underwent detailed transthoracic echocardiographic examinations in the left lateral position according to the recommendations of the American Society of Echocardiography[18] and a local research protocol previously described by Mavinkurve-Groothuis *et al.*[19] Every examination was performed at rest, without using sedation. Images were obtained with a 3.0-MHz (S3) or a 5.0-MHz (S5) phased-array transducer using a commercially available system (Vivid 7; GE Vingmed Ultrasound AS, Horten, Norway). The choice of an S3 or an S5 transducer depended on the age and posture of the child. Quantification of cardiac chamber size, ventricular mass, and systolic LV function was performed in accordance with the recommendations for chamber quantification by the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group.[18] LV systolic function was characterized using fractional shortening, ejection fraction, pulsed-wave Doppler–derived LV myocardial performance index (or Tei index), and rate-corrected velocity of circumferential fiber shortening.[20-22] Ejection fraction was calculated using the modified Simpson's rule. The obtained values of LV mass (corrected for body surface area) were compared with those previously described in normal, healthy children.[23,24]

2DSTE Data Acquisition

Two-dimensional multiframe B-mode (grayscale) images were obtained from the apical four-chamber, the parasternal midcavity short-axis view (at the level of the papillary muscle), and parasternal basal short-axis view (at the level of the mitral valve). A sector scan angle of approximately 60° was chosen, and frame rates of 60 to 90 Hz were used because these rates are considered to be optimal for 2D speckle tracking.[7] Data were stored at the same frame rate as the acquisition frame rate. Preferably, images from five cardiac cycles triggered by the R wave of the QRS complex were digitally saved in cine loop format. Offline strain analysis was performed using speckle-tracking software for echocardiographic quantification (EchoPAC version 6.1.0; GE Vingmed Ultrasound AS). The timing of aortic valve closure and mitral valve opening with respect to peak strain and peak systolic strain were manually obtained, using single gated pulsed-wave Doppler or continuous wave Doppler blood flow velocity images of the LV outflow tract. For these measurements, special care was taken to keep the heart rate in the same range as