Insights into dyssynchrony in Hypoplastic Left Heart Syndrome

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BACKGROUND Cardiac resynchronization therapy has been proposed for treatment of hypoplastic left heart syndrome (HLHS) patients with right ventricular (RV) failure. The role of dyssynchrony, however, is poorly understood in this population.

OBJECTIVE The purpose of this study was to better understand the relationship between electrical and mechanical dyssynchrony in HLHS using 3-dimensional electrical mapping, tissue Doppler indices of wall motion, and vector velocity imaging.

METHODS Eleven HLHS subjects with normal RV function and ten normal subjects (age 3–18 years) were studied. Electrical and mechanical activation times and dyssynchrony indices (electrical dyssynchrony index, mechanical dyssynchrony index) were calculated using 3-dimensional electrical mapping, tissue Doppler indices, and vector velocity imaging.

RESULTS No differences in measures of electrical dyssynchrony were seen when comparing HLHS patients and normal patients (electrical activation time 63.3 $\pm$ 22.8 ms vs 56.2 $\pm$ 11.2 ms, $P =$ .38; electrical dyssynchrony index 13.7 $\pm$ 6.3 ms vs 11.6 $\pm$ 3.0 ms, $P = .34$). However, measures of mechanical dyssynchrony were markedly abnormal in HLHS patients despite normal RV function (mechanical activation time 16 $\pm$ 11.3 ms vs 0.9 $\pm$ 1.9 ms, $P =$ .01; mechanical dyssynchrony index 7.5 $\pm$ 5.5 vs 0.4 $\pm$ 0.8, $P <$.01).

CONCLUSION Patients with HLHS and preserved RV systolic function have normal electrical activation when compared to patients with normal right and left ventricles. In contrast, these patients demonstrate mechanical dyssynchrony compared to patients with normal right and left ventricles. This finding raises important questions about the indications for cardiac resynchronization therapy in this patient population.

KEYWORDS Congenital heart defects; Dyssynchrony; Hypoplastic left heart syndrome; Pediatrics; Resynchronization

ABBREVIATIONS **CRT** = cardiac resynchronization therapy; **EP** = electrophysiology; **HLHS** = hypoplastic left heart syndrome; **LV** = left ventricle; **RV** = right ventricle

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Background

With improvements in surgical technique, patients with hypoplastic left heart syndrome (HLHS) are more frequently surviving into adulthood. These patients exhibit long-term sequelae of their disease, including systemic right ventricular (RV) heart failure. Unfortunately, few effective therapies for systemic RV heart failure in this population are available.

Cardiac resynchronization therapy (CRT) is a powerful tool in adult heart failure that has led to improved left ventricular (LV) function, improved quality of life, decreased rate of hospitalizations, and decreased all cause mortality.[1–4] Several small studies have shown that CRT is also beneficial in a subset of children with poor function and heart failure symptoms. However, there is an erratic response to CRT in all pediatric patients, particularly in single-ventricle populations.[5–8]

Investigators have used both mechanical and electrical dyssynchrony indices to predict response to CRT.[9–11] Mechanical dyssynchrony, measured by echocardiography, has been demonstrated in children with HLHS; however, electrical and mechanical interactions in systemic single ventricles are not well understood.[12] In order to better define CRT indications, electrical and mechanical dyssynchrony must be further elucidated.

The purpose of this study was to evaluate RV electrical activation using 3-dimensional electrical mapping in patients with HLHS compared with normal ventricles to assess for electrical dyssynchrony. Echocardiographic techniques were used to evaluate for mechanical dyssynchrony in patients with HLHS compared with normal ventricles, and the relationship between electrical and mechanical dyssynchrony was explored in this patient population.

Methods

Patient population

Patients aged 2 months to 18 years with HLHS and normal RV function undergoing a clinically indicated cardiac catheterization at Lucile Packard Children's Hospital

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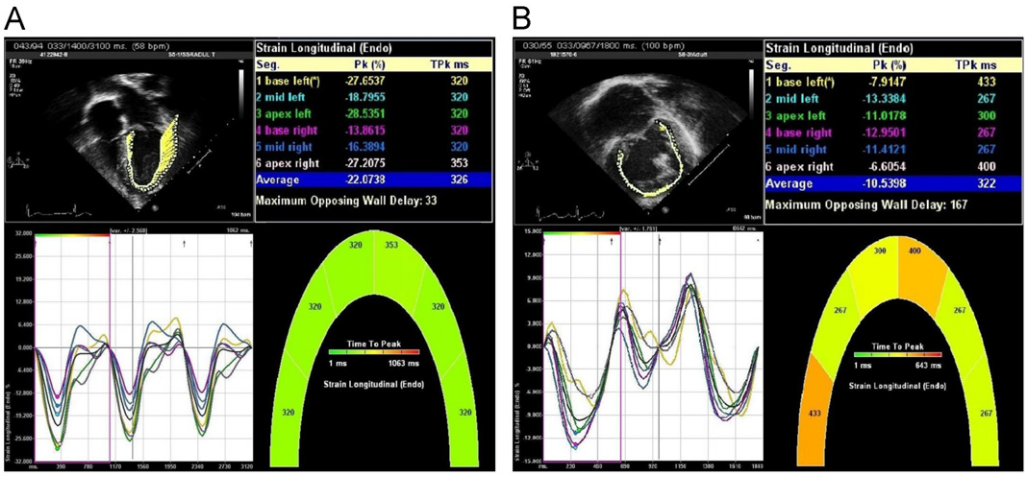

Figure 1 Example of strain curves derived by vector velocity imaging software displayed as time to peak strain among 6 cardiac segments in the apical 4-chamber view (or equivalent) for a control subject (**A**) and a hypoplastic left heart syndrome subject (**B**). Variable times to peak strain are shown among the cardiac segments in the hypoplastic left heart syndrome subject compared with the control subject reflecting mechanical dyssynchrony.

(LPCH) were prospectively identified and recruited as study subjects. Patients aged 2 months to 18 years with normal echocardiograms undergoing a clinically indicated electrophysiologic (EP) study at LPCH were prospectively identified and recruited as control subjects. Any patients who were actively paced, had a nonsinus rhythm at baseline, had ventricular arrhythmias, were taking antiarrhythmic medications, had ventricular preexcitation, or (in control patients) had a bundle branch block at baseline were excluded. The study was approved by the Stanford University institutional review board, and the subjects gave informed consent.

Measuring mechanical dyssynchrony by echocardiography

Echocardiography was performed on all subjects using a Philips iE33 xMATRIX echo system (Philips Medical Systems, Bothell, WA). Images were acquired at a frame rate between 70 and 150 Hz. A standard 4-chamber and parasternal short-axis view of the systemic ventricle was obtained. Equivalent views of the systemic RV were obtained in HLHS patients. Global ventricular function was assessed qualitatively by echocardiography.

Vector velocity imaging

Vector velocity imaging was performed using the Syngo system (Siemens Medical Solutions USA, Mountain View, CA). The endocardial border was traced manually in peak systole. In the standard 4-chamber view, both the RV and LV borders were traced for control subjects, and the RV was traced in HLHS subjects. In the parasternal short-axis view, the systemic ventricle was traced for both the control and the HLHS subjects. The parasternal short-axis view was found to be unreliable for vector velocity imaging tracking of the RV in control subjects and thus was not included in the analysis. The measured contours were then automatically tracked by the computer algorithm through its frame-to-frame displacement over one cardiac cycle, yielding the local velocity, strain, and strain rate. For each of the parameters (velocity, strain, strain rate), the degree of mechanical dyssynchrony was quantified as the standard deviation of time to peak event among six cardiac segments in a 4-chamber or equivalent view (Figure 1) and a parasternal short-axis view (Figure 2).

Pulsed-wave tissue Doppler imaging

Using the standard apical 4-chamber views in control subjects and views equivalent to a standard apical 4-chamber in HLHS subjects, pulsed-wave tissue Doppler imaging was sampled at 4 prespecified locations (basal septum, mid-septum, basal free wall, and mid-free wall) for each ventricle (Figure 3). Local mechanical activation time was defined as the time from onset of the QRS on the surface ECG lead to the onset of isovolumic acceleration for each location (Figure 4A). The total mechanical activation time was defined as the difference between the longest and shortest local mechanical activation times for each ventricle. The mechanical dyssynchrony index was defined as the standard deviation of all 4 local mechanical activation times for each ventricle. This method is a minor modification of the method used by Friedberg et al[12] in an earlier study.

Measuring electrical dyssynchrony by 3-dimensional electrical mapping

Three-dimensional electroanatomic maps of the single RV in HLHS subjects and both the RV and LV in control subjects were created using EnSite NavX Navigation & Visualization Technology (St. Jude Medical, St Paul, MN). Using an impedance-based localization method, a 3-dimensional geometry of the chamber can be generated by sampling multiple endocardial sites. Electrical activation is recorded simultaneously and superimposed on the chamber shell with the electrical activation information color-coded. A minimum of 100 endocardial sites were sampled for each ventricle.

Three measurements were made from these maps: local electrical activation time, total electrical activation time, and