Insights into the Evolution of Myocardial Dysfunction in the Functionally Single Right Ventricle between Staged Palliations Using Speckle-Tracking Echocardiography

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Background: The long-term prognosis of hypoplastic left heart syndrome is limited by progressive right ventricular dysfunction. The aim of this study was to determine the trends in single right ventricular systolic function between staged palliative surgeries using speckle-tracking and conventional echocardiography.

Methods: There were 76 patients with functionally single right ventricles at the (1) pre-Norwood (n = 26), (2) pre–bidirectional cavopulmonary anastomosis (BCPA; n = 19), (3) pre-Fontan (n = 16), and (4) post-Fontan (n = 15) stages, compared with 30 controls of similar ages. Speckle-tracking-derived longitudinal and circumferential strain and strain rate, postsystolic strain index, and mechanical dyssynchrony index were compared with conventional measures of ventricular function. Differences between stages were analyzed using analysis of variance ($P < .05$).

Results: Strain rate was highest at the pre-Norwood stage and decreased at the other stages (longitudinal $P < .0001$, circumferential $P = .0002$), as opposed to controls, in whom strain rate was maintained. Longitudinal strain was significantly decreased at the pre-BCPA stage compared with the pre-Norwood stage ($P = .004$), but circumferential strain was maintained, resulting in a corresponding decrease in the ratio of longitudinal to circumferential strain, which failed to resemble that of controls. Longitudinal ($P = .003$) and circumferential ($P = .002$) postsystolic strain indices were greatest at the pre-BCPA stage.

Conclusions: A decline in contractility occurred at the pre-BCPA stage. Although there was evidence of adaptation of the single right ventricle, this failed to resemble the normal left ventricle and may be insufficient to handle the chronic volume load or insult from previous surgery. These findings suggest an intrinsic inability of the single right ventricular myocardium to fully adapt to chronic systemic pressures. (J Am Soc Echocardiogr 2014;27:314-22.)

Keywords: Speckle-tracking imaging, Single ventricle, Ventricular function, Strain, Echocardiography

Advances in surgical techniques and perioperative care over the past decade have been associated with improved early and long-term survival of patients with hypoplastic left heart syndrome (HLHS).[1,2] Even patients with less favorable hemodynamics than those outlined by the original selection criteria are now undergoing the Fontan procedure.[3] However, single right ventricular (RV) function may deteriorate over time.[4-6] Understanding the mechanisms of myocardial dysfunction may allow the early optimization of medical management.[4] Risk factors for long-term outcomes include tricuspid regurgitation, unfavorable ventricular morphology, diastolic dysfunction, and afterload mismatch.[7] Other postulated mechanisms include impaired coronary flow reserve and mechanical dyssynchrony.[8-12]

Serial assessment of ventricular function is important in the long-term care of these patients.[13,14] However, there is no widely accepted technique by which to quantify single RV function, because of the right ventricle's complex asymmetric geometry.[4] Conventional echocardiographic indices of ventricular function are largely qualitative, while quantitative methods are limited by their load dependency and geometric assumptions. Systolic function as assessed by cardiac magnetic resonance imaging is reliable and accurate, but it provides only a global index of ventricular function, and it does not assess the complex contraction mechanics in the single right ventricle.[15-17] Speckle-tracking echocardiography measuring ventricular function using strain and contractility from strain rate (SR) are angle-independent and reproducible methods of quantifying ventricular deformation.[18] Furthermore, as shown in our previous longitudinal study of HLHS between the pre-Norwood and pre–bidirectional cavopulmonary anastomosis (BCPA) stages, these methods enable the assessment of both longitudinal and circumferential contractility,

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0894-7317/$36.00

http://dx.doi.org/10.1016/j.echo.2013.11.012

Abbreviations

BCPA = Bidirectional cavopulmonary anastomosis

EDAi = Indexed right ventricular end-diastolic area

FAC = Fractional area change

HLHS = Hypoplastic left heart syndrome

IVA = Isovolumic acceleration

MDI = Mechanical dyssynchrony index

PSSi = Postsystolic strain index

RV = Right ventricular

SR = Strain rate

2D = Two-dimensional

providing important insights into the adaptive changes that occur within the single right ventricle when facing systemic pressures.[18] The aim of this study was to gain insight into the evolution of systolic dysfunction in functionally single right ventricles between the stages of palliative surgery using speckle-tracking echocardiography.

METHODS

Study Subjects

Since 2007, we have embarked on a prospective, longitudinal study of ventricular function in patients with HLHS and its variants (i.e., functionally single right ventricle) at the Stollery Children's Hospital, University of Alberta. This cross-sectional study was performed in patients selected from our study population at four different stages of surgical palliation, and thus each patient was only included once.

Clinical Variables

Demographic and clinical data collected included age, body surface area, oxygen saturation, blood pressure, and medications at the time of echocardiography. Note was made if patients were sedated at the time of the study. At the pre-Norwood stage, mechanical ventilation, blood pH and lactate, antenatal diagnosis, and modified inotrope score were recorded.[19] The use of angiotensin-converting enzyme inhibitors was noted.

Subjects

Patients with functionally single right ventricles presenting to the Stollery Children's Hospital were included. Patients were studied at a single time point at one of four possible surgical stages: the (1) pre-Norwood (pre–surgical intervention), (2) pre-BCPA, (3) pre-Fontan, and (4) post-Fontan stages. These were chosen to represent different volume-loading conditions. Echocardiography was performed shortly after diagnosis at the pre-Norwood stage and at the time of presurgical assessment at the pre-BCPA or pre-Fontan stage. If the post-Fontan echocardiographic assessment was close to the time of discharge, it was performed once chest tubes were removed and there were no pleural effusions. All patients with the intent to proceed to the next stage of surgery were included whether they subsequently underwent the surgical procedure or not (i.e., an "intention-to-treat" approach). The type of Fontan procedure performed (lateral tunnel or extracardiac conduit) and the presence of a fenestration were recorded, as well as the time frame between the Fontan procedure and post-Fontan echocardiography. Exclusion criteria were arrhythmias, pacemakers, and inability to cooperate for an adequate functional echocardiographic study. Patients who did not undergo stage I procedures under cardiopulmonary bypass were excluded.

Control Population

Healthy volunteers between day 1 of life to 3.5 years of age, to represent the normal maturational changes for speckle-tracking echocardiographic parameters, were recruited from the Stollery Children's Hospital and the University of Nebraska. Because the pre-Fontan and post-Fontan stages were of the same age, we divided the controls into only three age groups of similar ages to patients with single right ventricles. All controls had no histories of cardiac pathology or respiratory disease and no family histories of cardiomyopathy. They had normal results on physical examination, 12-lead electrocardiography, and echocardiography. The parents of all subjects enrolled gave informed consent to participate in the study, which was approved by the health research ethics boards of both institutions.

Echocardiographic Protocol

All echocardiographic studies were performed using a Vivid 7 ultrasound machine (GE Medical Systems, Milwaukee, WI) with electrocardiographic and respiratory gating and stored on an offline EchoPAC (version 7.1) system (GE Medical Systems) for later analysis. A standard anatomic evaluation and functional examination were performed only by technicians or physicians experienced with our institution's detailed single-ventricle functional protocol. All pre-BCPA patients were sedated for their studies, most receiving chloral hydrate (60–80 mg/kg); three studies were performed during general anesthesia in association with other procedures.

Two-Dimensional Echocardiography. Traditional parameters for the assessment of ventricular systolic function applicable to the single right ventricle were measured as described in previous studies.[4,15,20] These included (1) tricuspid annular plane systolic excursion of the RV free wall indexed to body surface area, a measure of longitudinal systolic function; (2) Doppler tissue imaging assessment of tricuspid annular velocity to determine S′ velocity and myocardial performance index; (3) isovolumic acceleration (IVA) from color tissue Doppler; (4) indexed RV end-diastolic area (EDAi) and systole, from the apical "four-chamber" view, as surrogates for ventricular volumes, as we have previously shown a good correlation between these two-dimensional (2D) measures and magnetic resonance imaging–derived volumes[18]; and (5) calculated 2D fractional area change (FAC). The presence of tricuspid regurgitation was classified subjectively as none, mild, moderate, or severe.

Speckle-Tracking Echocardiography. Two-dimensional grayscale images captured at the equivalent apical "four-chamber" (longitudinal) and basal short-axis (circumferential) planes optimized for higher frame rate (115 ± 33 Hz) were analyzed by a single observer. Speckle-tracking imaging measured global longitudinal and circumferential strain and SR. The ratio of longitudinal to circumferential strain was calculated to determine their relative contribution to contraction. The postsystolic strain index (PSSi) was calculated as [(peak strain − peak systolic strain)/peak strain] and expressed as a percentage. Mechanical dyssynchrony in the longitudinal and circumferential dimensions was measured as the standard deviation of segmental time to peak strain. Measurements were made in the single right ventricle in the study patients and the normal left ventricles of controls. We previously reported low interobserver variability, a small 1.96 × within-subject standard deviation, and high intraclass correlation coefficients for all the reported parameters, indicating good repeatability of these novel parameters in an anatomically similar cohort of patients with single right ventricles using the same equipment and analytic software.[18] Because of the importance of accurate timing of these parameters, we noted the heart rate at the time of our