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Three Dimensional (3D) Echocardiography as a Tool of Left Ventricular Assessment in Children with Dilated Cardiomyopathy: Comparison to Cardiac MRI

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Abstract

BACKGROUND: Left ventricular (LV) volumes and ejection fraction (EF) is Strong prognostic indicators for DCM. Cardiac MRI (CMRI) is a preferred technique for LV volumes and EF assessment due to high spatial resolution and complete volumetric datasets. Three-dimensional echocardiography is a promising new technique under investigations.

AIM: Evaluate 3D echocardiography as a tool in LV assessment in DCM children about CMRI.

PATIENTS AND METHODS: A group of 20 DCM children (LVdiastolic diameter < 2 Z score, LVEF < 35%) at Children s Hospital, Ain-Shams University (gp1) (mean age 6.6 years) were compared to 20 age and sex-matched children as controls (gp2). Patients were subjected to: clinical examination, conventional echocardiography, automated 3D LV quantification, 3D speckle tracking echocardiography (3D-STE) (VIVID E9 Vingmed, Norway) and CMRI (Philips Achieva Nova, 1.5 Tesla scanner) for LV end systolic volume (LVESV), LVend diastolic volume (LVEDV) that were indexed to body surface area, EF% and wall motion abnormalities assessment.

RESUTS: No statistically significant difference was found between automated 3D LV quantification echocardiography, 3D-STE, and CMRI in ESV/BSA and EDV/BSA assessment (p = 1, 0.99 respectively), between automated LV quantification echocardiography and CMRI in EF% assessment (p = 0.99) and between CMRI and 3D-STE in LV Global hypokinesia detection (P = 0.255). As for segmental hypokinesia CMRI was more sensitive [45% of patients vs. 40%, (P = 0,036), basal septal hypokinesia 85% vs. 75%, (p = 0.045), mid septal hypokinesia 80% vs. 65%, (p = 0.012) and lateral wall hypokinesia 75% vs. 65%, (p = 0.028)].

CONCLUSION: Automated 3D LV quantification echocardiography and 3D-STE are reliable tools in LV volumetric and systolic function assessment about CMRIas a standard method. 3D speckle echocardiography is comparable to CMRI in global wall hypokinesia detection but less sensitive in segmental wall hypokinesia which mandates further studies.

Introduction

Pediatric dilated cardiomyopathy (DCM) is a serious often life-threatening condition. Left ventricular (L V) volumes and LV ejection fraction (EF) provide fundamental measures of function and are Strong prognostic indicators for patients with DCM [1]. In DCM, LV ejection fraction is the strongest predictor of progression to heart failure, while LV volume and mass are independently correlated with mortality and morbidity; therefore accurate quantification of all these parameters is essential for adequate patient's evaluation and also to monitor the progression of disease and response to different therapeutic agents [2]. CMR can be considered the reference technique for the quantification of ventricular volumes and functional parameters and ventricular mass in patients with DCM [3].

Three dimensional (3D) and 3D speckle tracking are promising new techniques that are still under investigations. The aim of the current study was To evaluate 3D echocardiography as a tool of LV assessment in children with DCM about CMR

Patients and Methods

The current cross-sectional study was conducted on 20 children with idiopathic dilated cardiomyopathy (IDCM) (LVdiastolic diameter > 2 Z score, LVEF < 35%) [4], attending the Pediatric Cardiology Clinic, Children's Hospital, Ain-Shams University (10 males and 10 females), and their ages ranged from 1 month to 14 years with a mean age of 6.6 years (gp1) that were compared to 20 age and sex-matched children as controls (gp2). Patients with any known cause of myocardial disease, underlying congenital heart disease, hypertrophic cardiomyopathy or secondary DCM, renal insufficiency (plasma creatinine > 2mg/dl), hepatic, autoimmune disorders or malignancies were excluded from the study. Informed consent was taken from parents/caregivers. The study was approved by the ethical committee. Studied groups were subjected to:

- Thorough history taking: laying stress on symptoms of heart failure, NYHA heart failure classification

- Detailed clinical examination with special emphasis on cardiac examination.

- Echocardiographic imaging.

Initially routine diagnostic imaging was performed and included Motion mode (M mode), two-dimensional echo (2D), Pulsed wave (PW), Continous wave (CW), as well as Colour flow (CF) Doppler studies. The following parameters were assessed by M-mode of left ventricle in short axis parasternal views: Left Ventricular End Systolic Volume (LVESV (ml), Left Ventricular End Diastolic Volume (LVEDV (ml), Ejection Fraction (EF%) Echocardiographic examinations were performed in a standard manner with use of a commercially available cardiac ultrasound unit device model (VIVId E9 ultrasound system, General electric Vingmed, Horten, Norway).

First, six-chamber views, as well as three short-axis views at different levels of the left ventricle from base to apex, were automatically selected from the RT3DE pyramidal dataset in the first time frame of the dataset, i.e. end-diastole. Then the anatomically correct, non-foreshortened apical views were identified by finding the largest long-axis dimensions. In these two planes, LV endocardial boundaries were manually initialised, while including the papillary muscles in the LV cavity. Then, the 3D endocardial surface was automatically reconstructed and tracked in 3D throughout the cardiac cycle. Finally, the endocardial surface was manually adjusted when necessary in the above five planes until the best match was visually verified. For each consecutive time frame, voxel count inside the detected endocardial surface was used to calculate LV volume. End-diastolic volume and ESV were then obtained from the LV volume curves as the maximum and minimum values, respectively**,** as well as detecting values of longitudinal strain and expressed as a percentage of the original length. The patient is considered to have wall motion abnormality if any segment showed longitudinal strain < 11 [5].

Pyramidal RT3DE datasets were analysed using the 3D wall motion tracking software (VIVId E9 ultrasound system (General Electric, Vingmed, Horten, Norway)) by an investigator experienced with STE analysis that was blinded to the results of cMRI measurements.

A Philips Achieva Nova (1.5 teslas) scanner superconducting system with 30 mt/mint gradient with cardiac coil was used in Radiology department (MRI unit) Ain Shams University for assessment of Ejection Fraction (EF%, End Systolic Volume (ESV) End Diastolic Volume (EDV).

The procedures of the MR examination were explained to the patient above 7 years old including breath hold instructions. The patients were briefly interviewed about MR contraindications, whether the patient has a pacemaker or any other implanted devices, or other foreign materials inside the body (in particular cerebral aneurysmal clips). Children below 7 years sedated with chloral hydrate and their parents were informed by precautions.

Patients were studied in the supine position, head first. The patients were offered cotton blankets for warmth. Headphones with the MRI machine were used to reduce repetitive gradient noise and at the same time allow the patients to hear the breath-hold instructions.

The first electrode was placed approximately 1 cm left of the xiphoid. The second and third electrodes (were positioned in such a way that they were aligned at approximately 90 degrees to each other, where the first electrode forms the right angle. The distance between the electrodes should be approximately 15 cm. The fourth electrode was placed below the first electrode. It was used to determine the cardiac frequency as it should be close to the patient's heart rate. The QRS complex was then checked on MRI monitor, adjustment of the site of the leads was made accordingly. The patient's heart rate was also detected on MRI monitor.

The respiratory sensor was placed over the maximum area of respiratory movement (abdomen and thorax) under the coil. A strap was used to fix the sensor. The respiratory signal was then checked as the respiratory wave appeared on the monitor and was used to detect the patient's respiratory rhythm and synchronise breath hold instructions to the patient's abilities.

The SENSE (sensitivity encoding) cardiac coil (6 elements phased array coil, receive only) was used. It has a rigid lower part and a flexible upper part. The coil was positioned on the chest so that the midline of its upper part lied just below the sternoclavicular notch and the lower part of the coil

lied underneath the patient. It was carefully strapped onto the patient. The connection to the magnet was checked.

Planning vertical long axis image from the axial orthogonal image at the level of the left ventricle, planning the horizontal long axis view from the vertical long axis view. Planning the short axis view from the horizontal long axis view. Breath-hold balanced turbo field echo sequence (b-TFE) in short axis view from the mitral annulus to the apex with the following parameters: TR (repetition time)/TE (echo time): 4.4/2.5, FOV (Field of view): 300, Phases: 25, NSA (Number of signal averages): 1, Flip angle: 15, Scan time: 7-12 sec, Slice thickness: 8 mm, Number of slices: 7.

Analysis of the CMR (DICOM) images was performed using Brilliance 170 P workstation. Left ventricular ejection fraction and volumes were quantified automatically from the cine images after manual tracing of LV endocardial border in the short axis images during end systole and end diastole for each slice position.

Results

Sixty-five per cent of studied patients (65%) were males and (35%) were females with males to females 2:1.

Thirty per cent of studied patients (30%) had increased heart rate for age, 55% had low systolic blood pressure for age, and 35% had low diastolic blood pressure for age.

Table 1: Comparison between 3D echocardiography, cMRI and 3D speckle echocardiography regarding ESV (ml) and EDV (ml) values indexed by BSA (m^2) and EF (%) mean values

	3D echocardiography		cMRI		3D speckle		One Way ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F	P-value
ESV (ml)/BSA (m^2)	58.58	23.89	58.65	24.11	58.58	23.88	0.000	1.000 (NS)
EDV (ml)/BSA (m^2)	92.69	27.44	93.41	27.33	92.84	27.29	0.004	0.996 (NS)
EF (%)	40.25	7.65	39.56	9.80	-	-	4.817	0.996 (NS)

One Way ANOVA comparing three groups, P-value > 0.05 is non-significant, SD: Standard deviation, ESV: End Systolic Volume, EDV: End Diastolic Volume, cMRI: cardiac Magnetic Resonant Imaging, BSA: Body Surface Area, NS: Non-Significant.

All patients were on Frusemide and Captopril therapy, 90% of them were on Digoxin and Spironolactone, 35% were on low dose aspirin, and 20% of them were on L-carnitine.

A statiscally significant increase was found in patients ESV/BSA and EDV/BSA and a statistically significant decrease was found in patients EF% assessed by 3D-LV quantification compared to controls (58.58 ± 23.89 vs. 24.16 ± 1.58, p = 0.000; 92.69 ± 27.44 vs. 61,24 ± 1.58, p = 0.001 and 40.25 ± 7.65 vs. 69.4 ± 4.55, p = 0.00 respectively).

Table 2: Comparison between cMRI and 3DSTE as regards cardiac wall motion abnormalities assessment

	CMRI		3D STE		Chi-square test	
	No.	%	No.	%	X^2	P-value
Global hypokinesia	16	80.0%	16	80.0%	2.727	0.255 NS
Apical hypokinesia	9	45.0%	8	40.0%	6.624	0.036 S
Septal wall dyskinesia	3	15.0%	2	10.0%	3.055	0.217 NS
Basal septal hypokinesia	17	85.0%	15	75.0%	6.190	0.045 S
Mid septal hypokinesia	16	80.0%	13	65.0%	8.750	0.012 S
Inferior wall hypokinesia	14	70.0%	12	60.0%	5.253	0.072 NS
Lateral wall hypokinesia	15	75.0%	13	65.0%	7.131	0.028 S
Inferior wall akinesia	2	10.0%	1	5.0%	2.105	0.349 NS

cMRI: Cardiac magnetic resonance imaging, 3DSTE: 3D speckle tracking echocardiography, P value > 0.05 is non-significant, P value < 0.05 is significant, NS: Non Significant, S: Significant.

A statistically significant increase was found in patients ESV/BSA and EDV/BSA assessed by 3D-STE compared to controls (58.58 ± 23.88 vs. 24.16 ± 15.8, p = 0.000 and 92.84 ± 27.29 vs. 61.24 ± 2.84, p = 0.001 respectively).

Also, a stastically significant increase was found in patients ESV/BSA and EDV/BSA and a statistically significant decrease was found in patients EF%assessedbyCMRI compared to controls (58.65 ± 24.11 vs. 26.02 ± 1.77, p = 0.000; 93.41 ± 27.33 vs. 63.03 ± 3.05, p = 0.002 and 39.56 ± 9.8 vs. 67.65 ± 3.07, p = 0.000 respectively).

Table 3: Intraobserver variability of 3DSTE regarding wall motion abnormalities

3DSTE	Observer. I		Observer. II		Chi-square test	
	No.	%	No.	%	X^2	P-value
Global hypokinesia	16	80.0%	13	65.0%	0.864	0.3526 NS
Apical hypokinesia	8	40.0%	6	30.0%	0.110	0.7403 NS
Septal wall dyskinesia	2	10.0%	1	5.0%	0.000	1.0000 NS
Basal septal hypokinesia	15	75.0%	13	65.0%	0.119	0.7301 NS
Mid septal hypokinesia	13	65.0%	11	55.0%	0.114	0.7469 NS
Inferior wall hypokinesia	12	60.0%	10	50.0%	0.101	0.7506 NS
Lateral wall hypokinesia	13	65.0%	11	55.0%	0.104	0.7469 NS
Inferior wall akinesia	1	5.0%	1	5.0%	0.545	0.4602 NS

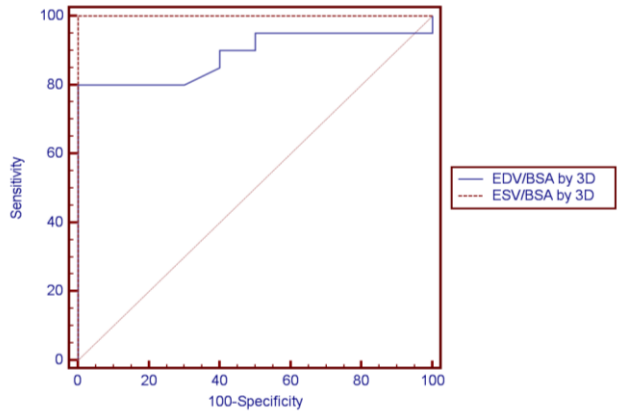
3DSTE: 3D speckle track echocardiography, P value > 0.05 is non significant, NS: Non Significant, Observ: Observation.

No statistically significant difference was found between automated 3D LV quantification echocardiography, 3D-speckle echocardiography, and cMRI in assessment of ESV/BSA (58.58 ± 23.89 ml/m^2), (58.58 ± 23.88 ml/m^2), (58.65 ± 24.11ml/m^2) respectively and EDV/BSA (92.69 ± 27.44 ml/m^2), (92.84 ± 27.29 ml/m^2), (93.41 ± 27.33 ml/m^2) respectively No statistically significant difference was found between automated LV quantification echocardiography and CMRI in EF% values (40.25 ± 7.65 vs. 39.56 ± 9.8, p = 0.99). All studied patients had global and segmental hypokinesia as assessed by 3D-STE and CMRI.

Table 4: Intraobserver variability of cMRI regarding wall motion abnormalities

cMRI	Observer. I		Observer. II		Chi-square test	
	No.	%	No.	%	X^2	P-value
Global hypokinesia	16	80.0%	14	70.0%	0.133	0.715 NS
Apical hypokinesia	9	45.0%	7	35.0%	0.104	0.746 NS
Septal wall dyskinesia	3	15.0%	1	5.0%	0.144	0.0578 NS
Basal septal hypokinesia	17	85.0%	15	75.0%	0.158	0.6926 NS
Mid septal hypokinesia	16	80.0%	13	65.0%	0.502	0.4788 NS
Inferior wall hypokinesia	14	70.0%	12	60.0%	0.110	0.7403 NS
Lateral wall hypokinesia	15	75.0%	13	65.0%	0.119	0.7301 NS
Inferior wall akinesia	2	10.0%	0	0.0%	0.526	0.4682 NS

cMRI: Cardiac magnetic resonance imaging, P-value > 0.05 is non significant, NS: Non Significant, Observer: Observation.

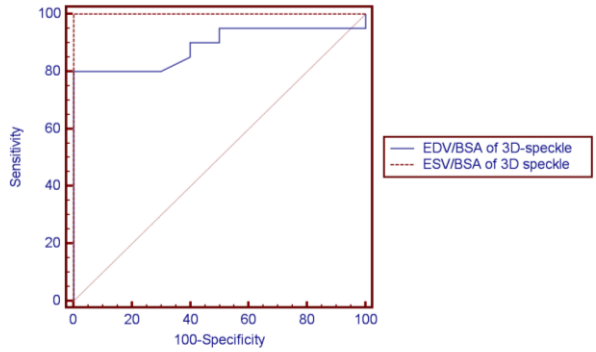


Parameters	Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
EDV(ml)/BSA(m^2) by 3D echocardiography	>65.4 *	88.8	80.00	100.00	100.0	71.4
ESV(ml)/BSA(m^2) by 3D echocardiography	>26.6	100.00	100.00	100.00	100.00	100.0

ESV: End Systolic Volume, EDV: End Diastolic Volume, BSA: Body Surface Area,+ PV: Positive Predictive Value, -PV: Negative Predictive Value, AUC: Area Under the Curve.

Figure 1: ROC curve detect sensitivity and specificity of 3D echocardiography in the prediction of EDV and ESV indexed by BSA

Sensitivity of 3D and 3D-STE echocardiography in prediction of EDV (ml)/BSA (m^2) was 80% and 100% in prediction of ESV (ml) /BSA (m^2) (Figures 1 and 2). Sensitivity and specificity of 3D-echocardiography and cMRI were 100% in the assessment of EF% (Figure 3).



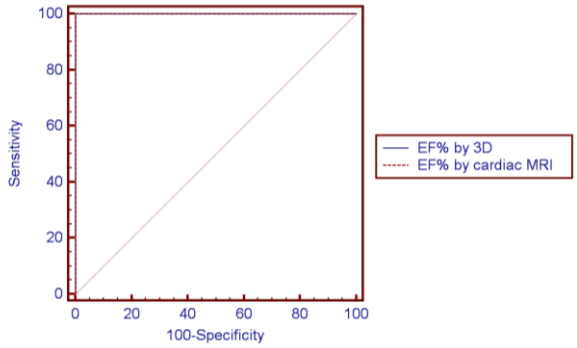
Parameters	Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
EDV(ml)/BSA(m^2) by 3D-STE	> 65.4	88.8	80.0	100.0	100.0	71.4
ESV(ml)/BSA(m^2) by 3D-STE	> 26.6	100.0	100.0	100.0	100.0	100.0

ESV: End Systolic Volume, EDV: End Diastolic Volume, BSA: Body Surface Area, + PV: Positive Predictive Value, -PV: Negative Predictive Value, AUC: Area Under the Curve.

Figure 2: Sensitivity and specificity of 3D-STE in the prediction of EDV (ml) and ESV (ml) indexed by BSA (m^2)

No statistically significant intraobserver variability was found as regards ESV/BSA,EDV/BSA and assessed by 3D LV quantification (58.5 ± 2.3 vs. 58.2 ± 3.5, p = 0.75 and 92.6 ± 3.5 vs. 92.3 ± 3.2, p = 0.71 respectively).

No statistically significant difference was found between CMRI and 3D-Speckle tracking echocardiography in detection of LV Global hypokinesia (P = 0.255). CMRI was found to be a better tool in segmental wall hypokinesia detection than 3D-STE [(apical hypokinesia 45% vs. 40%, (P = 0,036), basal septal hypokinesia 85% vs. 75%, (p = 0.045), mid-septal hypokinesia 80% vs. 65%, (p = 0.012) and lateral wall hypokinesia 75% vs. 65%, (p = 0.028).



Parameters	Cut off point	AUC	Sensitivity	Specificity	PPV	NPV
EF% by 3D	≤49	100.0	100.0	100.0	100.0	100.0
EF by cardiac MRI	≤ 48.5	100.0	100.0	100.0	100.0	100.0

PV: Positive Predictive Value, -PV: Negative Predictive Value, AUC: Area Under the Curve, cMRI Cardiac magnetic resonance imaging.

Figure 3: ROC curve detect sensitivity and specificity of 3D echocardiography and cMRI in the prediction of EF

Also, no statistically significant intraobserver variability was found as regards ESV/BSA, EDV/BSA and EF% assessed by 3D-STE (58.45 ± 3.7, p = 0.923; 92.65 ± 3.4, p = 0.855) and no statistically significant intraobserver variability was found as regards EF% assessment by 3D LVquantification (40.25 ± 8.75 vs. 40.5 ± 7.95, p = 0.908) and by CMRI (39.56 ± 15 vs. 39.34 ± 15.8, p = 0.992).

Also, no statistically significant intraobserver variability was found as LV segmental wall motion abnormalities by 3D-STE and CMRI.

Discussion

The current study aimed to compare 3-D echocardiography versus cMRI in the assessment of left ventricular functions of children with dilated cardiomyopathy.

Thirty per cent of studied patients (30%) had increased heart rate for age, 55% had low systolic blood pressure for age, and 35% of them had low diastolic blood pressure for age which came in accordance with Marx et al., 2013 and can be attributed to decreased cardiac output and medications received [6]. All studied patients were on Frusemide, and Captopril therapy, 90% of them were on Digoxin and Spironolactone, 35% were on low dose aspirin, and 20% of them were on L-carnitine

which agreed with Daubeney et al., (2006) who reported that long-term medical therapy for congestive heart failure is the main treatment strategy in patients with DCM and include diuretics, digoxin, afterload reducing agents (usually ACEI), an aldosterone antagonist and beta-blockers, they also added that congestive heart failure is severe among children with DCM and although early mortality is high, the clinical status of long-term survivors is good with adequate management [7].

In the current study, no statistically significant difference was found between 3D-echocardiography and cMRI as regards EF% assessment (40.25 ± 25 vs 39.56 ± 9.80%, p = 0.996). This agreed with Jenkins et al., (2004) and (Hoffmann et al., 2006) and disagreed with Feng Wang et al., (2009) who reported an overestimation of LVEF by 3D-echocardiography compared to CMRI (30 ± 7%:19 ± 8%), and explained this overestimation by the delay of cardiac MRI gating so that the first frame was not always end-diastolic, and therefore EDVs of Cardiac MRI was sometimes underestimated [8], [9], [10]. Also, by the assumption that, in hypocontractile and enlarged ventricles, the difference in temporal resolution between 3D-echocardiography and cardiac MRI becomes less relevant than in contractile ventricles with a good LVEF or hypertrophy of the myocardial wall.

No statistically significant difference was found between 3D-echocardiography, 3D-speckle echocardiography, and cMRI as regards ESV/BSA [(58.58 ± 23.89 ml/m^2), (58.58 ± 23.88 ml/m^2), (58.65 ± 24.11 ml/m^2) respectively (P = 1)] and EDV/BSA[(92.69 ± 27.44 ml/m^2), (92.84 ± 27.29 ml/m^2), (93.41 ± 27.33 ml/m^2) respectively (P = 0.996)] which came in accordance with Gutierrez-Chico et al., (2005) and Hans-Joachim Nesser et al., (2009)and disagreed with Hakan Demir et al., (2007) who reported that the values of EDV and ESV were under estimated by cMRI (EDV 91.1 ± 38.0 ml, ESV 41.8 ± 26.9 ml) compared to ECHO (EDV 127.5 ± 42.2 ml, ESV 59.9 ± 37.6 ml) and attributed this difference in their study to exclusion of basal portions of left ventricle and high spatial resolution of (CMRI) [11], [12], [13]. Hakan Demir et al., (2007) exclusion of major vascular structures and valves from ventricular volume slices of CMRI were minimally repositioned to the midventricular region at the base of the heart. So, inclusion or exclusion of the most basal slice, which consists of parts of LV myocardium, outflow tract, and left atrium, could be the main reason for the difference between previous studies and the present study [13]. Also, Feng Wang et al., (2009) and Faber et al., (2001), reported underestimation of EDV and ESV measured by cMRI and explained that, trabeculation and papillary muscles are clearly visualized on cardiac MRI images, so they are usually excluded from the volume on analysis of cardiac MRI images and that cMRI allows inclusion of outflow tract tissue, which is not a part of LV volume acquisition [10], [14]. On the other hand, Sugeng et al., (2006) and Jenkins et al., (2007) reported that real-time 3D echocardiography underestimated MRI-derived end-diastolic LV volume (mean 168 ml) by 15 ml while 2D echocardiography underestimated MRI derived end-diastolic LV volume by 57 ml [8], [15].

No statistically significant difference was found regarding Global LV hypokinesia (P = 0.255), septal wall dyskinesia (P = 0.217), inferior wall hypokinesia (P = 0.072) and inferior wall akinesia (P = 0.349) measured by cMRI and 3D-STE. Hans-Joachim Nesser et al., (2009) [12] reported that the new 3D-STE technology is likely to become the method of choice for the assessment of regional LV function, replacing TDI. However, for this to happen, 3D-STE needs to be validated against an established reference technique. But because there is no non-invasive ‘gold standard’ technique that can be used in human subjects to validate regional ventricular function in three dimensions, it is essential to test the accuracy of 3D-STE using a global index, such as LV volume, against the current standard CMR reference. This is the first study designed to address this need.

In conclusion, automated 3D LV quantification echocardiography and 3D-STE are reliable tools in LV volumetric and systolic function assessment about CMRIas a standard method. 3D speckle echocardiography is comparable to CMRI in global wall hypokinesia detection but less sensitive in segmental wall hypokinesia assessment which mandates further studies.

More objective techniques are needed for assessment of segmental wall hypokinesia. More studies are needed on a larger number of patients to validate normal values of 3D speckle in children.

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