Frequent Activation Delay–Induced Mechanical Dyssynchrony and Dysfunction in the Systemic Right Ventricle

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Background: Patients with systemic right ventricles frequently experience progressive heart failure and conduction abnormalities leading to abnormal ventricular activation. Activation delay–induced mechanical dyssynchrony can contribute to ventricular failure and is identified by a classic strain pattern of paradoxical opposing wall motion that is an excellent predictor of response to cardiac resynchronization therapy in adults with left bundle branch block. The specific aims of this study were to compare right ventricular (RV) mechanics in an adult systemic right ventricle population versus control subjects, evaluate the feasibility of this RV strain pattern analysis, and determine the frequency of the classic pattern.

Methods: Young adults ($n = 25$) with d-transposition of the great arteries, status post Mustard or Senning palliation (TGA-MS), were ambispectively enrolled and compared with healthy young adults ($n = 30$) who were prospectively enrolled. All subjects were imaged using novel three–apical view (18-segment) RV longitudinal speckle-tracking strain analysis (EchoPAC) and electrocardiographic data.

Results: Patients with TGA-MS had diminished RV global peak systolic strain compared with control subjects ($-12.0 \pm 4.0\%$ vs $-23.3 \pm 2.3\%$, $P < .001$). Most patients with TGA-MS had intrinsic or left ventricular paced right bundle branch block. A classic pattern was present in 11 of 25 subjects (44%), but this pattern would have been missed in four of 11 based only on the RV four-chamber (six-segment) model. Only three subjects underwent cardiac resynchronization therapy. Both subjects who had the classic pattern responded to cardiac resynchronization therapy, whereas the one nonresponder did not have the classic pattern.

Conclusion: Systemic right ventricles demonstrated decreased function and increased mechanical dyssynchrony. The classic pattern of activation delay–induced mechanical dyssynchrony was frequently seen in this TGA-MS population and associated with activation delays. This comprehensive RV approach demonstrated incremental value. (J Am Soc Echocardiogr 2016;■:■-■.)

Keywords: Atrial switch, Strain pattern analysis, Dyssynchrony, Cardiac resynchronization therapy, Right ventricle, Mustard, Senning

Progressive right ventricular (RV) failure is a nearly universal problem for adults with systemic right ventricles. Understanding how ventricular activation abnormalities contribute to RV dysfunction and the potential for cardiac resynchronization therapy (CRT) may avoid transplantation or prevent death in properly selected patients. Before the arterial switch procedure became the gold standard repair for patients born with d-transposition of the great arteries, the Mustard and Senning palliations were the surgical procedures of choice. They both effectively baffle the systemic venous return to the left heart and the pulmonary venous return to the right heart, which solved the problem of the parallel left and right heart circulations but maintained the morphologic right ventricle as the systemic pumping ventricle. Most institutions transitioned to the arterial switch procedure >20 years ago, so patients with d-transposition of the great arteries, status post Mustard or Senning palliation (TGA-MS), now constitute an adult congenital population in their 20s to 40s. In this aging population, there is almost universal progressive RV failure in adults that is due partly to a lifetime systemic pressure load.[1-4] However, abnormal ventricular activation causing mechanical dyssynchrony may also contribute to this progression,[5,6] which has been demonstrated in the left ventricles of patients with normal anatomy with left bundle branch block (LBBB).[7-9] Patients with TGA-MS frequently have activation abnormalities of their systemic

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Abbreviations

18S = 18-segment

ADI-MD = Activation delay–induced mechanical dyssynchrony

CRT = Cardiac resynchronization therapy

FAC = Fractional area change

LBBB = Left bundle branch block

LV = Left ventricular

NYHA = New York Heart Association

PLS = Peak longitudinal systolic strain

RBBB = Right bundle branch block

RV = Right ventricular

RV4 = Right ventricle–centered four-chamber apical

TAPSE = Tricuspid annular plane systolic excursion

TGA-MS = D-transposition of the great arteries, status post Mustard or Senning palliation

TTP = Time to peak

TTP_{op} = Maximal opposing wall delays of the time to peak strain

TTP_{SD} = SD of all time-to-peak strain intervals

right ventricles, such as intrinsic right bundle branch block (RBBB) or left ventricular (LV) pacing–induced RBBB. RBBB often leads to progressively mechanical RV dyssynchrony and dysfunction, and studies have shown that a subgroup of patients with TGA-MS benefit from CRT.[10-15] However, the high CRT nonresponse rate is a major clinical problem[10,11,13] and highlights the need for a specific predictive marker for CRT response in the systemic right ventricle.

In adults with LV cardiomyopathy, predicting CRT response by traditional time to peak (TTP) echocardiographic strain indices or prolonged QRS duration on electrocardiography leads to an unacceptably high nonresponse rate.[7,9,16-18] Recently, a classic pattern of dyssynchrony has been identified using regional strain pattern analysis that more strongly predicts both short- and long-term CRT response[7,8] and is associated with LBBB criteria on electrocardiography.[19] This pattern analysis identifies the physiology of opposing wall motion caused by a significant activation delay, referred to as activation delay–induced mechanical dyssynchrony (ADI-MD). The paradoxical wall motion of ADI-MD consists of early septal contraction opposed by early stretch in the activation-delayed RV free wall, followed by late free wall contraction causing early termination of septal contraction. Independent groups have also reported on a similar strain pattern analysis with strong CRT response predictive characteristics.[20-22] This pattern has also been identified in both the left and right ventricles of various patient populations, including case reports in the systemic right ventricle.[23-25]

In the past, RV longitudinal strain analysis has used only a right ventricle–centered four-chamber apical (RV4) view despite potential heterogeneities in the systemic right ventricle.[5,26] Recently, a comprehensive 18-segment (18S) strain analysis model, using three apical RV images, has been introduced in a normal adult population to more comprehensively evaluate complex regional RV mechanics.[23] The aims of this study were to (1) compare RV mechanics in a young adult systemic right ventricle population versus control subjects and (2) evaluate for the presence of the classic pattern of ADI-MD in the right ventricle in this systemic right ventricle population. We hypothesized that the classic pattern would be present in a subgroup of patients with systemic right ventricles and would be associated with electrical activation abnormalities.

METHODS

Study Subjects

The TGA-MS population consisted of all the adult subjects who were identified for strain-protocol echocardiography with the three apical RV views during routine adult congenital heart clinic visits from June 2010 to September 2012 at Duke University Medical Center. The patients with TGA-MS for this study were ambispectively identified, with subjects imaged before January 2012 retrospectively identified and those after that date prospectively enrolled. However, all subjects with TGA-MS in this study were imaged with the same echocardiographic protocol, including comprehensive RV apical acquisitions on the GE Vivid E9 (GE Vingmed Ultrasound AS, Horten, Norway) optimized for strain analysis, because the protocol was implemented in early 2010 for all patients with systemic right ventricles. This is believed to represent a consecutive capture of all subjects with TGA-MS imaged during this period. No subjects were excluded because of inadequate image quality. Health information and electrocardiograms were obtained from the medical record. A small subset of this population was previously described as pilot data.[23]

The control population was prospectively enrolled from a population of healthy young adults recruited for a study to assess echocardiographic predictors of pulmonary edema when diving underwater. In the normal population, feasibility of the 18S RV strain analysis, normal ranges, and reproducibility were previously presented.[23] A normal cohort ($n = 30$) was age- and sex-matched to the TGA-MS population. All subjects underwent comprehensive screening echocardiography with the comprehensive apical RV views with strain analysis. Inclusion criteria for control subjects were age ≤18 years, no history of cardiac abnormalities, and normal echocardiographic findings, including anatomy, LV ejection fraction, fractional area change (FAC), and tricuspid annular plane systolic excursion (TAPSE). Exclusion criteria for control subjects were any abnormal echocardiographic findings, prolonged QRS duration, and serious systemic disease. This study was approved by the institutional review board at Duke, and all prospectively enrolled subjects provided informed consent.

Echocardiography with Comprehensive Apical RV Views

Echocardiography was performed with grayscale images optimized for longitudinal speckle-tracking strain analysis (50–90 frames/sec). Three apical RV views were obtained with the subject in the standard left lateral recumbent position. The three apical RV views have equivalent imaging planes to the four-, two-, and three-chamber LV apical views with the transducer angled rightward (Figure 1), as previously published.[23] To name the apical RV views, the view with the outflow tract (transducer notch at 1 o'clock) was named the RV outflow view. The view isolating the RV inflow and apical regions (transducer notch at 11 o'clock) was named the RV inflow view. The RV four-chamber view name was maintained (transducer notch at 3 o'clock). Optimizing these views often required repositioning of the transducer a few centimeters toward the axillary line from the typical LV-focused apical view and angling the imaging plane anteriorly and rightward. All echocardiographic studies were acquired with a Vivid E9 using a 3.5-MHz ultrasound probe. RV systolic function was also assessed by FAC and TAPSE.[27]

In the planning stage of this study, efforts were made to obtain high-quality short-axis views of the right ventricle for circumferential strain assessment. However, imaging of the anterior right ventricle was