Echocardiographic Evaluation of the Single Right Ventricle in Congenital Heart Disease
– Results of New Techniques –
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Right ventricular (RV) function is increasingly recognized as having prognostic significance in various disease processes. The current gold standard for noninvasive measurement of RV function is cardiac magnetic resonance imaging; however, because of practical considerations, echocardiography remains the most often used modality for evaluating the RV. In the past, because of its complex morphology, echocardiographic assessment of the RV was usually qualitative in nature. Current advances in echocardiographic techniques have been able to overcome some of the previous limitations and thus quantification of RV function is increasingly being performed. In addition, recent echocardiographic guidelines for evaluating the RV have been published to aid in standardizing practice. The evaluation of RV function almost certainly has no greater importance than in the congenital heart population, especially in those patients that have a single RV acting as the systemic ventricle. As this complex population continues to increase in number, accurate and precise evaluation of RV function will be a major issue in determining clinical care.

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Advances in congenital heart procedures, both surgical and interventional, have increased the life expectancy of patients with complex congenital heart disease (CHD). This holds especially true for patients with single right ventricle (RV) physiology. A major medical issue that these patients are experiencing with increasing life expectancy after surgical palliation is progressive heart failure, with a reported incidence as high as 40%. Adult guidelines for treatment of heart failure are mainly based on level A evidence; however, most guidelines for pediatric/congenital heart failure treatment are based on, at best, level B evidence and more often level C evidence, the latter being the only evidence supporting heart failure treatment guidelines in patients with single-ventricle physiology.

Multiple reasons exist for the lack of evidence for heart failure treatment in this complex population, but a definite reason is the inability to accurately and precisely assess RV function. The RV is difficult to image echocardiographically because of its anterior position in the chest, its course muscular trabeculations making chamber margins difficult to ascertain, and its relatively thin wall. Because of these difficulties, cardiac magnetic resonance imaging (cMRI) is considered the gold standard for non-invasively evaluating RV function. However, because of practical considerations, echocardiography still remains the most often used modality for evaluating the RV. Current advances in echocardiographic techniques have been able to overcome some of the previous limitations in evaluating the RV and correlations with cMRI have been documented. In addition, recent echocardiographic guidelines for evaluating the RV have been published to aid in standardizing practice in both pediatric and adult populations.

In this review, we briefly discuss the characteristics of the RV and how this may differ in a single RV vs. a biventricular physiology. We also review the current available literature on the echocardiographic assessment of patients with single RV physiology using newer echocardiographic techniques.

**RV’s Characteristics**

The RV differs embryologically, structurally, and functionally from the left ventricle (LV). These differences are likely related to both genetic/gene expression and physiology, and the interactions between them. These interactions have been described in the “normal” RV in a biventricular physiology, but significantly less is known about how a “normal” RV should develop in a single-ventricle physiology.

The heart forms from a single tube after fusion of the bilateral heart fields. This tube consists essentially of the inflow and outflow limbs. The RV, conus, and truncus comprise the outflow limb. Embryologically, the RV develops from cells that originate in the secondary heart field, whereas the LV...
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originate from cells that originate from the anterior plate mesoderm. With C-looping of this heart tube, a bulboventricular fold is created that will eventually separate the RV and LV. Trabeculation of the heart is also occurring during this time and is one of the earliest signs of differentiation between the two ventricular chambers. The conus of the heart is also distinctly different from the RV, though in practise is considered part of the RV. The conus originates from the anterior heart field, but never becomes trabeculated. The cells of the conus also have different properties to those of the cells in the ventricles. All these differences are likely because the RV is acting as an active pump whereas the conus serves more as a conduit. The LV does not have as prominent a conus component.

From a genetic/gene expression standpoint, there are multiple and complex interactions that occur in the development of the RV. Gene expression may be turned on and off according to the stage of RV heart development. Chamber-specific gene expression between the atria and ventricles has been well documented in various animal models. For example, Hand2-null mice develop a hypoplastic RV, whereas Tbx5-null mice develop a hypertrophic LV. In addition, gene expression has been noted to be different in the RV compared with the LV in response to the particular hemodynamic conditions that are present. Furthermore, the RV’s capacity to adapt to different hemodynamic conditions via gene expression may be limited by when these conditions occur during a patient’s lifetime. For example, patients with CHD and pulmonary hypertension have markedly improved survival compared with patients who develop pulmonary hypertension later in life. This is probably because the RV in CHD patients is constantly exposed to elevated pressures whereas in patients who develop pulmonary hypertension later in life it is not so exposed. Variation in the ability for gene’s to express during a person’s lifetime likely plays a role in the adaptive response and subsequent outcome. These differences in genetic expression in the single RV physiology are yet to be fully elucidated.

Structurally, the mature RV is thin-walled and trabeculated, with a crescent shape that wraps around the LV. The cell orientation is mostly longitudinal in the RV, whereas LV cell orientation is mostly radial in nature. This functionally explains the contraction pattern of the respective ventricles, with the predominant contraction pattern of the RV being in the longitudinal direction and the LV contraction pattern is predominantly radial and circumferential with torsional components also present. However, in patients with transposition of the great arteries following a Mustard/Senning operation, the contraction pattern of the systemic RV has been shown via cMRE to be more like that of the LV, with predominantly circumferential contraction pattern. Though that report was in patients with a biventricular physiology, the RV was the systemic ventricle, which is analogous to patients with a single RV physiology. In a similar vein, RV pressure-volume loops are more trapezoidal in shape compared with the rectangular pressure-volume shape of the LV. This physiology allows for the most efficient contractility possible, with the RV working against a lower resistance pulmonary system and the LV working against a higher resistance in the systemic system. However, the pressure-volume loop of the RV changes in shape and becomes more rectangular when exposed to a pressure load. Inversely, the pressure-volume loop of the LV in patients following a Mustard/Senning repair becomes more trapezoidal. Both those studies imply that the contraction pattern of the RV is affected by the hemodynamic conditions present and not necessarily solely by the intrinsic properties of the RV myocardium. The implication for a single RV physiology is that the single RV attempts to become more like a LV physiologically, despite being embryologically different. Despite these potential adaptive mechanisms, the single RV is still under unfavorable hemodynamic conditions in a Fontan circulation compared with a biventricular circulation.

It is this setting that makes the accurate and precise echocardiographic assessment of single RV function complicated, but imperative.

Echocardiography

In the past, RV function was graded qualitatively, with minimal quantification performed because of the difficulties previously mentioned. With adult and pediatric echocardiographic guidelines now available and with advances in echocardiographic technology constantly occurring, assessment of the RV should continue to improve. Specifically, the newest echocardiographic techniques of tissue Doppler imaging (TDI), speckle tracking echocardiography (STE) for strain and strain rate analysis, and 3-dimensional (3D) analysis have been performed on patients with single RV physiology to evaluate function. Each of these modalities shows promise for improving the quantitative assessment of function in this complex population.

TDI

TDI essentially measures the RV myocardial longitudinal velocity when performed from the apical 4-chamber view (Figure 1). By convention, the RV free wall at the level of the tricuspid valve is evaluated, though any segment of the RV may be analyzed. An early diastolic wave (e’), atrial contraction wave (a’), and systolic wave (s’), as well as contraction times, can also be obtained (Figure 2). The contraction times may be used to calculate a myocardial performance index (MPI) to quantify overall systolic and diastolic function.

Another measurement that can be obtained via TDI is the myocardial acceleration during isovolumic contraction (IVA). IVA has been shown to be load-independent and has correlated well with end-systolic elastance obtained via cardiac catheterization, the gold standard for myocardial contractility assessment. Measurements can be acquired via spectral Doppler or color Doppler analysis, but the absolute velocity values obtained will differ, with the spectral Doppler analysis usually 20–30% higher. This is because spectral Doppler measures the peak velocity of the region of interest, whereas color Doppler measures the mean velocity of the region of interest. Most contemporary normative pediatric data were obtained via spectral Doppler analysis, and current adult guidelines recommend using spectral Doppler analysis.

TDI has been used extensively in the adult setting and has increasingly been used in the pediatric population to assess RV function in various disease processes. In the setting of single RV physiology, a study compared RV function with TDI in patients with hypoplastic left heart syndrome (HLHS) undergoing Norwood palliation using a modified Blalock-Taussig shunt (NW-BT) vs. Norwood palliation using a RV to pulmonary artery conduit (NW-RVPA). They found no significant differences in TDI values between the 2 groups over time from pre-Norwood procedure to post-bidirectional Glenn procedure. The investigators did note that the TDI s’ wave velocity, e’ wave velocity, and MPI worsened during that time period, suggesting both progressive systolic and diastolic dysfunction. Another study, comparing TDI values between
healthy patients with a single RV status post-Fontan completion vs. patients with normal biventricular physiology, showed significant differences in all the TDI RV values measured. Both those studies demonstrate that TDI can be used to detect RV abnormalities that would have otherwise have been missed by standard echocardiographic assessment.

Studies in adult subjects have correlated RV TDI values to invasive hemodynamic measurements, and similar findings have been documented in the pediatric setting. Specifically, the tricuspid early diastolic blood flow velocity wave (E) to RV TDI e’ wave ratio (E/e’) has been correlated with RV end-diastolic pressures. One study examining 32 patients with single-ventricle physiology, 17 of whom had single-RV physiology, showed a positive correlation between the RV E/e’ measurements and catheterization values of ventricular end-diastolic pressures. Receiver-operating characteristic curve analysis using an E/e’ cutoff of 12 showed a sensitivity of 90% and specificity of 75.0% for identifying a ventricular end-diastolic pressure >10 mmHg. The investigators also documented a positive correlation between echocardiographic values of ejection fraction and TDI s’ wave. However, in another study of 137 single-ventricle patients post Fontan procedure, of which 27% had single RV physiology, the authors did not find a correlation between the TDI s’ wave and the cMRI-derived ejection fraction. This finding is contradictory to a study in adult patients that found good correlation between RV TDI values and cMRI RV ejection fractions, albeit in 2-ventricle physiology. Neither of the pediatric studies specifically stated the underlying diagnosis of the patients with a single RV or the previous surgeries. This lack of infor-
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Information may have relevance, because another study showed cMRI-derived ejection fraction has a weaker correlation with the TDI s’ wave in patients with repaired tetralogy of Fallot and moderate or severe dysfunction of the RV outflow tract area compared with those who had normal RV outflow tract function. Because the RV outflow tract may be affected in patients with HLHS undergoing the NW-RVPA, TDI analysis may not be as accurate for assessing RV function in this specific single-RV patient population, which could explain some of the discrepancies between studies. Regardless, it is without question that larger studies are needed to better delineate the situations where TDI analysis may be most reliable in assessing single-RV function.

The advantages of TDI analysis include its ease of use and reproducibility. The major disadvantage of TDI is its angle dependency, whereby velocities may be underestimated if the angle of interrogation is excessive. TDI values of myocardial segments may also be affected by adjacent segmental movement (translational, torsional, and rotational). This “tethering” will move abnormal myocardium when the adjacent normal myocardial segments pull the abnormal segment. This phenomenon will therefore give a false value when interrogating the abnormal segment. TDI is also not totally preload or afterload independent; therefore, it does not measure intrinsic contractility of the muscle per se. In addition, TDI analysis is regional in nature and does not necessarily give a global assessment unless the entire heart is evaluated.

Strain and Strain Rate

Strain is the measurement of myocardial shortening or lengthening and is defined as the change in distance between 2 points divided by the initial length. The unit of strain is a percentage. Strain is measured in the longitudinal, radial, or circumferential direction depending on the echocardiographic view acquired. Most studies evaluating the RV have used the apical 4-chamber view to obtain longitudinal strain values (Figure 3). By convention, negative strain signifies contraction. Strain rate is the first derivative of strain and is defined as the change in velocity between 2 points divided by the distance between the 2 points. The unit of strain rate is seconds⁻¹. A strain rate early diastolic wave (SRe’), strain rate atrial contraction wave (SRA’), and strain rate systolic wave (SRs’) can be obtained.

Both strain and strain rate measure myocardial contractility and are less preload dependent than conventional measurements, though not totally independent. Strain rate is thought to be less preload-dependent than strain. These values can be obtained via color Doppler analysis or speckle tracking analysis. Similar to TDI, strain and strain rate values acquired

Figure 3. Two-dimensional speckle tracking strain analysis of a single-RV patient. Segments are color coded as follows: yellow=basal interventricular septum; light blue=mid interventricular septum; green=apical interventricular septum; red=basal right ventricular free wall; dark blue=mid right ventricular free wall; purple=apical right ventricular free wall. (Top left) Strain curve with global right ventricular strain value. (Bottom left) Segmental strain values. (Top right) Color-coded segmental strain curves. Dashed white line=global strain curve. (Bottom right) Color M-mode for strain.
Speckle tracking analysis measures “speckles” of myocardium and follows the movement of these “speckles” to achieve displacement information and thus the strain and strain rate values. Speckle tracking is thought to be angle-independent or at least less dependent than color Doppler analysis. Normative data for strain and strain rate are available in pediatric patients, though the populations evaluated were small.

Analogous to TDI, strain and strain rate analyses have been performed in the pediatric population to assess RV function in various disease processes. In the single-RV physiology, strain and strain rate analyses have been used to measure longitudinal changes, compare patients with different types of cardiac anatomy, and compare results of different surgeries. In the longitudinal studies, subtle changes in RV strain and strain rate that were not evident by conventional echocardiographic RV measurements were detected. In the study comparing different subtypes of HLHS, slightly better RV strain and strain rate values in patients with aortic atresia/mitral atresia subtype vs. other subtypes were documented, which was not noted by other echocardiographic techniques. These echocardiographic changes potentially support the clinical finding of improved outcomes in certain subtypes of HLHS. Similarly, differences in strain and strain rate values have been noted in patients with HLHS undergoing the NW-BT procedure vs. the NW-RVPA procedure, which were not otherwise detected by more conventional methods or TDI evaluation. Because controversy remains over which surgical procedure is more advantageous for patients with a single RV, strain and strain rate analyses could be used as another possible indicator to help resolve this issue. In any case, all these studies indicate that strain and strain rate analyses may be more sensitive in detecting subtle RV dysfunction.

Strain and strain rate values have correlated with catheterization measures of LV hemodynamics as well as RV hemodynamics in patients with biventricular physiology, though the correlations were sometimes variable. There are no data available correlating echocardiographic strain and strain rate values with catheterization data in patients with single-RV physiology. One study has correlated cMRI values of ejection fraction with strain values in patients with HLHS.

Advantages of strain and strain rate analyses include sensitivity in detecting RV abnormalities compared with other echocardiographic techniques, as well as angle independence.
in the case of speckle tracking. One disadvantage is the need for relatively high frame rates in relation to heart rates for adequate post-processing evaluation, which is significant in the pediatric population where heart rates are substantially higher than in adults. Another disadvantage, which is a significant limitation, is that strain and strain rate values may not necessarily be equivalent, depending on which vendor is used. Until this major obstacle is overcome, comparisons between published studies and institutions cannot be performed. Strain and strain rate analyses are currently not recommended for routine evaluation of RV function, but this recommendation may change as more data become available.

**3D Echocardiography**

3D echocardiographic analysis has markedly improved, with live acquisition and off-line analysis being significantly faster than in the past. Currently, there are 2 methods of obtaining a 3D volume set: manual tracking whereby the endocardial borders are traced over different image slices and a summation of disks is performed to obtain a volume (Figure 4); and semi-automated border detection whereby points are placed at pre-specified areas and then the computer performs a volumetric reconstruction. RV volume and ejection fraction can thus be obtained via 3D echocardiography. Newer techniques, such as 3D speckle tracking, may also improve quantification of the heart by combining both methods to obtain a regional strain and strain rate in a more homogeneous manner. Image acquisition theoretically can be performed from any view (Figure 5).

Multiple adult and pediatric studies have documented good correlation between RV volumes obtained via 3D echocardiography and those from cMRI. Most of those studies have shown 3D echocardiography usually underestimates RV volume anywhere from 10% to 40%, with this occurring more frequently in the dilated RV. Despite this underestimation of volume, ejection fraction usually has good agreement between the 2 modalities, thus suggesting that the underestimation is a systemic rather than a random error. In the single-RV population, 1 study has compared 3D echocardiography by disc summation method with cMRI and documented that there was a strong correlation between 3D echocardiography and cMRI when measuring end-diastolic and systolic RV volumes, and a moderate correlation with ejection fraction. However, 3D echocardiography significantly underestimated end-diastolic volume by 9% and ejection fraction by 11%. All the measurements had good inter- and intra-observer agreement, except for interobserver measurements of ejection fraction.

The major advantage of 3D echocardiography is the fact that all 3 planes of the cardiac chamber can be evaluated simultaneously, which theoretically should allow for a more accurate assessment of ventricular function in relation to time. Disadvantages include the need for relatively good-quality images to perform analysis, the relatively low frame rates available for acquisition, therefore limiting picture quality, the need for off-line analysis, and the limited validation of this technique in the single-RV population. Because of these issues, 3D echocardiography is still considered better suited as a research tool for assessing RV function; however, this will likely change as more data become available.

It must be stated that none of these newer echocardiographic techniques used to quantitate single-RV function has been shown to predict clinical outcomes, in contrast with the adult data. This is almost certainly because of the small number of single-RV patients who have been studied, as well as the lack of longitudinal follow-up data currently available. There is every reason to believe that these methods will have prognostic significance as they gain wider usage in this population over time.

**Cardiac Resynchronization Therapy (CRT)**

CRT has been clearly shown to improve clinical outcomes in adult patients with heart failure, and guidelines for therapy have been endorsed. CRT is increasingly being used in the pediatric population to also treat heart failure both in 2-ventricle and single-ventricle physiology, but indications and inclusion criteria are imprecise. In addition, the prognostic role of mechanical dyssynchrony measured via echocardiography is still vague in the adult population, much
less the pediatric population. Case reports in the pediatric literature using echocardiographic techniques noted above to aid in CRT have been described, but the significance of these reports is unclear at best. Increased mechanical dysynchrony has been reported in patients with single-RV physiology, but adult definitions for adult dysynchrony may not necessarily be valid in the pediatric population. All these questions need to be addressed so that unambiguous guidelines can be made for CRT in the pediatric population, especially the single-RV population. Undoubtedly, the echocardiographic techniques described will play an important part in quantifying effectiveness of treatment, as well as possibly having predictive capabilities.

Patients with single-RV physiology are a complex population who are at an increased risk for cardiac morbidity and mortality. Accurate, quantitative, and precise evaluation of RV function is thus crucial to aid in their management, and qualitative assessment of RV function should become a thing of the past. With advances in echocardiography, this goal is closer to being attained. These latest techniques have given us insight into the intrinsic properties of the RV and, hopefully, with enhanced understanding of RV function, improved clinical outcomes will occur.

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