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Original Article

Advanced functional echocardiographic imaging of the failing heart in children*

Anitha Parthiban, Girish Shirali

Ward Family Heart Center, Children's Mercy Hospital, Kansas City, Missouri, United States of America

Abstract Over the past decade, new echocardiographic techniques such as three-dimensional echocardiography and the imaging of myocardial deformation (strain) have been developed, and are increasingly used in clinical practice. In this article, we describe the rationale and methodology, review available guidelines for practice, and discuss the advantages and limitations of each of these modalities. When available, we have also summarised the scientific evidence for the clinical application of these techniques to detect heart failure in children.

Keywords: Heart failure; children; myocardial strain; three-dimensional echocardiography; advanced imaging

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Background

Echocardiography is the most frequently used modality for imaging and serial follow-up of the failing heart. As we have shown, standard measurements of ventricular thickness and function that are obtained using two-dimensional and M-mode echocardiography remain the mainstay of echocardiographic imaging. Although investigators have had the opportunity to critically study these modalities over the past several decades, the critical evaluation of the prognostic value and reproducibility of these modalities and measurements in children appears to have started only recently.[1–5]

Over the past decade, advances in the speed of computerised processing and in the miniaturisation of electronics have led to an increasing momentum among the industry and investigators in search for more reliable, sensitive, and automated measurements of regional and global myocardial mechanics.[6] These techniques have been utilised in the clinical context to varying degrees. Given the relatively recent development of these techniques, the inconsistency of adoption of each technique among centres, and the challenges that are unique to quantitation in CHD and paediatric echocardiography, it is unsurprising that none has been evaluated, to date, as critically as established echocardiographic techniques have been.

In this article, we shall discuss three-dimensional echocardiography and the imaging of myocardial deformation (strain). We describe the rationale and methodology, review available guidelines for practice, and discuss the advantages and limitations of each of these modalities. When available, we have also summarised the scientific evidence for the clinical application of these techniques to detect heart failure in children.

Considerations that are specific to paediatric and CHDs

Most of these techniques and modalities have been developed and studied in adults. Therefore, when they are used in children, consideration must be given to the varying range of body sizes, heart rates, and maturational changes in myocardial mechanics. The development of transducers and algorithms that are applicable to children typically lags behind similar developments in adults: a factor that compounds the challenges of new technology. Somatic growth is associated with changes in heart rates, loading conditions, and the size and thickness of the heart, all of which challenge the ability to interpret findings. For new measurements, there is paucity of

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Correspondence to: A. Parthiban, MD, Ward Family Heart Center, Children's Mercy Hospital, 2401 Gillham Road, Kansas City, MO 64108, United States of America. Tel: +816 234 3947; Fax: +816 302 9987; E-mail: aparthiban@cmh.edu

meaningful normative data in children. The wide range of pathology that underlies the failing heart in children, such as the failing univentricular heart or the systemic right ventricle, further complicates the extrapolation of these techniques in children.

Three-dimensional echocardiography

At present, three-dimensional echocardiography enables the acquisition of the entirety of a cardiac chamber or valve in a single data set.[7] Software that enables quantitation based on such data sets provides the potential for measuring the size and function of chambers and valves in a manner that would be free of geometric assumptions, independent of the size, shape, or morphology of a structure.[8] Starting about 15 years ago, advances in piezoelectric technology have led to the development of single crystals of piezoelectric material that are cut into thousands of elements that are arrayed in a matrix.[9] Simultaneously, advances in the miniaturisation of transducers and faster processing have made three-dimensional echocardiography a reality with clinical applications.[10] The development of transducers that are capable of imaging at higher frequency and with smaller footprints has extended this application of this modality to children.[11]

Furthermore, three-dimensional echocardiograms can be acquired using one of two main methods. The first of these is live imaging, in which a narrow pyramidal echocardiographic image is displayed in real time. At present, applications of this mode centre on interventional cardiology or localised abnormalities of cardiac structures or valves. The second method uses multiple narrow pyramidal images that are obtained from multiple cardiac cycles and are stitched together to develop a wide data set. This allows for acquisition of larger structures such as ventricles and enables the quantitation of volumetrics and function. Three-dimensional echocardiography has two main roles in the assessment of the dysfunctional ventricle – the measurement of ventricular volumes and ejection fraction and providing insights into the mechanism, and potentially the quantitation, of valvar regurgitation.

Left ventricular size and function

The ability to perform three-dimensional echocardiographic measurement of the left ventricular volumetrics requires the software to detect the chamber that is of interest, delineate its boundaries, and then track its borders throughout the cardiac cycle. Owing to the complexity of performing this on a rapidly moving structure, the algorithms that are in widespread clinical use are based on computerised modelling of cardiac structures and motion. They require that the user designate specific locations for the hinges of the mitral valve and the apex of the left ventricle, and then use a form of automated detection of endocardial borders followed by counting of voxels to determine the volume of the ventricle; three-dimensional measurements of left ventricular volumes and ejection fraction that are based on these algorithms have been validated using cardiac MRI as a reference standard. A recent meta-analysis of 95 such studies involving over 3000 adults showed that left ventricular ejection fraction obtained using three-dimensional echocardiography exhibited excellent correlation with MRI, whereas left ventricular volumes were systematically underestimated.[12] Similar studies have been performed in children, both with structurally normal hearts and with CHD, with similar results.[13–15]

If three-dimensional echocardiography was, in fact, more accurate than two-dimensional techniques, then its ability to detect smaller changes in volume or ejection fraction of the ventricle in a manner that is more reproducible when compared with two-dimensional techniques would add incremental value; two recent studies have evaluated these features. Dorosz et al[16] published a meta-analysis of studies that compared left ventricular volumes and ejection fraction that were performed using two- and three-dimensional echocardiography with measurements obtained using cardiac MRI. They collated 23 studies that included over 1600 echocardiograms. They found that under controlled settings and in patients with adequate image quality, three-dimensional echocardiography provides better accuracy and precision in measuring the volume and ejection fraction of the left ventricle when compared with two-dimensional echocardiography; however, when compared with MRI, it underestimates true left ventricular volumes. Thavendiranathan et al[17] compared the temporal variability of left ventricular ejection fraction that was measured using two-dimensional echocardiography with that obtained using three-dimensional echocardiography in the setting of normal global longitudinal strain. They interpreted the temporal variation in left ventricular ejection fraction as being attributable to physiological differences and intrinsic variability of the measurement, rather than to dysfunction. They showed that the temporal variability of two-dimensional echocardiographic measurement of left ventricular ejection fraction was ~10%, whereas the temporal variability of three-dimensional echocardiographic measurement of the left ventricular ejection fraction was ~6%. Baker et al,[18] among others, have shown that left ventricular volumetrics in children can be performed quickly and that it is a reproducible technique.

The American Society of Echocardiography and the European Association of Cardiovascular Imaging published guidelines that delineate the role of three-dimensional echocardiography in adults in 2012;[19,20] these guidelines were updated in 2015.[20] The routine use of three-dimensional echocardiography for measuring left ventricular volumetrics and ejection fraction is recommended in adults because it is more accurate and reproducible than two-dimensional techniques. This stance has been re-iterated in recent guidelines for serial monitoring of patients who have received cardiotoxic chemotherapy.[21] Guidelines do not exist, at present, for the use of three-dimensional echocardiography in children.

The right ventricle and the univentricular heart

Dilation and dysfunction of the right ventricle are frequently encountered in paediatric cardiology. The retrosternal position of the right ventricle, its complex pyramidal shape, and the prominence of trabeculations that obscure the border between the endocardium and the cavity are all factors that greatly complicate the echocardiography of the right ventricle. Although these factors pose a challenge to two-dimensional echocardiography, they should not, in theory, affect three-dimensional echocardiography, because with three-dimensional echocardiography there ought to be fewer assumptions about the shape of the ventricle. There are two echocardiographic approaches to volumetrics for the right ventricle: summation of discs and semi-automated detection of borders.

The method of summation of discs is most directly comparable with the technique that is used for MRI. It correlates well with volumes obtained by MRI, but underestimates volumes consistently. This method does not rely on left ventricular landmarks for the purposes of developing a model of the right ventricle. It can be applied to abnormal left ventricles, the systemic right ventricle, and the univentricular heart. Unfortunately, this method has been removed as an option from commercial platforms for three-dimensional quantification.

Semi-automated detection of borders is a validated method[22–24] that is in widest usage for right ventricular volumetrics. It requires that the user first define both right and left ventricular anatomic landmarks, and then manually draw the contours of the ventricle in three orthogonal views in both end diastole and end systole. This method has been validated in adults, but the need for the definition of left ventricular landmarks – in locations that are anatomically correct – poses a major challenge to the application of this technique in many situations that are encountered commonly in paediatric practice. Nevertheless, the feasibility, reproducibility, and accuracy of three-dimensional echocardiographic quantitation of the size and function of the right ventricle has been evaluated in a variety of CHDs including tetralogy of Fallot, the univentricular heart, and the systemic right ventricle.[25–31] Overall, three-dimensional echocardiography is feasible in this population with acceptable inter- and intra-observer variability. Correlation with MRI is good when the right ventricle is normal in size and function, and is moderate when the right ventricle is enlarged or dysfunctional. Moreover, three-dimensional echocardiography yields right ventricular volumes that are typically underestimated compared with cardiac MRI; the two modalities are not interchangeable.

Valvar structure and function

Routine three-dimensional imaging of the mitral valve is recommended in adults because it provides the best physiological and morphological assessment of the valve;[19] three-dimensional colour Doppler imaging of the mitral valve allows for quantitation of the number of jets and measurement of the regurgitant orifice.[32]

Imaging of myocardial deformation (strain)

Strain is a dimensionless index that reflects the regional deformation of ventricular myocardium during a cardiac cycle as a function of its initial length or thickness. This form of quantitation uses deformation as a direct measure of ventricular contraction and relaxation, in contrast to indices that measure the overall change in dimensions of the cavity of the ventricle, such as shortening fraction or ejection fraction. The rationale behind the use of deformation imaging is that the direct measurement of myocardial mechanics may detect early changes in the health of the myocardium, before overall changes in function become evident using shortening fraction or ejection fraction. The measurement of deformation of the myocardium may be useful in recognising pre-clinical disease, in surveillance for disease, and in stratifying patients for their risk of developing disease. As strain does not rely on assumptions regarding the geometry of cardiac chambers, this method could be useful in quantifying myocardial function in the context of CHD, particularly in quantifying the function of the morphological right ventricle or of the univentricular heart. Strain imaging can also identify patterns of dyssynchronous contraction of the ventricles.

Strain is expressed as a percentage; the value may be positive or negative depending on whether there is shortening or lengthening of the myocardial segment. Strain is measured in each of the three planes – longitudinal, circumferential, and radial – in which a chamber deforms during the cardiac cycle. Segmental strain refers to deformation within a segment of the ventricle, whereas global strain refers to the average of all strains for all segments of the ventricle; in practice, global longitudinal strain is the type of global strain measurements that is used. With any measurement of strain, a corresponding strain rate can be measured. Strain rate is the rate of change in strain over time; it is expressed as per second. Both strain and strain rate can be measured in systole or diastole. Strain is imaged using speckle tracking echocardiography, a technique that tracks "speckles" that are ultrasonic patterns of reflection within the myocardium, throughout the cardiac cycle to determine deformation.

There are some caveats to the imaging of strain. It requires high temporal resolution: frame rates between 40 and 80 frames/second are recommended in adults, and even higher frame rates are required in patients who have high heart rates. In addition, the quality of the image has to be optimal, such that it includes the apex of the ventricle without foreshortening and ensures that views of the short axis of the left ventricle are not off-axis. Although measurements of strain that are based on two-dimensional speckle tracking have been believed to be independent of the angle of insonation, a recent study in children[33] demonstrated that left ventricular peak longitudinal systolic strain is modestly dependent on the angle of insonation as well as on the depth of the target. Although strain is, conceptually, independent of the angle of insonation or the depth of the target, echocardiography itself is not – for example, if a structure is imaged in the axial plane when imaged from one window, and in the lateral plane in another window, then it is unrealistic to expect images that have identical resolution from both windows. The same logic holds for the depth of the target. As a corollary to this, the ability to track speckles may well depend on the well-known differences in the resolution of an echocardiographic image in different planes and at differing depths. Two-dimensional analysis of strain is fundamentally challenged by the loss of speckles of ultrasound due to motion outside the plane of imaging,[34] which is inherent to the complex, three-dimensional nature of myocardial contraction. Three-dimensional speckle tracking is in its infancy; it faces many challenges,[35] and is therefore not discussed further.

Since 2011, the American Society of Echocardiography and the European Association of Echocardiography have published three statements that reflect a consensus on the methodology and clinical applications of myocardial deformation imaging.[20,21,36] Together, these statements point to the potential value of deformation imaging in the recognition of sub-clinical diseases such as cardiotoxicity from chemotherapeutic agents, serial monitoring of cardiomyopathy, and pulmonary artery hypertension as well as in the assessment of myocardial ischaemia and viability. They conclude that global longitudinal strain measured by two-dimensional speckle tracking echocardiography is reproducible and provides incremental prognostic data over left ventricular ejection fraction, although the variability of measurements among vendors and among different versions of software makes it difficult to recommend normal values or lower limits of normal range. In a recent meta-analysis of over 1500 adults who had received cardiotoxic chemotherapy, Thavendiranathan et al[37] found that a decline in left ventricular global longitudinal strain precedes a decrease in left ventricular ejection fraction. Similar findings have been reported in children with Duchenne's muscular dystrophy,[38] Friedrich's ataxia,[39] and after cardiotoxic chemotherapy for childhood cancer.[40,41] It is unknown, however, whether using strain as a primary marker of cardiotoxicity to initiate cardioprotective therapy is superior to an approach that is based on ejection fraction, or whether a sub-clinical decrease in ejection fraction predicts subsequent heart failure.

Measurements of strain have been found to be predictive of outcomes in adults with hypertrophic cardiomyopathy: left ventricular global longitudinal strain below 15% has been shown to independently predict adverse cardiac events, adding incremental value to the stratification of risk that is possible with the use of traditional variables.[42,43] Studies on adults with heart failure suggest that left ventricular global longitudinal strain and circumferential strain add to the ability of a model that uses ejection fraction and tissue Doppler measurements to predict re-hospitalisation or death.[44] In adults with pulmonary hypertension, right ventricular longitudinal strain has been shown to add incremental value to a model that predicts mortality.[45] Such data are lacking in children. Guidelines do not exist at present for the use of the imaging of myocardial deformation (strain) in children.

Other measurements

The list of additional echocardiographic measurements that can be performed on children with ventricular dysfunction is long and can be overwhelming for the sonographer and echocardiographer, to say nothing of providing a potentially vast amount of numeric information for the clinician. Some such measurements, such as the ratio of the peak transmitral inflow Doppler velocity to the peak mitral annular velocity in early diastole – E:E' ratio – and the index of myocardial performance – Tei index – are in wide clinical usage. Others, such as the slope of propagation of transmitral inflow as measured by colour M-mode, and the slope of isovolumic acceleration of the myocardium at the level of the annulus of the mitral or tricuspid valve, or at the septum, are not. To date, there are neither practice guidelines nor high levels of evidence that would make a strong case for performance of these measurements in either children or adults. On the contrary, all the measurements that are listed in this paragraph have, in fact, been evaluated critically[2,4] and have been found to have poor reproducibility and/or a lack of ability to predict outcomes. Similarly, the echocardiographic assessment of mechanical ventricular dyssynchrony is a controversial topic that lacks guidelines or high levels of evidence that might help build a case for its routine use.

The future

New echocardiographic modalities and technologies have great potential for clinical applications in children. Maturity of hardware and software platforms, coupled with operability across vendors, would be an important foundation to establish the reproducibility and normal paediatric values of the various new parameters. It is likely that the automation of measurements would help improve their reproducibility. Finally, large prospective studies with follow-up over the long term – with analysis of echocardiograms in core facilities – would be needed to establish the clinical significance, prognostic, and incremental value of these modalities in the evaluation and management of heart failure in children.

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Conflicts of Interest

There are no relevant conflicts of interest.

Ethical Standards

The authors assert that all procedures contributing to this study comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

References

1. Parthiban A, Shirali G. Echocardiographic evaluation of the failing heart. Cardiol Young 2015; (prior submission).
2. Colan SD, Shirali G, Margossian R, et al. The ventricular volume variability study of the Pediatric Heart Network: study design and impact of beat averaging and variable type on the reproducibility of echocardiographic measurements in children with chronic dilated cardiomyopathy. J Am Soc Echocardiogr 2012; 25: 842–854; e6.
3. Lee CK, Margossian R, Sleeper LA, et al. Variability of M-mode versus two-dimensional echocardiography measurements in children with dilated cardiomyopathy. Pediatr Cardiol 2014; 35: 658–667.
4. Molina KM, Shrader P, Colan SD, et al. Predictors of disease progression in pediatric dilated cardiomyopathy. Circ Heart Fail 2013; 6: 1214–1222.
5. Margossian R, Chen S, Sleeper LA, et al. The reproducibility and absolute values of echocardiographic measurements of left ventricular size and function in children are algorithm dependent. J Am Soc Echocardiogr 2015; 28: 549–558.
6. Pellikka PA, Douglas PS, Miller JG, et al. American Society of Echocardiography Cardiovascular Technology and Research Summit: a roadmap for 2020. J Am Soc Echocardiogr 2013; 26: 325–338.
7. Nanda NC, Kisslo J, Lang R, et al. Examination protocol for three-dimensional echocardiography. Echocardiography 2004; 21: 763–768.
8. Corsi C, Lang RM, Veronesi F, et al. Volumetric quantification of global and regional left ventricular function from real-time three-dimensional echocardiographic images. Circulation 2005; 112: 1161–1170.
9. Gururaja TR, Panda RK, Chen J, Beck H. Single crystal transducers for medical imaging applications. Proc IEEE Ultrason Symp 1999; 2: 969–972.
10. Sugeng L, Weinert L, Thiele K, et al. Real-time three-dimensional echocardiography using a novel matrix array transducer. Echocardiography 2003; 20: 623–635.
11. Acar P, Abadir S, Paranon S, et al. Live 3D echocardiography with the pediatric matrix probe. Echocardiography 2007; 24: 750–755.
12. Shimada YJ, Shiota T. A meta-analysis and investigation for the source of bias of left ventricular volumes and function by three-dimensional echocardiography in comparison with magnetic resonance imaging. Am J Cardiol 2011; 107: 126–138.
13. Friedberg MK, Su X, Tworetzky W, et al. Validation of 3D echocardiographic assessment of left ventricular volumes, mass, and ejection fraction in neonates and infants with congenital heart disease: a comparison study with cardiac MRI. Circ Cardiovasc Imaging 2010; 3: 735–742.
14. Bu L, Munns S, Zhang H, et al. Rapid full volume data acquisition by real-time 3-dimensional echocardiography for assessment of left ventricular indexes in children: a validation study compared with magnetic resonance imaging. J Am Soc Echocardiogr 2005; 18: 299–305.
15. Riehle TJ, Mahle WT, Parks WJ, et al. Real-time three-dimensional echocardiographic acquisition and quantification of left ventricular indices in children and young adults with congenital heart disease: comparison with magnetic resonance imaging. J Am Soc Echocardiogr 2008; 21: 78–83.
16. Dorosz JL, Lezotte DC, Weitzenkamp DA, et al. Performance of 3-dimensional echocardiography in measuring left ventricular volumes and ejection fraction: a systematic review and meta-analysis. J Am Coll Cardiol 2012; 59: 1799–1808.
17. Thavendiranathan P, Grant AD, Negishi T, et al. Reproducibility of echocardiographic techniques for sequential assessment of left ventricular ejection fraction and volumes: application to patients undergoing cancer chemotherapy. J Am Coll Cardiol 2013; 61: 77–84.
18. Baker G, Flack E, Hlavacek A, et al. Variability and resource utilization of bedside three-dimensional echocardiographic quantitative measurements of left ventricular volume in congenital heart disease. Congenit Heart Dis 2006; 1: 309–314.
19. Lang RM, Badano LP, Tsang W, et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. J Am Soc Echocardiogr 2012; 25: 3–46.
20. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an

update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015; 28: 1–39.

21. Plana JC, Galderisi M, Barac A, et al. Expert consensus for multimodality imaging evaluation of adult patients during and after cancer therapy: a report from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2014; 27: 911–939.
22. Jenkins C, Chan J, Bricknell K, et al. Reproducibility of right ventricular volumes and ejection fraction using real-time three-dimensional echocardiography: comparison with cardiac MRI. Chest 2007; 131: 1844–1851.
23. Leibundgut G, Rohner A, Grize L, et al. Dynamic assessment of right ventricular volumes and function by real-time three-dimensional echocardiography: a comparison study with magnetic resonance imaging in 100 adult patients. J Am Soc Echocardiogr 2010; 23: 116–126.
24. Tamborini G, Marsan NA, Gripari P, et al. Reference values for right ventricular volumes and ejection fraction with real-time three-dimensional echocardiography: evaluation in a large series of normal subjects. J Am Soc Echocardiogr 2010; 23: 109–115.
25. Khoo NS, Young A, Occleshaw C, et al. Assessments of right ventricular volume and function using three-dimensional echocardiography in older children and adults with congenital heart disease: comparison with cardiac magnetic resonance imaging. J Am Soc Echocardiogr 2009; 22: 1279–1288.
26. van der Zwaan HB, Helbing WA, McGhie JS, et al. Clinical value of real-time three-dimensional echocardiography for right ventricular quantification in congenital heart disease: validation with cardiac magnetic resonance imaging. J Am Soc Echocardiogr 2010; 23: 134–140.
27. Grewal J, Majdalany D, Syed I, et al. Three-dimensional echocardiographic assessment of right ventricular volume and function in adult patients with congenital heart disease: comparison with magnetic resonance imaging. J Am Soc Echocardiogr 2010; 23: 127–133.
28. Dragulescu A, Grosse-Wortmann L, Fackoury C, et al. Echocardiographic assessment of right ventricular volumes: a comparison of different techniques in children after surgical repair of tetralogy of Fallot. Eur Heart J Cardiovasc Imaging 2012; 13: 596–604.
29. Kutty S, Graney BA, Khoo NS, et al. Serial assessment of right ventricular volume and function in surgically palliated hypoplastic left heart syndrome using real-time transthoracic three-dimensional echocardiography. J Am Soc Echocardiogr 2012; 25: 682–689.
30. Bell A, Rawlins D, Bellsham-Revell H, et al. Assessment of right ventricular volumes in hypoplastic left heart syndrome by real-time three-dimensional echocardiography: comparison with cardiac magnetic resonance imaging. Eur Heart J Cardiovasc Imaging 2014; 15: 257–266.
31. Soriano BD, Hoch M, Ithuralde A, et al. Matrix-array 3-dimensional echocardiographic assessment of volumes, mass, and ejection fraction in young pediatric patients with a functional single ventricle: a comparison study with cardiac magnetic resonance. Circulation 2008; 117: 1842–1848.
32. Thavendiranathan P, Phelan D, Collier P, et al. Quantitative assessment of mitral regurgitation: how best to do it. JACC Cardiovasc Imaging 2012; 5: 1161–1175.
33. Forsha D, Risum N, Rajagopal S, et al. The influence of angle of insonation and target depth on speckle-tracking strain. J Am Soc Echocardiogr 2015; 28: 580–586.
34. Geyer H, Caracciolo G, Abe H, et al. Assessment of myocardial mechanics using speckle tracking echocardiography: fundamentals and clinical applications. J Am Soc Echocardiogr 2010; 23: 351–369.
35. Gayat E, Ahmad H, Weinert L, et al. Reproducibility and inter-vendor variability of left ventricular deformation measurements by three-dimensional speckle-tracking echocardiography. J Am Soc Echocardiogr 2011; 24: 878–885.
36. Mor-Avi V, Lang RM, Badano LP, et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. J Am Soc Echocardiogr 2011; 24: 277–313.
37. Thavendiranathan P, Poulin F, Lim KD, et al. Use of myocardial strain imaging by echocardiography for the early detection of cardiotoxicity in patients during and after cancer chemotherapy: a systematic review. J Am Coll Cardiol 2014; 63: 2751–2768.
38. Mertens L, Ganame J, Claus P, et al. Early regional myocardial dysfunction in young patients with Duchenne muscular dystrophy. J Am Soc Echocardiogr 2008; 21: 1049–1054.
39. Dedobbeleer C, Rai M, Donal E, et al. Normal left ventricular ejection fraction and mass but subclinical myocardial dysfunction in patients with Friedreich's ataxia. Eur Heart J Cardiovasc Imaging 2012; 13: 346–352.
40. Poterucha JT, Kutty S, Lindquist RK, et al. Changes in left ventricular longitudinal strain with anthracycline chemotherapy in adolescents precede subsequent decreased left ventricular ejection fraction. J Am Soc Echocardiogr 2012; 25: 733–740.
41. Cheung YF, Hong WJ, Chan GC, et al. Left ventricular myocardial deformation and mechanical dyssynchrony in children with normal ventricular shortening fraction after anthracycline therapy. Heart 2010; 96: 1137–1141.
42. Reant P, Reynaud A, Pillois X, et al. Comparison of resting and exercise echocardiographic parameters as indicators of outcomes in hypertrophic cardiomyopathy. J Am Soc Echocardiogr 2015; 28: 194–203.
43. Hartlage GR, Kim JH, Strickland PT, et al. The prognostic value of standardized reference values for speckle-tracking global longitudinal strain in hypertrophic cardiomyopathy. Int J Cardiovasc Imaging 2015; 31: 557–565.
44. Cho GY, Marwick TH, Kim HS, et al. Global 2-dimensional strain as a new prognosticator in patients with heart failure. J Am Coll Cardiol 2009; 54: 618–624.
45. Fine NM, Chen L, Bastiansen PM, et al. Outcome prediction by quantitative right ventricular function assessment in 575 subjects evaluated for pulmonary hypertension. Circ Cardiovasc Imaging 2013; 6: 711–721.