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Echocardiography

Speckle Tracking Echocardiography in Pediatric and Congenital Heart Disease

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Assessment of myocardial strain using speckle tracking echocardiography is an emerging echocardiographic technique that is increasingly used in the diagnosis and management of acquired heart disease in adults. In pediatric heart disease, this is still mainly considered as a research tool as the application of this technology has been slowed by the lack of vendor-independent technology and of normative data across the different age ranges. We believe that the technology has potential applications for the early detection of myocardial dysfunction, the quantification of ventricular function in congenital heart disease, and the detection of dyssynchrony. (Echocardiography 2013;30:447-459)

Key words: myocardial deformation, speckle tracking, strain and strain rate, pediatric heart disease

Over the last decade, there has been significant interest in the development of myocardial strain imaging as a technique that may be able to reliably quantify regional and global myocardial function. Strain imaging directly measures myocardial properties rather than relying on geometric changes, as in the measurement of ejection fraction (EF). Two main methods of strain imaging can be used; initially a tissue Doppler technique was employed and more recently speckle tracking echocardiography (STE) has gained popularity and has now been widely accepted as technique of choice. The majority of research in this field has focused on left ventricular (LV) function in the adult population with ischemic and nonischemic cardiac pathology. However, this technology has potential for the assessment of cardiac function in the pediatric population as well. In this review, we focus on the recent developments of STE within pediatric cardiology and areas of potential future development.

Two-Dimensional Speckle Tracking Echocardiography:

The fundamental principles behind strain imaging are well described[1–4] and it is not the focus of this review. The initial deformation imaging techniques relied on a tissue Doppler technique[5,6] measuring the differences in instantaneous velocities within a myocardial wall or segment representing strain rate, extrapolating the strain data by temporal integration of the strain rate curves. Being a Doppler technique, it was angle dependent and allowed calculation of myocardial deformation only in those directions that can be well aligned with the angle of the echo beam (typically longitudinal and radial strain). The method is associated with significant variability and requires extensive postprocessing.[7] Its advantage is the high frame rates associated with color tissue Doppler that can be advantageous in patients with high heart rates as are seen in pediatrics. More recently, two-dimensional (2D) STE has been introduced as a more reproducible method for measuring strain parameters. STE is based on B-mode gray scale tracking of 2D "speckles" or "kernels." Using the end-diastolic dimensions as a surrogate for original length and reference point, these speckles can be tracked as they move through the cardiac cycle to determine degree of deformation.[1,3] The method is angle independent and requires less postprocessing, but has the disadvantage that the frame rates are lower, which specifically impacts peak strain rate measurements. It should be noted that the commercially available vendors employ different postprocessing algorithms for 2D STE, which impact the results. As most algorithms are proprietary, the softwares function as a kind of "black box" generating output from a given imaging input. Each vendor uses slightly different tracking algorithms. An example of this that is

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widely reported in the literature is velocity vector imaging (VVI) (Siemens Medical Systems, Malvern, PA, USA). While employing 2D B-mode images, some systems rather than tracking the speckles in a region of interest, track user-defined points along the manually traced endocardial border. The motion of these tracked points between frames over a given time period will give tissue velocity. Strain can be calculated if the change in relative distances of traced points are combined with the difference in the relative displacement of the tissue motion behind the tracked points.[8,9]

Strain is a dimensionless parameter that represents the fractional change in length of a segment relative to its original length and is expressed as a percentage (%). Strain rate is a measure of the rate of deformation or strain per unit time and is expressed as 1/sec. While strain correlates well with EF, strain rate relates better to parameters reflecting myocardial contractility like end-systolic elastance. Loading conditions influence both parameters, but overall strain seems less affected by preload and afterload changes. Myocardial deformation is typically described in a geometrical coordinate system describing longitudinal, radial, and circumferential deformation as major strains. In addition, rotational mechanics can be described reflecting shear strains. Rotation is the relative clockwise or counterclockwise motion of the LV around the long axis of the heart when viewed in the short axis and is expressed as degrees (°). By convention, counterclockwise rotation is displayed as positive when viewed from the apex. In the normal heart, there is a wringing motion with an early counterclockwise and then more dominant clockwise rotation at the base, and counterclockwise rotation at the apex.[10] This motion results in a net gradient between the base–apex and is referred to as net LV twist and is expressed in degrees (°).[11]

Technical Considerations:

For speckle-tracking analysis, good-quality 2D gray scale images are required at adequate frame rates. The majority of commercially available picture archiving and communication system (PACS) systems will store data using digital imaging and communications in medicine (DICOM) format, which is often defaulted to a frame rate of 30 Hz. When performing strain analysis at this lower frame rate, there is a real potential for the underestimation of peak strain rate values.[12–14] It is generally accepted that frame rates of 50–90 Hz provide optimal 2D images for subsequent strain analysis. Standard views for radial and circumferential strain should be acquired in the short axis with true circular views of the LV demonstrated. For basal analysis, a view at the level of the mitral valve is required, for the mid-ventricle view the papillary muscles should be seen but no mitral valve leaflet tissue, and for the apical view a section below the level of the papillary muscles is required. For longitudinal measurements, an apical four-chamber view should be attained with care taken not to foreshorten the LV. Strain calculation requires offline analysis; this can either be performed on the machine or on a separate designated workstation. For measurement of regional strain, the ventricle is divided using standard nomenclature,[15] with global or mean strain being the average of the different segments in any 1 plane. The software is a semiautomated program with manual tracing of the endocardial border in end-systole, which then performs analysis following an automated tracking algorithm. Current software packages are able to display individual and mean strain curves along with schematic representations (Fig. 1).These automated applications are easy to use and have been shown to correlate well with angiographic-derived EF with good reproducibility.[16]

In general, strain analysis is performed on a vendor-specific software package with significant variation in strain values recorded both between different systems and when attempting to use cross-vendor image acquisition and postprocessing technologies.[9,14,17,18] Manovel et al. compared 28 adult patients who had prospectively acquired radial, circumferential, and longitudinal strain data on 2 vendor platforms. While longitudinal strain was relatively well correlated with relatively narrow limits of agreement, radial and circumferential data demonstrated poorer levels of agreement.[17] These findings are even more evident in the pediatric population. Koopman et al. compared 3 software deformation packages, 2 employing STE and the other a tissue Doppler-derived strain package. The 2 STE systems used were the GE healthcare vivid 7 and EchoPac (GE Healthcare, Milwaukee, WI, USA) and the Phillips iE33 and QLAB (Philips Medical Systems, Best, The Netherlands). A total of 34 children had standard strain parameters measured on both systems with longitudinal and circumferential strain showing relatively good agreement with narrow levels of agreement and low inter- and intraobserver variability. Longitudinal strain intra- and interobserver coefficient of variation with EchoPac was 9% and 8%, and QLAB 5% and 6%. Circumferential values were 12% and 9% for EchoPac, and 11% and 13% for QLAB. For radial strain, there was poor agreement both across vendors with a difference of

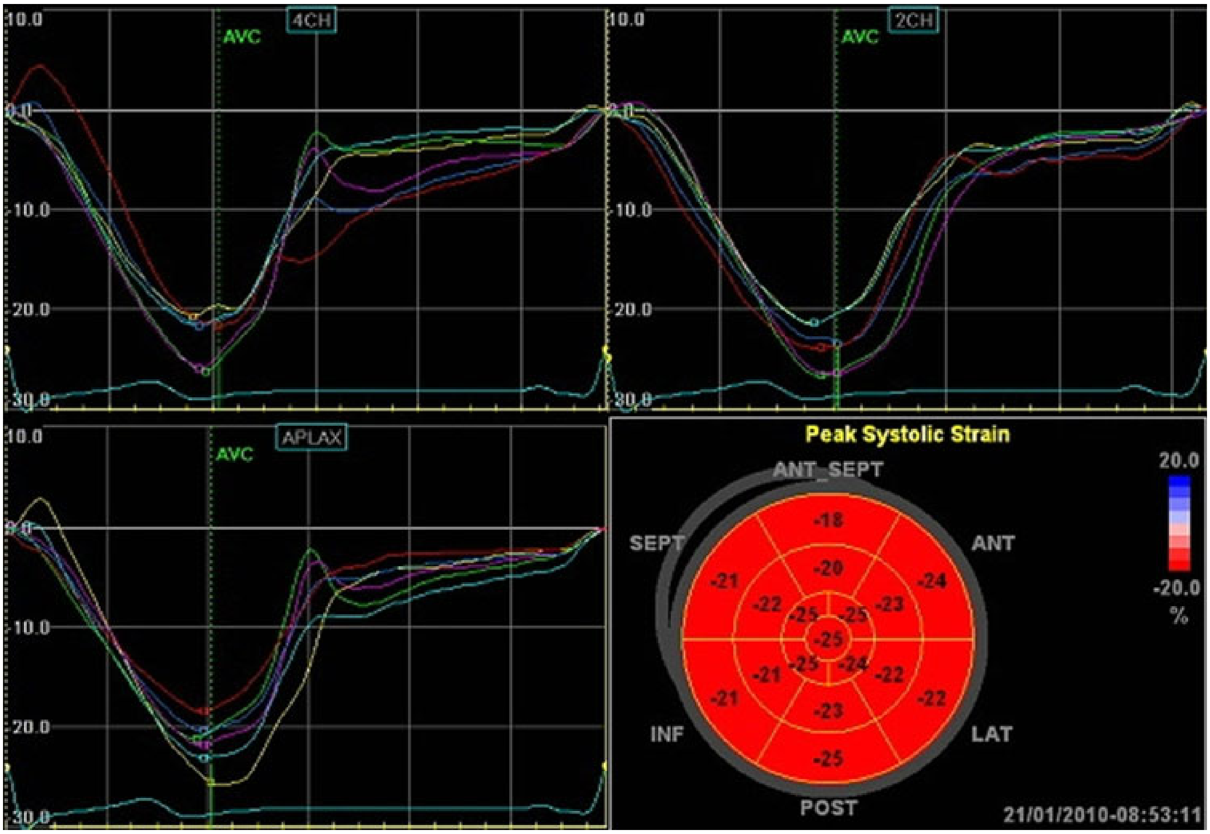

Figure 1. Normal longitudinal strain curves obtained from a standard apical four-chamber (4CH), two-chamber (2CH), and apical long axis (APLAX). The "bull's eye" schematic in the lower right of the image is a uniform red color, which represents normal peak systolic strain in all segments with values given for each subsegment. AVC = aortic valve closure; ANT_SEPT = anteroseptal; ANT = anterior; LAT = lateral; POST = posterior; INF = inferior; SEPT = septal.

50% between QLAB and EchoPac and with intra and interobserver variability in the posterior wall of 12% and 24% for EchoPac and 39% and 56% for QLAB.[18] This is a major ongoing concern; the lack of industry standardization limits the clinician's ability to utilize data from research using different postprocessing platforms. The poor reproducibility of radial strain has certainly influenced our center's practice, where we no longer report on radial strain for clinical purposes concentrating only on circumferential and longitudinal data.

Validation and Normal Values:

Speckle tracking echocardiography as a technique is well validated in the adult population with numerous studies comparing against both sonomicrometry and tagged magnetic resonance imaging (MRI).[19–22] To understand how to interpret the findings of potentially altered strain parameters in pathological process, it is imperative to have good normal data. Until relatively recently, normal pediatric values for strain, strain rate, and rotation were lacking. In the last few years, there have been several studies which have tried to address this deficiency. In 2008, Lorch et al. published normal values for longitudinal strain using VVI in 284 children. They reported mean values for the septal wall of $-18.3 \pm 6.67\%$ and for the lateral wall $-20.68 \pm 8.08\%$ with no change in absolute strain with age.[23] In this study, a wide range was noted in the normal data, limiting the applicability of the technology in clinical practice. In 2009, a small study by Bussadori et al.[24] investigated 30 adults and only 15 children (mean age 8 ± 2 years) used a novel tissue-tracking program (XStrain, Esaote, Florence) to add normal circumferential data. They demonstrated an increase in circumferential strain from base to apex, base $-22 \pm 4\%$, midventricle $-24 \pm 6\%$, and apical $-32 \pm 7\%$; however, these data are somewhat limited by low numbers. While other studies have demonstrated an increase in strain toward the apex, the gradient has not been as large as reported in the Bussadori study. Most recently, Marcus et al.[25] have published a larger dataset of normative values for longitudinal, radial, and circumferential data in 139 children and 56 young adults acquired using the Vivid-7 system (GE Healthcare). Initial postprocessing was performed on vendor-specific software (EchoPac; GE Healthcare); however, strain curves were then imported into custom-made software for further analysis. Global peak systolic strain values are detailed in Table 1. In contrast to Lorch et al.,[23] they describe a quadratic relationship for peak strain and age, with highest values during teenage years (15–19 years) and lowest values seen in infants and >30-years age group. Given these contrasting findings, and the relatively small number of patients in each age subgroup, further study will be required.

Rotational data in children have been reported by 2 groups, both employing the same vendor-specific image acquisition and postprocessing software (GE Healthcare).[10,26] In the largest of these, Takahashi et al.[10] acquired rotational data on 111 normal subjects aged between 3 and 40 years (68 patients <24 years), analysis was performed using EchoPac and a custom-made analysis package in MATLAB (The MathWorks, Inc., Natick, MA, USA). Using basal and apical short-axis views and values averaged over 3 heart beats, complete rotational data were possible in 66% of patients. Their results supported early tissue Doppler work[27] with increased net twist (termed torsion in their article) with age as a result of increased apical counterclockwise rotation. Apical rotation increases from 6.5 ± 2.3° (3–9 years) to 10.1 ± 1.9° (33–40 years), with basal clockwise rotation remaining relatively constant at between −4 and −5°, there is a resultant increase in net twist from 10 ± 3.3° to 14.2 ± 3.1° with advancing age, however, the net twist when corrected for LV length was constant across the age groups. Time to both systolic peak rotation and diastolic untwisting increase with age, leading the authors to conclude that the young heart tends to twist, untwist, and deform faster, while maintaining normalized twist (torsion) profile with age.[10]

One patient population which has little normative data is the neonatal age group with the majority of published work in patients <1 month age using tissue Doppler strain analysis. Pena et al. calculated normal values for 55 infants within the first few days of life and then reassessed at 1-month of age using tissue Doppler-derived strain. They report with good levels of reproducibility, normal values for both longitudinal and radial (basal posterior wall) systolic strain (−24.8 ± 3% and 49.7 ± 12.9%, respectively) with values falling slightly by a month.[28] There are only limited normal data for STE in this very young population in part due to the technical

TABLE 1

Published Normal Mean Peak Systolic Strain Values

Variable	Age Group							
	<1 Year n = 24	1–4 Years n = 34	5–9 Years n = 36	10–14 Years n = 29	15–19 Years n = 21	20–24 Years n = 25	25–29 Years n = 13	30–40 Years n = 13
Longitudinal strain								
Global	−18.3 ± 1.9	−20.7 ± 1.3	−21.0 ± 1.3	−21.8 ± 1.3	−22.5 ± 1.3	−20.9 ± 1.3	−20.6 ± 1.2	−18.9 ± 1.0
Radial strain								
MV posterior wall	60.5 ± 6.0	58.5 ± 7.7	61.2 ± 7.4	62.2 ± 6.5	63.0 ± 5.8	62.5 ± 6.0	59.5 ± 4.3	60.1 ± 4.4
MV global	49.9 ± 4.3	50.0 ± 5.7	52.3 ± 4.5	54.9 ± 5.4	56.1 ± 3.8	54.9 ± 5.4	52.8 ± 4.1	52.2 ± 4.3
Radial strain								
PM posterior wall	63.2 ± 11.6	61.1 ± 8.9	64.8 ± 7.1	66.3 ± 5.5	66.8 ± 4.1	66.4 ± 5.5	63.1 ± 5.8	62.2 ± 5.6
PM global	52.0 ± 9.9	53.5 ± 6.7	54.9 ± 5.5	58.0 ± 5.4	58.1 ± 4.0	57.3 ± 5.0	54.6 ± 5.3	54.2 ± 4.7
Circumferential strain								
Global MV	−17.5 ± 2.5	−19.7 ± 2.0	−20.9 ± 2.0	−21.5 ± 1.7	−21.9 ± 2.1	−21.1 ± 1.3	−21.0 ± 1.6	−20.2 ± 1.4
Global PM	−18.6 ± 3.3	−21.3 ± 2.0	−23.4 ± 1.7	−23.5 ± 1.8	−23.6 ± 2.0	−21.8 ± 1.5	−21.1 ± 1.9	−20.6 ± 2.2

Data are expressed as mean ± SD percentage.
MV = mitral valve; PM = papillary muscle.
Adapted from Marcus et al.[25]

difficulties of high heart rate, a small myocardial area, and so a reduced number of speckles and high degrees of artifact making adequate tracking for analysis problematic. There are significant changes in both preload and afterload during the first month of life, with changes in vascular resistance and closure of the arterial duct. How these normal physiological changes impact on normal values during this period remains unknown.

Clinical Applications in Acquired Heart Disease:

Detection of Preclinical Disease:

The early detection of myocardial disease prior to a reduction in LV EF has generated much research interest. Using tissue Doppler-derived strain measurements, it has been shown that changes in myocardial deformation can be detected in young patients with Duchenne muscular dystrophy, which further decreased with age.[29] Marcus et al.[30] found that patients with mitochondrial disease had reduced global strain values in all 3 directions compared with normal, while EF remained in the normal range. This has also been demonstrated in Friedreich's ataxia patients with normal EF,[31] and in children with Prader–Willi syndrome.[32] The prognostic value of these findings is still uncertain and will require further longitudinal follow-up data. Our group detected abnormalities in myocardial strain parameters, which were related to vascular changes in obese children with known lipid abnormalities.[33] Childhood obesity was found to be associated with reduced longitudinal end-systolic LV strain, global strain, and reduced diastolic strain rate. Similar findings were also found in children with diabetes, who exhibit reduced longitudinal strain with compensatory increase in torsion.[34,35] Two patient populations undergoing regular echo surveillance for which early detection of myocardial dysfunction is of the utmost importance are chemotherapy survivors and cardiac transplantation patients. In chronic survivors, Cheung et al.[36] showed reduced circumferential and longitudinal strain parameters in adolescent patients who had been exposed to chemotherapy, which correlated with cumulative anthracycline dose. In the subacute phase, Poterucha et al.[37] found significant changes in longitudinal strain 4 months after starting chemotherapy, while significant changes in EF could only be detected at 8 months. In women treated for breast cancer with the cardiotoxic combination of anthracyclines and trastuzumab, the reduction in longitudinal strain at 3 months was shown to be predictive for a reduction in EF at 6 months.[38,39] Rotational dynamics have also been demonstrated to be altered in childhood cancer survivors. Cheung et al. compared LV rotation in childhood leukemia survivors treated with anthracycline therapy. Although there was a reduction in EF compared with normal controls, they also demonstrated a subgroup of patients who had a normal EF, but a reduction in peak torsion, apical untwisting, and LV systolic twisting velocity.[40] All these findings strongly indicate that abnormal strain measurements reflect early changes in myocardial function prior to a decline in EF. This is also important for graft surveillance in pediatric patients postcardiac transplantation. Kailin et al.[41] found a reduction in longitudinal strain, but preservation of circumferential strain at 12 months. In adult patients, Sarvari et al.[42] showed that global longitudinal strain was an independent predictor of 1-year mortality posttransplant ($P = 0.02$). In addition, Marciniak et al.[43] also showed that strain monitoring might be useful in myocardial acute rejection monitoring. The same group also suggested that tissue Doppler-derived strain imaging was more accurate in detecting cardiac allograft vasculopathy using quantitative dobutamine stress echocardiography when compared with subjective visual assessment.[44] The exact clinical role of strain imaging after cardiac transplantation should be explored further in the next few years.

Disease Surveillance and Risk Stratification:

One patient population that has generated significant research interest is hypertrophic cardiomyopathy. The majority of the work in this area has been undertaken in the adult population with established hypertrophy. It is well recognized that there is reduced longitudinal strain in segments of hypertrophy and delayed untwisting of the LV contributing to impaired diastolic function.[45–48] At this time, there is little evidence that STE can reliably detect preclinical disease with normal strain parameters demonstrated between controls and known genotype-positive patients.[49] One potentially interesting application is the role STE may be able to play in risk stratifying patients at risk of developing tachydysrhythmia and potentially sudden death.[50] Di Salvo reports that in the presence of 3 or more segments with peak systolic strain $\geq -10\%$, there was a sensitivity of 81% and specificity of 97.1% for predicting nonsustained ventricular tachycardia during the follow-up. The true additional value of STE independent of more established parameters needs to be fully evaluated, but does show potential for future development.[51]

There is increasing evidence that in the setting of both acute and stable heart failure, STE offers incremental value in predicting outcome. Cho et al.[52] report an incremental value of global longitudinal and more markedly global circumferential strain in addition to EF in predicting cardiac events in acute heart failure patients. Longitudinal strain has been demonstrated to be an independent predictor of outcome in stable heart failure patients. Cutoff values of −9% for the LV and −21% for the right ventricle (RV) have been proposed as superior discriminators for poor outcome than conventional measures.[53,54]

Congenital Heart Disease:

While STE was initially developed for LV assessment, it has been applied to quantify RV and single ventricle deformation.[55–57]

Right Ventricle:

As the RV is often affected by congenital heart disease (CHD), quantification of RV function is an important topic. Particularly in postoperative tetralogy of Fallot patients (TOF), there is a lot of interest in better characterizing the effect of pulmonary regurgitation on RV function.[58–60] Earlier studies using tissue Doppler–derived strain measurements have shown that longitudinal RV strain is reduced in pediatric patients and that this correlates with exercise capacity and the severity of pulmonary regurgitation.[61,62] Not surprisingly, this was confirmed using STE, Kutty et al.[60] used VVI to demonstrate that longitudinal RV strain values were reduced compared with normal with some effect of pulmonary valve implantation on strain measurements. We found an increase in RV and septal strain in a small group of children in the first 2 days following catheter pulmonary valve implantation.[63] However, in the medium and long term, RV strain tends to be decreased after pulmonary valve replacement. Knirsch et al.[64] showed that pulmonary valve replacement resulted in a further decrease in longitudinal strain early after surgery with a slow improvement in strain at 6 months, although values remained lower than preprocedure values and lower than control values. These findings are not entirely surprising, as a reduction in RV output after removing the pulmonary regurgitation will result in a reduction of RV deformation. The interpretation of strain data is complicated by the fact that multiple factors can be expected to influence the strain measurements: increased RV output related to the regurgitant volume will result in increased strain, while progressive RV dilatation will cause a reduction in strain parameters. This makes the interpretation of strain measurements in this population difficult, as they do not directly reflect intrinsic myocardial contractile function in these settings. Strain imaging can also be used to study RV dyssynchrony and RV–LV interactions.[58,65,66] Data on biventricular dyssynchrony after TOF repair are still contradictory with no evidence of RV and LV mechanical dyssynchrony at rest in children, while exercise seemed to induce a more dyssynchronous contractile pattern.[58,67] In contrast, adults post TOF have demonstrated RV and LV dyssynchrony.[68] It is possible that this reflects a different era of surgery or that mechanical dyssynchrony becomes more prominent with advancing age. The dilated and often dysfunctional RV influences LV function with a reduction in LV deformation and LV twist. A recent study has demonstrated that reduced LV longitudinal strain was predictive for the occurrence of sudden cardiac death and ventricular arrhythmia.[69] Also RV diastolic dysfunction could potentially be studied using STE. Friedberg et al.[59] described diastolic abnormalities for both the RV and LV employing strain rate as a marker of early diastolic function.

Other studies have looked at the use of STE to assess RV function in patients with atrial septal defects,[70,71] congenitally corrected transposition of the great arteries,[72] and patients after the atrial switch operation for transposition of the great arteries.[73,74] Interestingly in patients after the Senning or Mustard procedure (atrial switch), a reduction in longitudinal strain in both the systemic RV and the subpulmonary LV were shown to predict clinical events and outcome, showing the importance of ventricular interaction in patients with right heart disease.[74]

Left Ventricle:

Speckle tracking echocardiography can also be used in children with left-sided congenital and acquired heart disease (Figs. 2 and 3). It could be especially useful looking at congenital defects causing chronic pressure loading. Specifically in patients with aortic stenosis (AS), a method capable of detecting myocardial damage early could possibly help selecting patients who might benefit from intervention on the valve. Marcus et al.[75] prospectively studied children undergoing balloon valvuloplasty for valvar AS using 2D STE with follow-up data to 3 years. They noticed a reduction in longitudinal strain parameters prior to intervention. Data collected at 6 months and then 3 years post procedure demonstrate that both global longitudinal and circumferential strain remain depressed, while radial strain returns to normal range. They conclude that while there is substantial recovery of myocardial deformation that there is incomplete recovery of strain parameters, which may indicate residual myocardial damage not appreciated by conventional

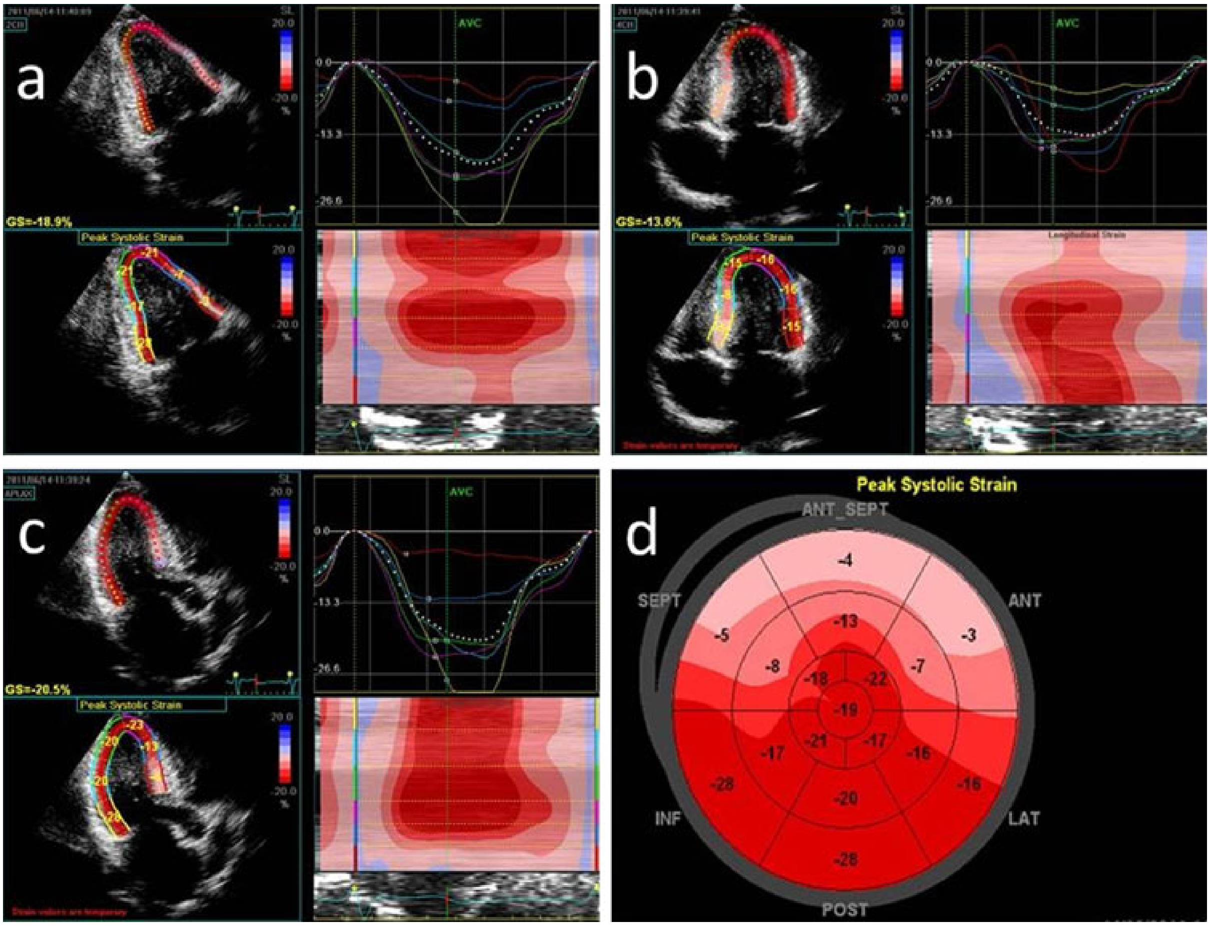

Figure 2. An 11-year-old boy with hypertrophic cardiomyopathy. Peak longitudinal systolic strain measured in the apical two-chamber **A.**, four-chamber **B.**, and long axis **C.**There is a characteristic reduction in basal anterio-septal and septal longitudinal strain represented by the lighter shaded segments in this "bull's eye" schematic (**D**). This corresponds to areas of hypertrophy predominantly affecting the basal and mid-ventricular setum. ANT SEPT = anteroseptal; ANT = anterior; LAT = lateral; POST = posterior; INF = inferior; SEPT = septal.

parameters. Similarly, cardiac MRI has demonstrated that in the setting of repaired coarctation even with no residual arch obstruction, LV radial and longitudinal strain remains reduced, but not circumferential strain.[76] The long-term significance of these findings is currently uncertain and will require further study.

Single Ventricle Circulation:

The functional assessment of the single ventricle is challenging due to the variable ventricular morphology and loading conditions. The use of STE has been investigated, but is challenging due to the variable geometry with dilatation and hypertrophy reflected by abnormal mass/volume ratio. Singh et al.[77] showed in a recent validation study comparing STE with myocardial tagging that reasonable reproducibility of the measurements and agreement could be obtained in patients with single ventricles. This study included only patients with tricuspid atresia, which are shaped more like normal LVs, with further validation in other types of univentricular hearts needed. Different studies have used STE to assess single ventricular function of both left and right ventricular morphology.[78,79] Menon et al.[80] used VVI to assess patients with hypoplastic left heart syndrome (HLHS) prior to and following a bidirectional cavopulmonary shunt. All patients had previously undergone first-stage Norwood operation with the Sano modification (RV to pulmonary artery conduit). They describe regional dysfunction at the ventriculotomy site using circumferential strain, postulating that this may have a deleterious implication for long-term RV function. A study by Khoo et al.[56] followed a cohort of 20 HLHS patients from prestage 1 Norwood/Sano to prebidirectional cavopulmonary shunt (stage 2) using both STE and cardiac MRI. Importantly, of their initial cohort of 46 patients, 65% were

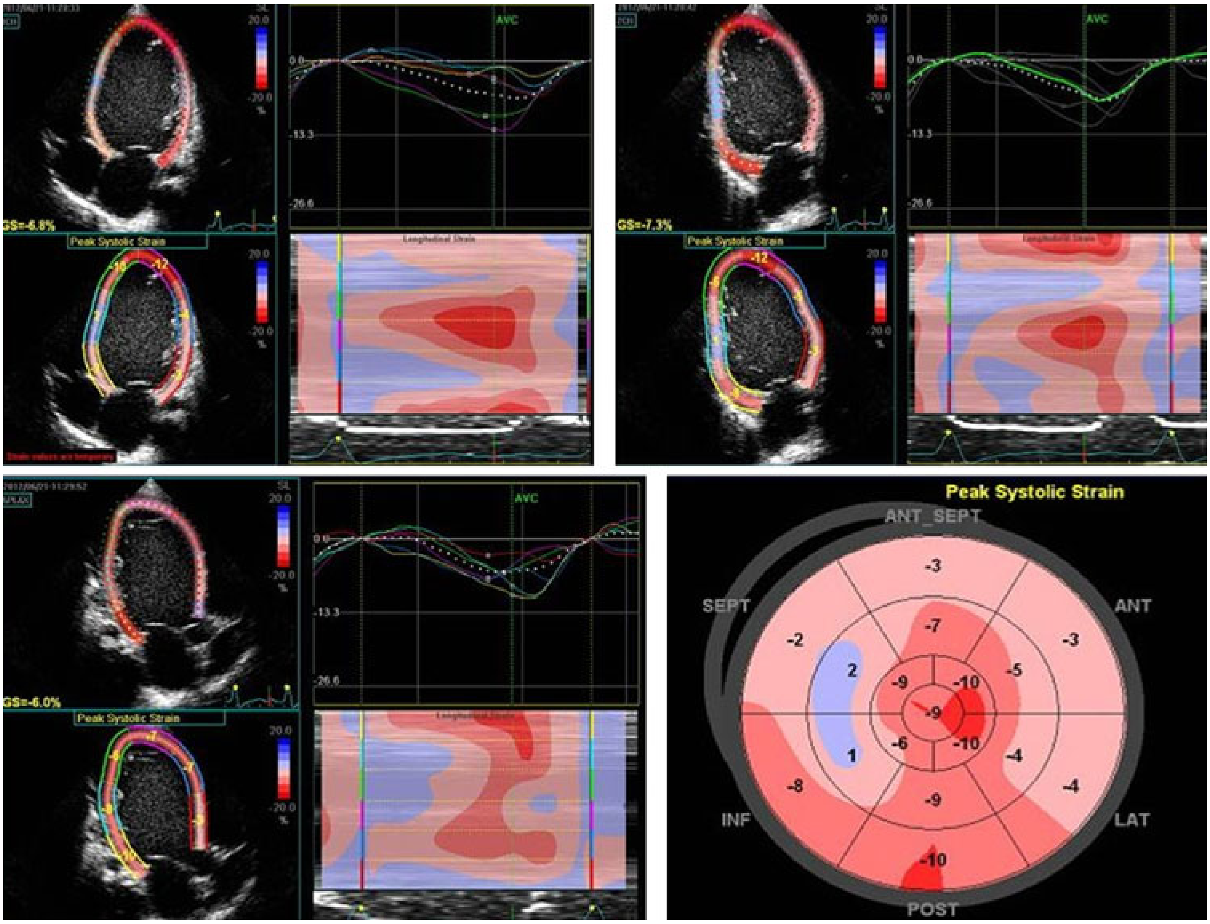

Figure 3. A patient with dilated cardiomyopathy. Longitudinal strain assessed from the apex in two-chamber, four-chamber, and long-axis views. There is marked reduction in global longitudinal function with heterogeneity of function and some postsystolic shortening.

prenatally diagnosed, 3 died within 30 days of Norwood/Sano (6.5%), and 7 died during the interstage period (15%) and therefore were excluded and no strain data reported. Using aortic valve closure as a marker of end-systole, they determined peak strain and peak systolic strain to calculate the postsystolic strain index (PSSI). There was a reduction in longitudinal systolic strain with preservation of circumferential systolic strain. In addition, they observed a delay in time to peak strain with a reduction in peak strain rate leading to an increase in PSSI. The MRI RV volumes correlated more closely with circumferential strain and strain rate than longitudinal values. These findings show that when the RV is placed in the systemic position that it changes from predominantly longitudinal shortening to an LV-type circumferential dominant pattern. Mechanical dyssynchrony (Fig. 4) may be an additional contributing factor to inefficient RV mechanics in these patients.[81] In the Khoo study, mechanical dyssynchrony (predominantly in the circumferential plane) was related to MRI-derived EF. However, circumferential strain is difficult to obtain reliably in the RV, and these results should be verified in additional populations. Nonetheless, these adaptive processes offer insight into the complex remodeling that occurs in these patients with better ventricular mechanics prior to bidirectional cavopulmonary shunt. The findings of PSSI are possibly related to myocardial ischemia and a mismatch of coronary flow reserve, but has also been reported with acute change in afterload.

Fetal Strain Imaging:

The assessment of fetal cardiac function poses interesting technical challenges. In part, given the unpredictability of fetal lie, the angle independence of STE may lend itself well in this situation. One major drawback has been low frame rates coupled with a high fetal heart rate. Most studies to date have retrospectively employed

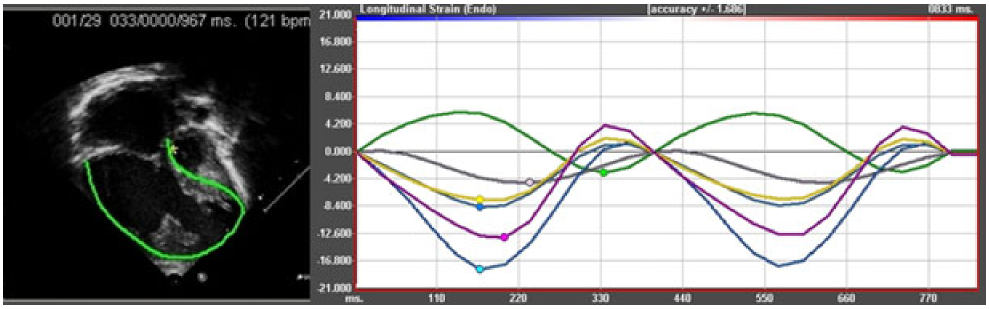

Figure 4. Longitudinal strain curves taken over 2 beats in a patient with hypoplastic left heart syndrome post Norwood operation. These strain curves were obtained from an apical four chamber stored as digital imaging and communications in medicine format and following manual tracing of the endocardial border processed using vendor-independent software (Image arena; TomTec imaging systems, Munich, Germany). There is marked heterogeneity in systolic function with the basal septal segment (in green) being stretched represented by a positive curve during systole and varying time to peak systolic strain in the other segments.

VVI at a frame rate of 30 Hz.[82–87] Higher frame rates may improve temporal data with Matsui et al.[83] comparing VVI with low and high frame rate, demonstrating an increased success rate for attaining adequate tracking and analysis (86% vs. 76%) and an increase in absolute strain, strain rate parameters at higher frame rates. Most studies have concentrated on longitudinal function as measured from a four-chamber view[82,83,86–90] with only 1 group reporting normal values for circumferential strain.[84] Reported normal values for mean RV strain range from −16% to 24.8%,[84,87] and for LV from −15.1% to 21.6%.[83,89] Circumferential strain values for the LV at the mid-ventricular level were $-18.7 \pm 3.3\%$.[64] Rychik et al. looked at the differences for both RV and LV function using both systolic and diastolic strain parameters in the setting of twin–twin transfusion syndrome. Compared with normal the donor (oligohydramniotic), twin demonstrated increase LV systolic strain rate. The recipient twin (polyhydramniotic) had significantly reduced strain (longitudinal), systolic and diastolic strain rates in both the LV and RV in comparison with controls. These ventricle-specific changes were attributed to the relative differences in loading conditions, both with altered preload due to hypovolemia in the donor and the changes in afterload due to relative imbalance of the cerebral and high-resistance placental bed.[85] Ishii et al. looked at a subset of patients with AS in the setting of normal-to-moderate LV dysfunction (as assessed by conventional techniques). They demonstrated characteristics ranging from global reduction in all values to relative preservation of circumferential strain in the setting of reduced longitudinal measurements.[84] More recently, VVI has been employed in the HLHS patient population with the systemic RV demonstrating evidence of remodeling in fetal life in keeping with changes recognized in the postnatal population. Brooks et al.[91] report on 48 fetuses, describing a more spherical RV due to an increase in RV diameter with reduced longitudinal strain compared with both normal RV and LV measurements.

Future prospective studies employing higher frame rate imaging have the potential to significantly add to our assessment of fetal cardiac function. The ultimate objective for STE is to provide reproducible quantitate values that may provide prognostic information for postnatal and long-term outcome.

The Future Three-Dimensional Strain?:

One limitation of 2D STE is that speckles can only be tracked in the plane of acquisition with loss of tracking for through plane motion; 1 possible solution to this is three-dimensional (3D) STE. As the spatial and temporal resolution of 3D imaging has improved, STE can now be performed on real time 3D datasets, potentially allowing tracking of speckles in all directions as long as they remain within the dataset.[92,93] The inherent limitations are similar to that of 2D STE in that if acoustic windows and imaging is poor on 2D this will only be amplified on 3D volumes leading some authors to suggest that only patients with good acoustic windows should undergo 3D STE.[94] To have a sufficiently large dataset to include the entire LV, there may be a compromise to frame rate. This in part may be overcome with acquisition over several heartbeats, but this requires a breath hold, which may be tolerated poorly in younger children and has the potential for significant stitching artifact. To address these issues, single-beat real time 3D imaging may be a solution as long as sufficiently high frame rates are maintained. Given the lower spatial resolution, care should be taken in ensuring adequate tracking of the myocardium as the epicardial and endocardial borders may be less well defined.[2]

This remains a new technique, and at this time validation is ongoing, there is an emerging body of literature reporting good correlation between 3D STE and both MRI and sonomicometry[95] coupled with high levels of technical feasibility.[93] In particular, Hayat et al.[96] report close correlation of global longitudinal strain with LV EF on MRI and Nesser et al.[97] reporting a closer agreement for LV-derived volume between 3D STE and MRI than 2D STE and MRI. The difficulty of vendor-specific imaging and software analysis packages present in 2D STE is also a major limitation for 3D STE. Gayat et al. looked specifically at the reproducibility and intervendor variability of 3D STE between 2 systems. They studied 30 adult patients attaining mean frame rates of 20 Hz, with only 15 datasets graded as "adequate to optimal" for subset analysis. Their findings led them to conclude that the intervendor technique agreement was poor (intraclass correlation coefficient [ICC] <0.4) and although intrinsic variability was relatively low, there was significant variation among parameters. For all comparisons, twist had the worst concordance with ICC <0.5.[98] Three-dimensional STE may struggle to be widely adopted until such time as the issues with frame rate can be addressed. While there are encouraging reports, further validation is required and at this time there seems to be little appetite from industry to standardize the postanalysis process so that both cross- and intervendor results can be compared.

Conclusion:

Echocardiography is an imaging modality, and while the advances of both 2D STE and 3D STE are exciting prospects for functional assessment, at their root is a need for good image acquisition, without which no amount of post processing will be able to generate accurate and reliable strain analysis. The angle independence and lack of geometric assumptions with STE are especially beneficial in the pediatric age range. The ability to gain quantitative information for both regional and global function in a quick and reproducible way make it ideal for both initial and serial assessment of children. Evidence for preclinical detection of myocardial dysfunction prior to the deterioration of traditional parameters is well recognized. The widespread inclusion of STE in routine functional assessment is in part hindered due to the time-intensive need for post processing and by a perceived lack of incremental value in the setting of reduced traditional parameters. Both of these issues are now being addressed with evidence from the adult population that not only does STE offer incremental value for prognostication but can also be accurately and reproducibly performed at the bedside.[99] At this time, 3D STE is hampered by the reduction in frame rate associated with full volume acquisition and poor reproducibility, and so will remain an exciting prospect until these issues can be overcome. Two-dimensional STE requires further validation and normative values in a pediatric population, ideally along with the standardization across different vendor systems, before we can fully integrate what is an excellent research tool into everyday clinical practice. However, there is an ever increasing number of publications demonstrating that STE is rapidly developing as the primary modality for assessment of myocardial deformation in pediatric heart disease.

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