

Mini Review

The Role of Advanced Imaging in Paediatric Cardiology: Basic Principles and Indications

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Abstract

Tissue Doppler Imaging and Speckle Tracking Echocardiography are newer echocardiographic modalities, that assess myocardial and valvular function in congenital and acquired heart diseases in childhood. In addition, cross-sectional imaging including Cardiac Magnetic Resonance (CMR) and Cardiac Computed Tomography has been widely used over the last decade in paediatric cardiology, in order to evaluate intra-cardiac and extra-cardiac anatomy. Cardiac Magnetic Resonance particularly allows detailed analysis of myocardial function, and shunt quantification and has applications even in fetal life. This mini-review summarizes the basic principles of the above-advanced modalities and highlights their main indications and clinical applications in childhood.

Introduction

Advanced echocardiographic techniques such as Tissue Doppler Imaging (TDI), Speckle Tracking Echocardiography (STE), including strain and strain rate imaging, and live 3-Dimensional (3D) echocardiography provide new perspectives in paediatric cardiology. These newer modalities may be a helpful clinical tool, in addition to a conventional echocardiogram, in order to assess myocardial and valvular function both in congenital and acquired heart diseases [1].

Moreover, Cardiac Magnetic Resonance imaging (CMR) and Cardiac Computed Tomography (CT) are essential tools in clinical practice and have replaced invasive cardiac procedures in many diseases [2]. In addition, fetal CMR could become an additional diagnostic tool that complements fetal echocardiography, whilst hybrid procedures, which are CMR-guided procedures in the cardiac catheterization laboratory, have been implemented in experienced centers [3].

The interpretation of the above techniques in children differs in many ways compared to adults. This mini-review summarizes the basic principles of advanced imaging in paediatric cardiology, highlighting the main indications and clinical use in childhood.

More Information

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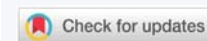
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Keywords: Tissue doppler imaging; Speckle tracking; Echocardiography; Children



Search strategy - methods

We performed a comprehensive search through Medline, Pubmed, and Google Scholar, using the following keywords in combination: Advanced imaging, pediatric, cardiac imaging, children, congenital heart disease, and acquired heart disease. Inclusion criteria were international reviews and studies written in the English language with specific emphasis on studies with tissue Doppler imaging, speckle tracking imaging, computed tomography, and magnetic resonance in children and adolescents. Exclusion criteria were studies that included only adult patients, inaccessible abstracts, and data from conference proceedings. All the collected articles were studied thoroughly and approved by the author team to be included in the review.

A. Tissue doppler imaging echocardiography - basic principles



Tissue Doppler Imaging is a specific form of echocardiography that measures the velocity of myocardial motion throughout the cardiac cycle, evaluating in this way both systolic and diastolic cardiac function. TDI has become an additional diagnostic tool to conventional Doppler for the assessment of both right and left-sided systolic and diastolic dysfunction [4]. Spectral tissue velocity curves from the atrioventricular valve annulus from the four-chamber view at the septal and lateral points are measured. TDI can be performed in Pulsed-Wave (PW) and Color (C) modes [4]. More specifically, Pulsed wave spectral tissue Doppler measures three annular velocities during a cardiac cycle: A positive peak velocity in Systole (S'), that reflects the systolic function and two negative peaks in diastole, (e' in early diastole and a' in late diastole) associated with atrial contraction, that estimate diastolic function [5]. Myocardial Performance Index (MPI), also known as Tei index, is a new Doppler index of combined systolic and diastolic function, that is defined as the sum of Isovolumic Contraction Time (ICT) and Isovolumic Relaxation Time (IRT), divided by Ejection Time (ET). The sum of ICT and IRT refers to the interval between cessation and onset of mitral inflow, while ET refers to the duration of the left ventricular outflow velocity time [6]. In summary, TDI assesses both global and regional myocardial function and is irrelevant to septal wall motion [6].

Clinical use in paediatric cardiology: There are studies in children with acquired or congenital heart disease investigating the clinical applications of TDI [7-9]. Data regarding children with aortic valve stenosis, show decreased TDI velocities in severe aortic stenosis, reflecting the negative impact of increased afterload on myocardial velocities. TDI in children with aortic stenosis is a reliable, non-invasive marker of filling pressures, therefore fall in TDI velocities reflects the severity. Contrastingly, in children with ventricular septal defects, there is minimal impact on TDI velocities from the increased ventricular preload [7]. On the other hand, in children with Atrial Septal Defect (ASD) following device closure, there is a significant decrease in right-sided TDI velocities, compared with pre-catheter velocities, reflecting an immediate improvement of right ventricular function after interventional ASD closure [8]. Similarly, in children with tetralogy of Fallot, TDI velocities decrease after surgical repair, and seems that they correlate with the degree of pulmonary regurgitation [9].

Age, sex, heart rate, myocardial mass, and in general cardiac growth influence TDI velocities in childhood [10]. Thus, further studies are needed to determine normal reference values in healthy children [4,11]. In general, subclinical myocardial dysfunction, due to the non-specific changes of the myocardium, starts from the subendocardium. Thus, TDI which evaluates longitudinal ventricular function, has been shown to be the most effective tool for assessing early dysfunction [10].

Therefore, the use of TDI velocities over the last decades

has been expanded in children with cardiomyopathies, both hypertrophic and dilated cardiomyopathy, highlighting the ratio of transmitral E velocity to septal E_a velocity ($E: E_a$) as a significant predictor of clinical outcome [12,13]. Moreover, TDI has been studied in children post-cardiac transplant, showing a positive correlation between lower velocities and graft rejection [14]. In children who received anthracyclines as chemotherapy, TDI was useful in detecting early subclinical myocardial dysfunction [15].

Finally, TDI velocities have been studied even in neonates, not only in healthy ones, in order to assess normal values, but also in critically ill (such as neonates with sepsis or congenital diaphragmatic hernia), in order to detect early myocardial abnormalities [16]. There are also limited studies showing that preterm infants have lower TDI velocities, which gradually increase during the neonatal period [17].

B. Speckle tracking echocardiography – basic principles

STE is another advanced echocardiographic technique that analyses the motion of cardiac tissues, by using random speckle patterns. Each region of the myocardium has a unique speckle pattern. By tracking the displacement of the speckles during the cardiac cycle, strain, and strain rate can be measured offline after adequate image acquisition. Strain is a measure of myocardial tissue deformation during systole and is expressed as a percentage. Strain analysis using STE could detect subclinical left ventricular dysfunction [18]. This technique is independent of angle, in comparison to tissue Doppler, as it doesn't use a Doppler signal [19].

Another measure of Left Ventricular (LV) systolic function is a Global Longitudinal Strain (GLS), which has superior prognostic value compared to left ventricular ejection fraction (LVEF), as it tends to be affected earlier than LVEF [18]. GLS requires reference values in children, in order to be widely used in all ages [20]. According to Levy et al, the normal mean LV global longitudinal strain in healthy children is -20.2% [20] On the other hand, Harrington, et al. found that reference values differed significantly with age and body surface, so z-scores should be used instead [21].

Clinical use in paediatric cardiology: To date, limited studies have been published in the literature regarding clinical applications of GLS in childhood. Myocardial strain imaging by speckle-tracking echocardiography has been applied in children with Duchenne Muscular Dystrophy (DMD) [22] and in children who received anthracyclines as a part of chemotherapy [23]. Indeed, in DMD, the presence of abnormal LV strain despite normal LVEF is an early marker of cardiomyopathy. In addition, it can be considered an important objective marker for prophylactic medical management initiation, in order to prevent the progression of cardiomyopathy [22].

Sporadic studies in children with non-alcoholic fatty liver



disease, [24] systemic lupus erythematosus, [25] renal failure [26] and cystic fibrosis [27] show that the GLS is an early marker of LV subclinical dysfunction, whilst conventional echocardiography measurements remain unremarkable.

Moreover, similar research, based on STE, has been done in children with different types of congenital heart disease, reflecting the value of GLS in the quantification of ventricular function in different complex cardiac morphologies [28]. The Assessment of ventricular function by strain has been evaluated in children with coarctation of the aorta and revealed that strain parameters did not differ significantly compared to healthy children. On the contrary, the strain parameters differed significantly in children with coexisting hypertension, compared to healthy ones [29].

Moreover, in children with repaired Tetralogy of Fallot, right ventricular strain analysis may provide a more comprehensive approach to Right Ventricular (RV) functional assessment, particularly as there are comparatively limited parameters for RV assessment [30].

STE studies, using strain measurements, have also been performed in neonates, mainly for the assessment of right ventricular function [31]. However, studies are sporadic, so these techniques are currently not included in routine clinical practice.

Finally, in post-cardiac transplant children, GLS is considered an early marker of myocardial dysfunction, even when conventional parameters are within normal limits [32].

C. Three-dimensional techniques - basic principles and clinical applications

3D echocardiography is based on three-dimensional views of the heart, using greater depth in comparison to 2-D. This results in the reconstruction of cardiac chambers in all dimensions, allowing more accurate visualization of the morphology of congenital heart defects. Basic principles of 3D reconstruction use the same principles applied to adults, with the only difference being the limitation of available smaller aperture high-frequency probes for smaller children and babies. Indeed, the European Association of Cardiovascular Imaging and the American Society of Echocardiography have published guidelines for the use of 3D echocardiography in the management of patients with congenital heart disease [33].

3D echocardiography in children not only allows detailed functional assessment of the heart but also offers better visualization and understanding of the spatial relationships of intracardiac structures, for cardiac surgeons in a variety of congenital heart diseases such as valvular abnormalities, atrioventricular septal defects, double outlet right ventricle and left ventricular outflow obstruction lesions [33,34]. The non-invasive visualization of the heart offered by 3D visualization is increasingly used, in order to provide more detailed information before cardiac surgery [35].

D. Cardiac computed tomography - basic principles

A cardiac computed tomography scan uses many X-rays from multiple angles to reconstruct images of the heart, using a scanner and a computer. Newer technology involves dual-source CT scanners with multi-detectors that allow a quick, detailed, and high-resolution acquisition of data within a single heartbeat, using intravenous contrast (to differentiate tissue from blood). However, the child's exposure to ionizing radiation remains a disadvantage to the technique. Previous CT technology used high doses of radiation, even up to 18 millisieverts (Msv), which was twice the dose used in a standard cardiac catheterization. However, newer-generation CT scanners provide excellent image quality at a much lower radiation dose. The ability to acquire data within a single heartbeat has transformed the ability of CT neonates and small children, as they can be scanned without the need for anesthesia and sometimes even without sedation [36,37].

Clinical use of CT in paediatric cardiology: The main clinical use of cardiac CT is to evaluate extra-cardiac anatomy and arterial/venous connections in congenital heart defects and to assess coronary arteries [37,38]. The rapid acquisition makes CT an effective tool in critically ill neonates or children for delineation of the anatomy. In addition, it contributes, along with the echocardiogram, to decision-making organization and management, allowing cardiac surgery to be better planned [37]. Moreover, in children with contraindications for CMR, cardiac CT can be performed particularly allowing the visualization of the cardiac and extra-cardiac anatomy [38]. When analyzing 3D modalities, 3D reconstruction with CT has an added benefit, particularly for complex aortic arch abnormalities, arthropathies, or even vascular rings. Moreover, in Tetralogy of Fallot, or pulmonary atresia with an intact ventricular septum and major aortopulmonary collaterals, cardiac CT allows a more detailed assessment of the anatomy of very small vessels including, pulmonary veins, distal pulmonary artery branches, and aortopulmonary collaterals [37,39]. Finally, cardiac CT is also the preferred modality for serial evaluation of patients with stents in vessels and surgical shunts, allowing the assessment of stent position, morphology, and patency [39].

E. Cardiac magnetic resonance imaging - basic principles

Cardiac Magnetic Resonance is an imaging technology that uses MRI techniques along with ECG gating, in order to suspend cardiac motion. The data acquisition has been performed over multiple heartbeats and the whole procedure may last for 60 minutes - 90 minutes in total. The length of scanning and the need for multiple hold breaths limits the use in young children, as general anesthesia is required [37]. In clinical practice, in the first decade of life, there is usually no need to do CMR, as the echocardiogram provides detailed information. However, the utility of CMR increases in adolescence [40].

Clinical use of CMR in paediatric cardiology: CMR has been used in paediatric cardiology as a non-invasive assessment of cardiac function and structure. Cardiac MRI is a dynamic procedure that provides accurate volumetric, functional, and flow analysis. For example, in adolescents with tetralogy of Fallot, CMR is the gold standard imaging modality for accurate quantification of volume and flow assessment, indicating the optimal timing for pulmonary valve replacement [39].

Furthermore, various CMR sequences also allow the assessment of myocardial tissue characteristics such as tissue edema, necrosis, and fibrosis [40]. Several indications for cardiac MRI in children with congenital or acquired heart disease have been published [40]. In summary, CMR in children should be performed in order to define morphology, assess function (including ventricular volumes and blood flow into the vessels), and define myocardial tissue properties, including myocardial perfusion imaging [40].

Finally, CMR should be considered a useful tool for imaging complex congenital heart diseases before surgical repair, guiding catheter intervention, or assisting in the surgical repair of complex cases [41].

In more complex congenital heart diseases, 3D CT and 3D MRI provide a more comprehensive anatomy demonstration. In addition, 3D CT images reproduce in detail the anatomy of the aortic arch, providing an excellent reconstruction of vascular rings. On the other hand, measures of flow could be obtained through 4D flow MRI data [42]. Finally, limited studies [41,43] have shown that 3D-printing models from MRI or CT data could be so useful as to modify the surgical plan.

Table 1 summarises the main advantages and disadvantages of both cardiac CT and cardiac MRI, providing an overview of the clinical use of both modalities.

Advanced imaging in assessing fetal heart

TDI and speckle-tracking echocardiography in fetal cardiology: TDI could be performed as part of fetal echocardiography, using the four-chamber view. However, there are several limitations, due to the very small size of the fetus, the high fetal heart rate, or incorrect Doppler angle due

to fetal positioning [44]. Despite these limitations, studies have shown that TDI could evaluate fetal cardiac function. Additionally, the Tei index has been suggested as a reliable marker for assessing systolic and diastolic cardiac function in fetuses [45].

To date, there is limited data on strain and strain rate measurements in healthy fetuses. Published studies suggest that throughout pregnancy strain values are higher in the fetal LV compared to the RV, while strain rates are similar in both ventricles [46]. In particular, Barker et al, using cardiac strain and strain rate, evaluated normal fetuses and fetuses with heart disease and suggested that global measurements may be a useful tool for estimating fetal cardiac function [47].

In summary, TDI seems more accurate than STE in assessing diastolic myocardial function in fetal life [48].

Fetal cardiac MRI

Imaging the fetal heart with cardiac MRI in early gestation remains a challenge, due to both fetal and maternal motion and increased fetal heart rate. However, advanced techniques could be used in the third trimester, such as 4D volumetric reconstruction [3]. Salehi, et al. noted that fetal CMR added diagnostic information in over 80% of cases where echocardiography was insufficient for diagnosis [49]. Volumetric reconstruction could provide an additional assessment of fetal cardiovascular anatomy, increasing diagnostic accuracy in fetal life. However, there are limited promising studies published so far in fetuses with various congenital heart diseases (such as atrioventricular septal defects, transposition of the great arteries, and left-sided heart disease) [50].

Advancements in the field and further perspectives

Non-invasive cardiac imaging, such as cardiac CT and MRI has significantly improved the diagnosis of congenital and acquired heart diseases. Conventional echocardiography has been an invaluable tool for many years. However, advanced techniques, as described above, could be an additional tool along with catheter angiography and echocardiography, for the assessment of cardiovascular disease in childhood.

In clinical practice, multiple techniques need to be combined, in order to better visualize cardiac anatomy and assess function. The decision between choosing the best technique depends on the clinical indication to be answered and the correct interpretation of data. Expert consensus statements and guidelines, for the clinical indications and management of advanced imaging techniques from infancy should be published, in order to progress further in the field. Higher-resolution MRI and CT scanners, 3D technology, and 4D Flow assessment should be gradually incorporated into clinical practice. Finally, artificial intelligence could potentially improve data collection and interpretation in the near future [51].

Table 1: Cardiac Magnetic Resonance and Cardiac Computed Tomography Overview.

	Cardiac Computed Tomography	Cardiac Magnetic Resonance
Clinical Use	Anatomy Surgical Planning Stents-Calcifications Lung-Bones If MRI is contraindicated	Functional Assessment (Ventricular Function and volumes) The flow of valves and vessels Tissue characterization/scarring Shunts Other vessels
Advantages	High Special Resolution Quick-Available	Dynamic Imaging No radiation Should be without contrast
Disadvantages	Radiation Burden Need for IV Contrast	Lower special Resolution Time-consuming/resource Need for Breath hold Need for General Anaesthesia



Conclusion

There is a variety of new advanced imaging modalities that can be used for assessing heart anatomy in childhood, which should be an increasing part of the routine conventional echocardiogram. However, more studies are needed in the paediatric population, in order to establish normal reference values for both TDI velocities and STE.

Awareness of the newer modalities in advanced imaging is imperative for clinicians dealing with children suffering from congenital or acquired heart diseases, as these new methods allow a more comprehensive assessment of the child, as well as myocardial structure and function.

Highlights

- 1) Indications and clinical use of advanced imaging modalities in children with congenital or acquired heart disease.
- 2) Variety of newer echocardiographic modalities of advanced imaging can be used for assessing heart anatomy and function in childhood.
- 3) Cardiac Magnetic Resonance Imaging and Cardiac Computed Tomography are essential tools in clinical practice to evaluate intra-cardiac and extra-cardiac anatomy.

Author contributions

Concept: Maria Kavga, Kyriaki Papadopoulou-Legbelou, writing: Maria Kavga, Tristan Ramcharan, Revising: Kyriaki Papadopoulou-Legbelou. All authors read and approved the final version of manuscript.

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