Quantification of Left Ventricular Mass Using Two-Dimensional Transthoracic Echocardiography - A Novel Method with High Accuracy and Reproducibility

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Abstract

Purpose

Increased left ventricular mass (LVM) is a strong independent predictor for adverse cardiovascular events, but conventional echocardiographic methods used to assess and monitor individuals are limited by poor reproducibility and accuracy. We aimed to develop an echocardiographic method for LVM-quantification that is simple, reproducible and accurate.

Methods

The novel method adds the mean wall thickness to the left ventricular end-diastolic volume acquired using the biplane model of discs. The mean wall thickness is acquired from the parasternal short axis view. Cardiac assessment was performed using echocardiography followed immediately by cardiac magnetic resonance in 85 subjects with different left ventricular geometries, ranging from patients with various cardiac disorders (n=41) to individuals without known cardiac disorders (n=44). We compared the novel two-dimensional (2D) method to various conventional one-dimensional (1D) and 2D methods as well as three-dimensional (3D) echocardiography.

Results

The novel method had better reproducibility in intra-examiner (coefficients of variation (CV) 9% vs. 11-14%) and inter-examiner analysis (CV 9% vs. 10-20%) than the other methods. Accuracy of the novel method was similar to 3D (mean difference±95% limits of agreement, CV): Novel: 2±50g,15% vs. 3D: 2±51g, 16%; and better than the 1D-method by Devereux (7±76g, 23%).

Conclusion

The novel 2D-based method for LVM-quantification had better reproducibility than the other echocardiographic methods. Accuracy was similar to 3D and better than conventional methods. As endocardial tracings using the biplane model forms part of the standard echocardiographic protocol, the novel method can easily be integrated into any echocardiographic software, without substantially increasing analysis time.

Introduction

Increased left ventricular mass (LVM) is a strong independent predictor for adverse cardiovascular events[1–3], and associated with impaired left ventricular (LV) myocardial function, coronary artery disease and arrhythmogenesis[4]. Unfavourable associations with increased LVM seem reversible through reduction of LVM[5], but clinical responses to treatment and prognosis using echocardiography

requires reliable LVM-quantification. As conventional methods for LVM-quantification lack reproducibility (precision) they are not suitable for serial comparisons, thereby not routinely deployed on individuals. This warrants a method with greater reproducibility to improve accuracy in detecting actual differences. Standard one-dimensional linear echocardiography (1DE) for LVM-quantification by the cube formula relies on a symmetrical shaped left ventricle (LV). Whilst technically simple, it is prone to inaccuracies[6] and more suitable for comparison on a population level. Conversely, three-dimensional echocardiography (3DE) is independent of LV symmetry and has higher concordance with the reference method cardiac magnetic resonance (CMR)[7, 8]. Since acquisition and analysis using 3DE are challenging and time-consuming, this presents disadvantages in busy echocardiography labs. We explored an alternative method to preserve the geometrical shape of the LV by applying the biplane model of discs by two-dimensional echocardiography (2DE) for LVM-quantification, without the need for troublesome epicardial boundary tracing in the apical views.

Our aims were to:

1) Develop a simpler, feasible and reproducible 2DE-based method for LVM-quantification that is less dependent on LV symmetry

2) Compare various well-known echocardiographic methods for LVM-quantification as well as our novel method to CMR, amongst subjects with assorted LV geometries.

Methods

Study design

This is a single-centre prospective cohort feasibility study. We included patients scheduled for echocardiography >18 years with sinus rhythm on the study days. Pregnant, breastfeeding or claustrophobic patients were excluded. We aimed to include a wide variety of subjects with different LV geometries. All subjects were assessed using echocardiography immediately followed by CMR (baseline); and re-assessed using echocardiography after a median of 6 days (IQR 3-18) (re-examination). To limit effects of hydration status, all subjects were instructed to abstain from oral intake ≥5 hours prior to both visits. The study was conducted in accordance with the second Helsinki declaration and approved by the local ethics committee (H-16029778). All participants provided written informed consent.

Echocardiography - acquisition and analysis

One experienced sonographer performed all examinations using a Vivid E95 ultrasound scanner (GE Healthcare, Norway), and M55c-D-matrix-array transducer (1.5-4.6 MHz) for 2DE and a 4V-D volume-phased array transducer (1.5-4 MHz) for 3DE. Subjects were studied in the left lateral decubitus position with parasternal long-axis view (PLAX), short-axis view (SAX), apical four-chamber view (4CH), apical two-chamber view (2CH), and 3DE. We reduced depth to focus on the LV. Framerate for 2DE was 65±7 frames/second, and for 3DE 26±8 volumes/second. The 3DE full volume dataset was acquired from the

apical window during breath-hold over four to six heart beats. The examinations were analysed using EchoPAC version 201.61 (GE Healthcare, Norway). End-diastole was defined as the first frame of mitral valve closure. We distinguished between end-diastolic-volume (EDV) defined by inner myocardial interface [endocardium (EDV_{ENDO})] and by outer myocardial interface [epicardium (EDV_{EPI})]. Conventional EDV (EDV_{ENDO}) was quantified by 3DE, 2DE (biplane model)[9] and 1DE (Teichholtz)[10]. LVM-quantifications were made at end-diastole. ECG-timing from PLAX was referenced to find the corresponding SAX-frame. All PLAX/SAX-measurements were made at the chordae level (Figure 1). In PLAX the region between the mitral valve and papillary muscle, just beneath the attachment of the chordae to the papillary muscle. In SAX this corresponded to the visible attachments of the chordae to the papillary muscle. In this view, the mitral valve should not be visible, and chordae should be separated from LV wall. We delineated the boundaries in SAX by using the blood-endocardium interface (inner tracing) and by the epicardium-blood/pericardium interface (outer tracing). We didn't use a leading-to-leading edge approach. Trabeculae or papillary muscles were considered part of the LV cavity, the pericardium was excluded from the tracing. 3DE LVM was quantified by the vendor-specific software package 4D Auto LVQ (EchoPAC, GE Healthcare, Norway). The full volume dataset was aligned for three apical views, which were manually adjusted, guided by the derived short-axis views.

The novel method

The novel method of LVM-quantification is based on adding the mean wall thickness (*t*) from a single SAX-recording to the EDV_{ENDO} acquired by the standard biplane model of discs in the apical 4CH- and 2CH-view (Figure 2). The EDV_{ENDO} is the sum of the sub-volumes of 30 unique discs, which are acquired during the conventional biplane tracing in apical views. EDV_{EPI} is the summation of 30 larger sub-volumes quantified by adding *t* to each unique sub-volume from the from the EDV_{ENDO}-tracing. An apical cap is added for EDV_{EPI}. The *t* was calculated from SAX by conversion from traced myocardial area, in the same manner as for the conventional 2DE methods. The difference between the EDV_{EPI} and EDV_{ENDO} was multiplied with the myocardial gravity of 1.05 g/ml. A more detailed description of the novel method is available in the **supplementary data**.

Left ventricular mass quantification using echocardiography

We evaluated six different methods for LVM-quantification (Figure 3)[11–14]. Four of these are widely recognized *(A, D, E, F)* and all except the novel method *(B)* and endo-/epicardial tracing in the 4CH- and 2CH-view by the biplane model of discs (BP) *(C)* and are recommended in current guidelines[6].

Cardiac magnetic resonance – acquisition and analysis

Accuracy of the echocardiographic methods was defined by agreement according to the CMR[15]. CMR images were obtained using a 1.5 Tesla system (GE Optima MR450W, GE Healthcare, Waukesha, WI) with a phased-array cardiac coil. Cine images were acquired during breath-hold using a steady-state free

precession cine sequence with retrospective gating. Slice thickness 8 mm, no gaps, field of view 300-360mm, 25 phases/cycle. Analysis was performed using CVI42 (Circle Cardiovascular Imaging Inc., Version 5.6.5, Canada). End-diastole was defined as for echocardiography. Endocardium and epicardium were manually delineated in the short-axis-stack, papillary muscles were considered part of the LV volume. The subjects were classified in four groups according to age, gender and indexed values[16] of the EDV_{ENDO} and LVM[17]; normal – dilatation – hypertrophy – dilatation and hypertrophy.

Reproducibility

Intra/inter-examiner examination were compared at baseline and day-to-day-variation between baseline and re-examination. All subjects were asked to walk around between baseline examinations and intra/inter-examiner exam. Intra-examiner exams (n=13) were acquired and analysed by the same examiner who performed the baseline and re-examination exams, inter-examiner exams (n=20) were acquired and analysed by another examiner.

Feasibility

Feasibility was estimated for the entire study cohort and for a small 'all-comers' cohort of twenty-six consecutive patients examined by a third sonographer during one week in our echo lab, no patients were excluded. Since 3DE is not routinely performed on all patients at our echo lab, we are unable to report reliable "all-comers" 3DE feasibility.

Classification of hypertrophy versus non-hypertrophy

Hypertrophy was defined by CMR according to age, gender and LVM-index[17]. The normal LVM-ranges for CMR were applied for the echocardiographic 3DE, novel method and BP-method[17]. Current echocardiographic guidelines were applied for normal LVM-ranges for the cube formula by Devereux (DEV), truncated ellipsoid (TE) and area-length (A-L)[6]. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for detection of hypertrophy was evaluated.

Statistics

Continuous variables were expressed as mean and standard deviation (SD) and categorical values expressed as frequencies (percentage). The accuracy of echocardiographic methods was defined according to agreement with CMR; evaluated by the Bland-Altman-method (BA) using paired t-test presented as mean difference (bias) and 95% limits of agreement (LOA)[18], and simple linear regression and Pearson's correlation. Reproducibility was assessed by the 95%LOA and by the coefficient of variation (CV) presented as percentages. P-values <0.05 were considered statistically significant. LVM-quantifications were performed in Windows Excel 2010 (Microsoft Office Professional Plus). Data analysis was performed in SPSS v25.0 (IBM Corp. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY).

Results

Study population

All 85 subjects had echocardiography and CMR at baseline. All were re-invited for re-examination; four subjects cancelled in advance, one subject was sent home because of technical problems, one subject did not show up for re-examination. Baseline characteristics of the population are presented in Table 1. Cardiac condition according to LV geometry in **supplementary data, Table S5**. Baseline EDV_{ENDO} and LVM by various methods in Table 2. We included all data for every methodology, although some subjects did not have feasible images for all methods. Data on the subjects with 100% feasibility (n=59) are specified in **supplementary data Table S7**.

Table 1
Baseline characteristics (n=85)

Age (yrs)	**44±14**
Male gender	57(67%)
Body mass index (kg/m^2)	25.5±4.2
Body surface area (m^2)	2.0±0.2
Systolic blood pressure (mmHg)	127±18
Diastolic blood pressure (mmHg)	76±13
Heart rate (bpm)	57±8
Cardiac disease	41(48%)
HCM	16(19%)
DCM	2(2%)
ARVC	1(1%)
Moderate-severe aortic valve stenosis	6(7%)
Moderate-severe aortic valve regurgitation	6(7%)
IHD	3(4%)
Others	7(8%)
Cardiovascular risk factors	44(52%)
Hypertension	17(20%)
Diabetes	3(4%)
Current/previous smoker	37(44%)
Peripheral artery disease	1(1%)
Stroke/TIA	2(2%)
Physical inactivity	8(9%)

HCM hypertrophic cardiomyopathy, **DCM** dilated cardiomyopathy, **ARVC** arrythmogenic right ventricular cardiomyopathy, **IHD** ischemic heart disease, **TIA** transient ischemic attack

Table 2
End-diastolic volumes and left ventricular mass, baseline (n=85)

	mean±SD
End-diastolic volume (ml)*	
CMR	197±60
3DE	147±51
2DE (BP)	151±50
1DE (Teichholtz)	131±43
Left ventricular mass (g)	
CMR	165±62
3DE	168±56
2DE (NOVEL)	167±62
2DE (BP)	178±66
2DE (TE)	163±60
2DE (A-L)	187±68
1DE (DEV)	172±70

*Delineated by the endocardium, EDV_{ENDO}

CMR cardiac magnetic resonance, **3DE** three-dimensional echocardiography, **2DE** two-dimensional echocardiography, **1DE** one-dimensional echocardiography, **BP** biplane model, **TE** truncated ellipsoid, **A-L** area-length, **DEV** cube formula, Devereux

Feasibility and Reproducibility

We report high feasibility for all methods, except the BP-method (74% vs. 95-100%) **(**Table 3**)**. All-comers' feasibility was lower; DEV 92%, TE/A-L/Novel 81%, BP 50%. We observe similar day-to-day-variations of the 2D/3D-methods (14-18%) and larger day-to-day-variation of the 1DE-method DEV (21%) **(**Table 3**)**. The novel method has better reproducibility in intra- (CV 9% vs. 11-14%) and inter-examiner (CV 9% vs. 10-20%) analysis **(**Table 3**)**.

Table 3
Feasibility and Reproducibility

	Feasibility	Day-to-day-variation		Intra-examiner-variation		Inter-examiner-variation	
	(%)	*Bias±95%LOA*	*CV(%)*	*Bias±95%LOA*	*CV(%)*	*Bias±95%LOA*	*CV(%)*
3DE	98	4±45	*14*	-8±51	*14*	6±54	*17*
NOVEL	95	-4±48	*15*	-1±27	*9*	4±27	*9*
BP	74	-3±63	*18*	-3±47	*14*	9±45	*15*
TE	95	-5±53	*15*	-3±34	*11*	0±30	*10*
A-L	95	-4±47	*15*	-1±40	*11*	2±34	*10*
DEV	100	-1±71	*21*	-21±45*	*13*	14±58	*20*

*p<0.05

Day-to-day-variation (n=79), intra-examiner (n=13) and inter-examiner (n=20) analysis

LOA limits of agreement, **CV** coefficient of variation, **3DE** three-dimensional echocardiography, **BP** biplane model, **TE** truncated ellipsoid, **A-L** area-length, **DEV** cube, Devereux

Agreement of LVM quantification by echocardiography and CMR

Baseline agreements between echocardiography and CMR are visualized in BA-plots and linear regression-plots (Figure 4). The novel method demonstrates equal distribution and limited proportional bias, based on the regression line (Figure 4B). **Table 4** presents the agreements between echocardiography and CMR at baseline. Figure 5 demonstrates the agreement of echocardiography and CMR among the defined LV geometries.

Diagnostic performance on detecting hypertrophy using echocardiography

The sensitivity, specificity, PPV and NPV for all methods and divided by LV geometry are presented in Table 5.

Table 4
Agreement between left ventricular mass by echocardiography and cardiac magnetic resonance, baseline

	Baseline *(n=85)*	
	Bias±95%LOA	*CV(%)*
3DE	2±51	*16*
NOVEL	2±50	*15*
BP	6±59	*17*
TE	-2±54	*17*
A-L	21*±56	*16*
DEV	7±76	*23*

* p<0.05

LOA limits of agreement, **CV** coefficient of variation, **3DE** three-dimensional echocardiography, **BP** biplane model, **TE** truncated ellipsoid, **A-L** area-length, **DEV** cube, Devereux

Table 5 Diagnostic performance on detecting hypertrophy

	Sensitivity (%)	**Specificity (%)**	**PPV (%)**	**NPV (%)**
3DE	71	87	74	86
NOVEL	82	95	88	92
BP	82	73	62	88
TE	52	98	93	80
A-L	85	89	79	92
DEV	36	96	83	75

3DE three-dimensional echocardiography, **BP** biplane model, **TE** truncated ellipsoid, **A-L** area-length, **DEV** cube, Devereux, **PPV** positive predictive value, **NPV** negative predictive value

Discussion

We present feasibility, reproducibility and accuracy of a novel echocardiographic method and various widely recognized echocardiographic methods for LVM-quantification. We found the following,

(1) The novelmethod has high feasibility and better intra/inter-examiner reproducibility than the other methods.

(2) Accuracy of the novel method is similar to 3DE and greater across all four defined LV geometries than 3DE-, 2DE-, and especially 1DE-methods.

(3) The novel method is simple, does not require specific training, and provides a reliable alternative or supplement to LVM-quantification

(4) Since the biplane model is already a standard procedure commonly utilised for echocardiography, this novel method should not cause any considerable delay. The formula can easily be integrated in any echocardiographic analysis software for automatic quantification and has the potential to provide a useful tool in busy echocardiography labs.

Pitfalls of applying linear measurements

It is unsurprising that the cube formula[11] has been the most common method for LVM-quantification since the 1970's, as this method is simple, feasible and useful in large population studies[1–3]. However, its simplicity makes it susceptible to measurement errors that make it less suitable for individual and serial measurements. For instance, recording a LVID of 45 mm with a small wall thickness measurement error of 11 mm instead of 10 mm yields 14% increase in LVM. Whereas wall thickness recordings using the novel method are derived from the whole circumferential area, and less sensitive to minor measurement errors. This vulnerability of methods deploying linear measurements to small differences that impact LVM measurement is reflected in the increased day-to-day- and intra-/inter-examiner variations for DEV compared to the novel method **(Table 3)**. High variations indicate decreased reproducibility and less ability to identify small yet significant real differences. Compared to the conventional method using DEV, our novel method presents lower variations and is thereby much more suited for monitoring serial measurements and comparing measurements by different examiners. **Figure 6** demonstrates three patients with excellent image quality where methods deploying linear measurements fail to accurately quantify LVM: Example A has hypertrophic cardiomyopathy (HCM) and asymmetry, focal septal hypertrophy results in overestimation of *t* and consequently overestimation of LVM by 100g. Whilst no echocardiographic method is ideal in focal/asymmetric HCM, 2DE/3DE correlate substantially better with CMR compared to 1DE. Example B has normal geometry with normal LVM and EDV_{ENDO}. However, the LV is short (78 mm), predisposing to overestimation of the LV length and consequently LVM by 44g. Other methods overcome this pitfall and correlate better with CMR. Example C has severe aortic regurgitation, the LV is both dilated and hypertrophied. Small measurement errors are particularly magnified amongst patients with large LVs, resulting in both overestimation and large variations (315-405g) despite very small, almost visually undetectable measured differences. This is also illustrated in **Figure 5** where this patient group (dilatation and hypertrophy) has large SDs, particularly amongst the method utilising linear measurements. Variations in LV geometry and size are common in cardiac disease, a cohort that particularly requires correct LVM-quantification, warranting exploration of improved methodologies.

Advantages and disadvantages with the novel method

The novel method is based on adding the mean wall thickness from a single SAX-recording to the conventional biplane tracings of the endocardium in the apical 4CH- and 2CH-view. The biplane model is traditionally applied for 2DE-quantification of volumes and function and better at correcting shape distortions compared to 1D-volume by Teichholtz or 2D-volume by A-L[6]. The biplane model can also be used for LVM-quantification, previous studies [7, 19–24] only report endo- and epicardial border delineation **(Figure 3C)**, not quantification **(Figure 3B)**. It is our experience that, the epicardium is more difficult to delineate than the endocardium. We envisaged advantages in measuring the myocardial thickness in another representative view and adding it to the EDV_{ENDO} to build up the EDV_{EPI}. This novel methodology preserves geometric variations from the biplane model and accounts for them during measurement. Compared to the BP-method, the novel method showed better feasibility, reproducibility and agreement to CMR. Several factors contribute to this observation: 1) reduced lateral resolution along the LV-walls impairs epicardial delineation in the apical views, 2) epicardial dropout, 3) echogenic pericardium, 4) small rotational errors causing the right ventricular wall to interfere with the epicardium of the inferior LV wall in the 2CH-view. It is important to remain mindful of disadvantages using the novel method, shape distortions beyond the 4CH/2CH-views are not accounted for and, inherent to 2DE-methods, inaccurate apical images and LV-foreshortening may underestimate the EDV_{ENDO} and LVM. Similar to the DEV, A-L and TE, the novel method is based on wall thickness estimation from a single imaging plane. Patients with distal wall thinning or basal septal hypertrophy are at risk of LVM-overestimation[25], conversely patients with focal hypertrophy are at risk of LVM-underestimation. Several cross sectional levels, at both base and apex may be considered with manifestly asymmetric geometry, although this may affect the feasibility and simplicity of the novel method.

Mean wall thickness

We recommend acquiring *t* using 2DE tracings in SAX **(Figure 1, right panel)**, where it is easier to ensure centred/aligned measurements. Alignment errors in PLAX such as eccentric alignment to the long-axis will yield falsely increased anterior and posterior wall thickness. In SAX, over- or under-rotation or lateral placement of the probe may also yield a falsely increased wall thickness, but not to the same extent, since the whole circumferential traced area is included and errors induced in some segments are countered by unchanged wall thickness in other segments. Initially we compared both 1DE (linear measurements, PLAX) and 2DE (tracings, SAX) at three LV levels, mitral, chordae, mid-papillary **(Figure S1 Supplementary data)**. 2DE at chordae level performed slightly better **(Table S3 Supplementary data)**. Current guidelines encourage 1DE-measurements at the mitral valve leaflet tip in PLAX and 2DE-tracings at the mid-papillary level in SAX[6]. However, results from *Chetrit M. et al*[26], *Guzzetti E et al*[25] and our findings suggest that the measurement level corresponding to the mitral valve leaflet tip provides inaccurate quantification of LVM and that the preferred level is located more towards the mid-ventricular level.

Accuracy of the novel method

We evaluated accuracy according to agreement with CMR. As envisaged, methods based on 2DE/3DE demonstrate better accuracy than 1DE. The novel method seems more accurate than other 1DE/2DE-methods, demonstrates high sensitivity and specificity for hypertrophy **(Table 5)** and, moreover, performs best regardless of LV geometry **(Figure 5)**. BA plots **(Figure 4B)** also reveal equal distribution and limited proportional bias, based on the regression line. The 3DE-agreement to CMR is consistent with recent studies[8], however, we observed underestimation of LVM by 30g among subjects with hypertrophy **(Figure 5)**, mostly HCM. Only 62% of the patients with geometry profiles of "hypertrophy" were correctly classified as being hypertrophic by 3DE **(Table S9 Supplementary data)**. This is similar to *Chang et al*[27], who also report underestimation of 20g and similar LOA in HCM, probably secondary to interpolation of small segments of the epicardium in the apex. Because of their larger LVs, the group with both hypertrophy and dilatation should also be prone to potential errors caused by interpolation of the epicardium in the apex, but we didn't observe the same pattern in this group. A plausible explanation for our findings may be slight overestimation of LVM by CMR in subjects with HCM and small/normal EDV. It may be hard to distinguish between trabeculae and LV cavity, delineation is easier among hypertrophied patients with increased EDV. Recognised difficulties in LVM-quantification amongst HCM are illustrated by relatively large LOAs' when comparing 3DE to CMR[28, 29].

Future aspects regarding implementation of the novel method

Our aim is to improve and facilitate echocardiographic LVM-quantification by developing a method that is simple, reproducible, accurate and reliable for monitoring individuals using serial measurements, without impairing workflow. The novel method does not require specific training and has substantially less post-processing analysis time than 3DE **(Table S8, Supplementary data)**. Time-efficacy may be even further improved by applying simultaneous bi-plane acquisition[30], which most vendors provide already. Any new method needs to be both *reproducible* and *accurate* compared to the reference method. For example, a method that always quantifies the LVM to 150 g is very reproducible but inaccurate and not able to detect differences. A method with high accuracy is not useful if reproducibility is poor when serial measurements are needed. The novel method performed better than conventional 1DE-methods on all parameters and was superior to 3DE in terms of reproducibility. Once integrated with the echocardiographic analysis software, an automated and accurate LVM, comparable to 3DE/CMR and with high reproducibility will be provided. Thus, it will increase reliability of quantified LVM, improve the ability to detect real differences in LVM, and facilitate clinical decisions. It potentially provides a useful tool in busy echocardiographic labs to enhance clinical management. The novel method is not yet validated according to normal LVM-range or outcome. We recognise our report may pose challenges to interpreting established data that relied on less reproducible methodologies, although this is not unique to our observations/ findings, future data is usually developed after adopting newer technologies and methods following a period of transition. We await validated normal LVM-ranges for both the 2DE/3DE-methods and hopefully, in time also for the novel method. We also recognize that there may be uncertainty regarding conventional geometrical classification according to relative wall thickness (RWT) and LVM index. Many clinical guidelines today are based upon linear measurements in PLAX. However, these measurements may also be ascertained by converting area to diameter using SAX-tracings.

Theoretically, this may be a more accurate way of achieving RWT, since all segments of the LV are represented, not only the anterior-posterior segments.

Limitations

We presumed that CMR represents the true LVM and propose comparison to other modalities. Developing and testing the model on the same population, may have biased the results. Although all measurements were performed blinded, we were not blinded to the purpose of the study, which may have affected the results. Also, the limited cohort size may have obscured potential trending in the BA plots. A validation cohort may have increased the strength of this study. Further and larger studies with various vendors or machines, contrast echocardiography, with/without contrast and with greater subject heterogeneity (including ages, obesity, LV shapes, hypertrophy and cardiac disorders) would provide corroboration, and widen interpretation and applicability of the findings. We encourage and await further validation on other populations.

Conclusion

The novel 2DE-based method for LVM-quantification has higher reproducibility than the other echocardiographic method. Accuracy is similar to 3DE and better than conventional 1DE by Devereux. As endocardial tracings using the biplane model forms part of the standard echocardiographic protocol, the novel method can easily be integrated into the echocardiographic software, without substantially increasing analysis time.

Declarations

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Conflicts of interest

The authors have no conflicts of interest.

Author contribution

CBK, RMo, CH and NV conceived and planned the study. CBK included the participants. CBK and KAM carried out the study. CBK developed the novel method, performed the data analysis and wrote the manuscript. KAM contributed to the inter-observer analysis. FFG and RMa provided critical feedback. All authors discussed the results and contributed to the manuscript.

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Figures

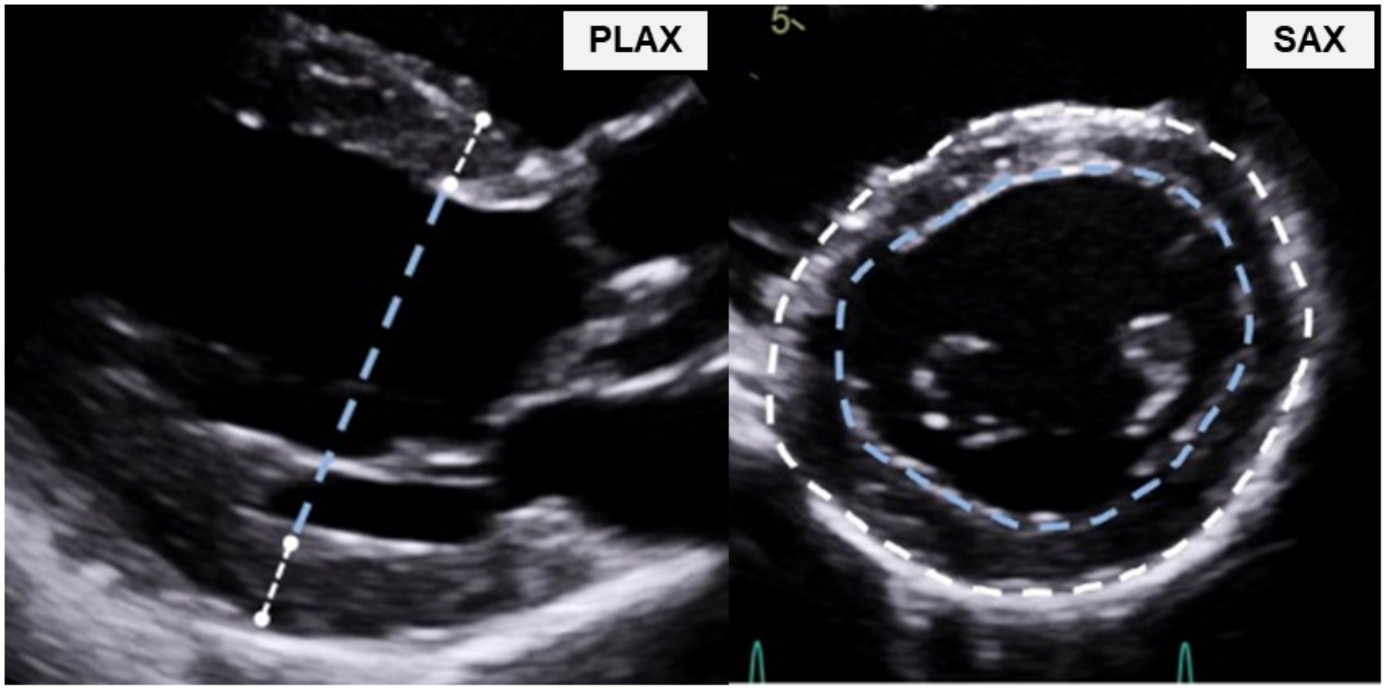


Figure 1

Wall thickness measurements at the chordae level PLAX parasternal long-axis, SAX parasternal short-axis

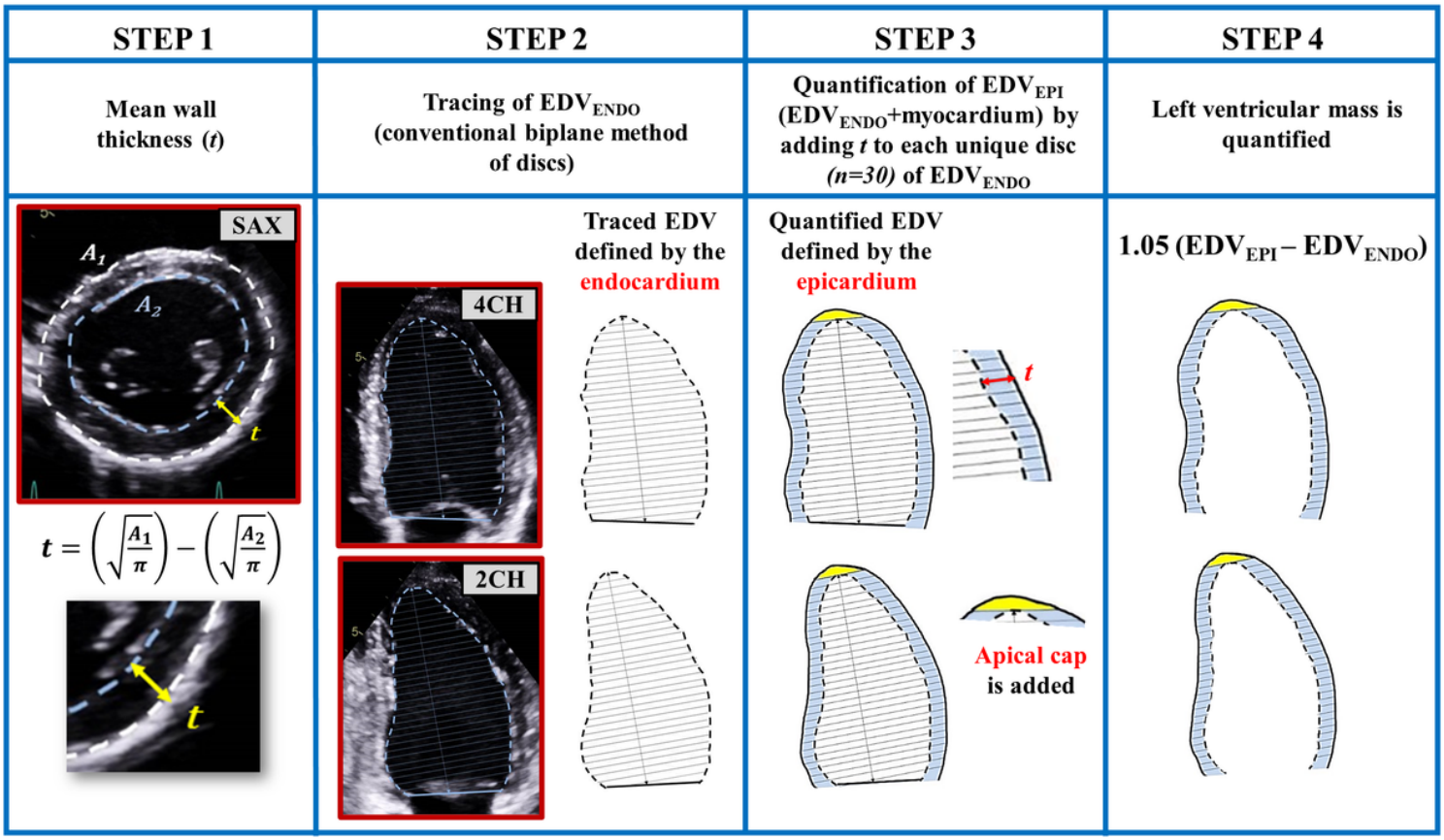


Figure 2

The novel method Step 1: Mean wall thickness (t) is calculated by tracing of the endocardial and epicardial border in the parasternal short axis view at the chordae level. Step 2: Conventional tracing in the apical four- and two-chamber view and for end-diastolic volume according to the biplane model of discs Step 3: The total volume defined by the epicardium is quantified by adding t to each unique disc from the tracings in step 2. An apical cap with the geometrical assumption of a prolate ellipsoid is added Step 4: Left ventricular myocardial volume is quantified by subtracting the traced volume defined by the endocardium (from step 2) from the quantified volume defined by the epicardium (from step 3). Left ventricular mass is quantified my multiplying the left ventricular volume with the myocardial gravity of 1.05 g/ml. t mean wall thickness, A1 outer delineation, A2 inner delineation, SAX short-axis view, EDV end-diastolic volume, 4CH four-chamber view, 2CH two-chamber view

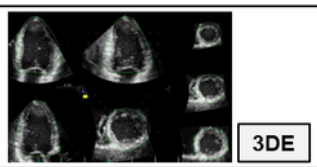
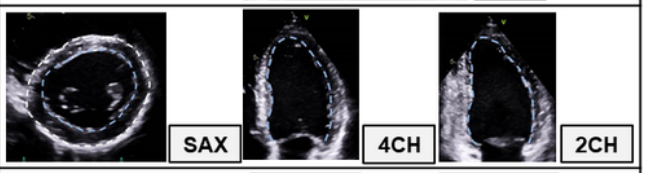
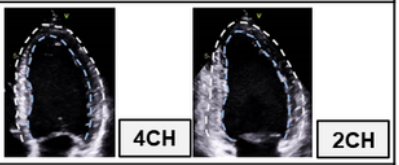
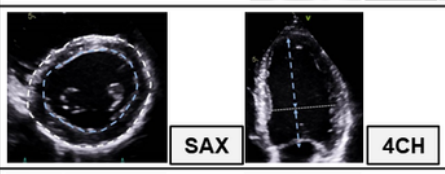
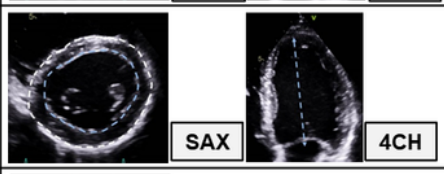
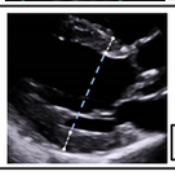
A	3DE	$1.05 \times (EDV_{EPI} - EDV_{ENDO})$	
B	NOVEL	$1.05 \times (EDV_{EPI} - EDV_{ENDO})$	
C	BP	$1.05 \times (EDV_{EPI} - EDV_{ENDO})$	
D	TE	$1.05\pi \left\{(b+t)^2\left[\frac{2}{3}(a+t)+d-\frac{d^3}{3(a+t)^2}\right] - b^2\left[\frac{2}{3}a+d-\frac{d^3}{3a^2}\right]\right\}$	
E	A-L	$1.05\left\{\left[\frac{5}{6}A_1(a+d+t)\right]-\left[\frac{5}{6}A_2(a+d)\right]\right\}$	
F	DEV	$0.8 \times 1.04 \times \left((IVS + LVID + LVPW)^3 - LVID^3\right) + 0.6$	

Figure 3A-1F: Left ventricular mass

3DE three-dimensional echocardiography, **EDV_{EPI}** end-diastolic volume defined by the epicadium, **EDV_{ENDO}** end-diastolic volume defined by the endocardium, **NOVEL** novel method, ***t*** mean wall thickness, **SAX** short-axis, **4CH** four-chamber, **2CH** two-chamber, **BP** endo-/epicardial tracing by the biplane model of discs, **TE** truncated ellipsoid, ***a*** length, apex to short-axis-plane, ***d*** length, short-axis-plane to mitral-plane, **A-L** area-length, **A_2** endocardial area (blue dotted lines) short-axis, **A_1** epicardial area (white dotted lines) short-axis, **DEV** cube formula, Devereux correction, **IVS** interventricular septum, **LVID** left ventricular internal diameter, **LVPW** left ventricular posterior wall

$b = \left(\sqrt{\frac{A_2}{\pi}}\right) \quad t = \left(\sqrt{\frac{A_1}{\pi}}\right) - \left(\sqrt{\frac{A_2}{\pi}}\right)$

Figure 3

See image above for figure legend

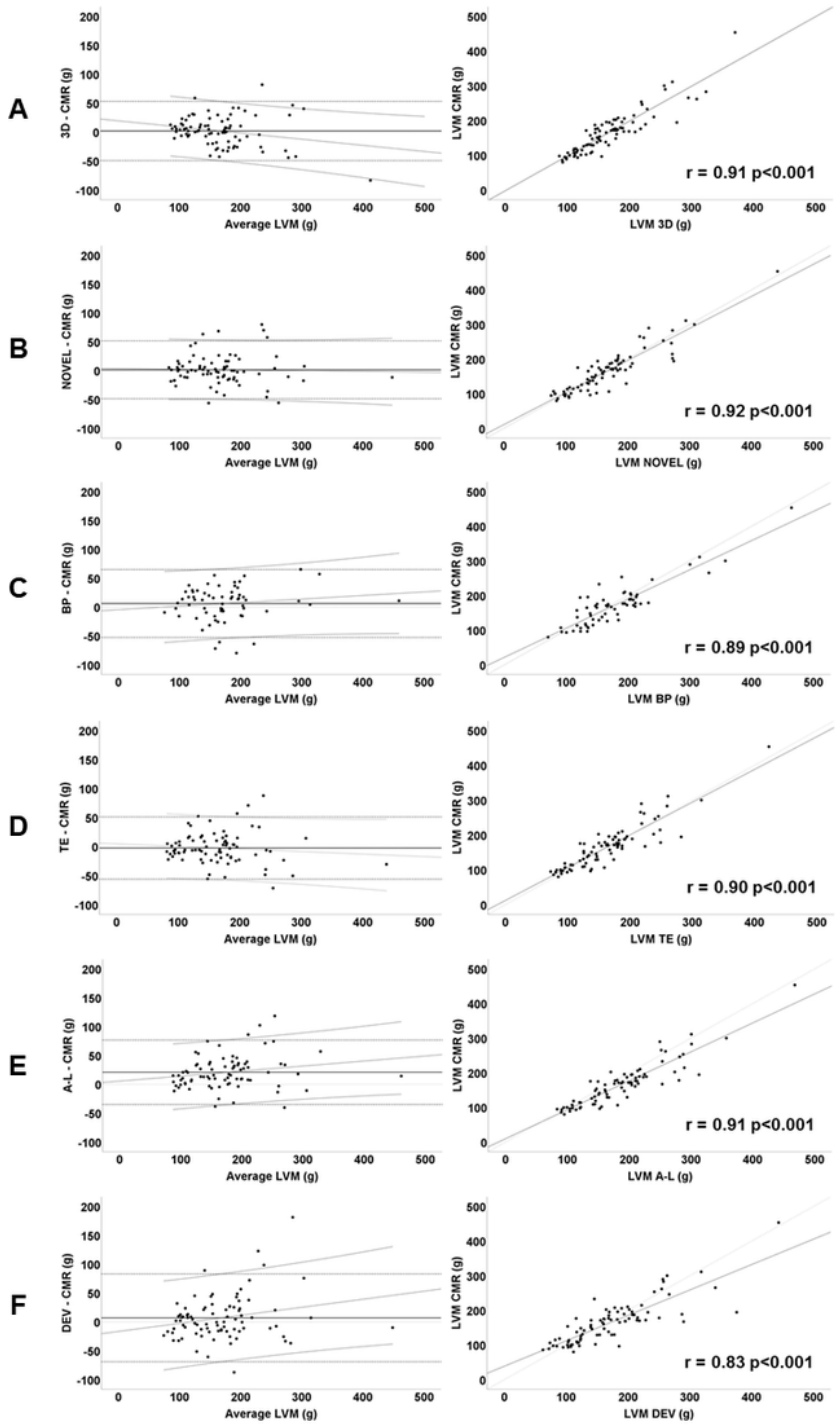


Figure 4

Agreement of left ventricular mass by echocardiography and cardiac magnetic resonance at baseline Left: Bland-Altman plots. Horizontal solid line=mean difference. Horizontal dashed line=95% limits of agreement. Solid/dashed diagonal lines=regression lines with 95% confidence interval. Right: Linear regression, pearson's correlation. (A) 3DE (B) novel (C) biplane model (D) truncated ellipsoid (E) area-length (F) cube formula, Devereux correction LVM left ventricular mass, CMR cardiac magnetic resonance

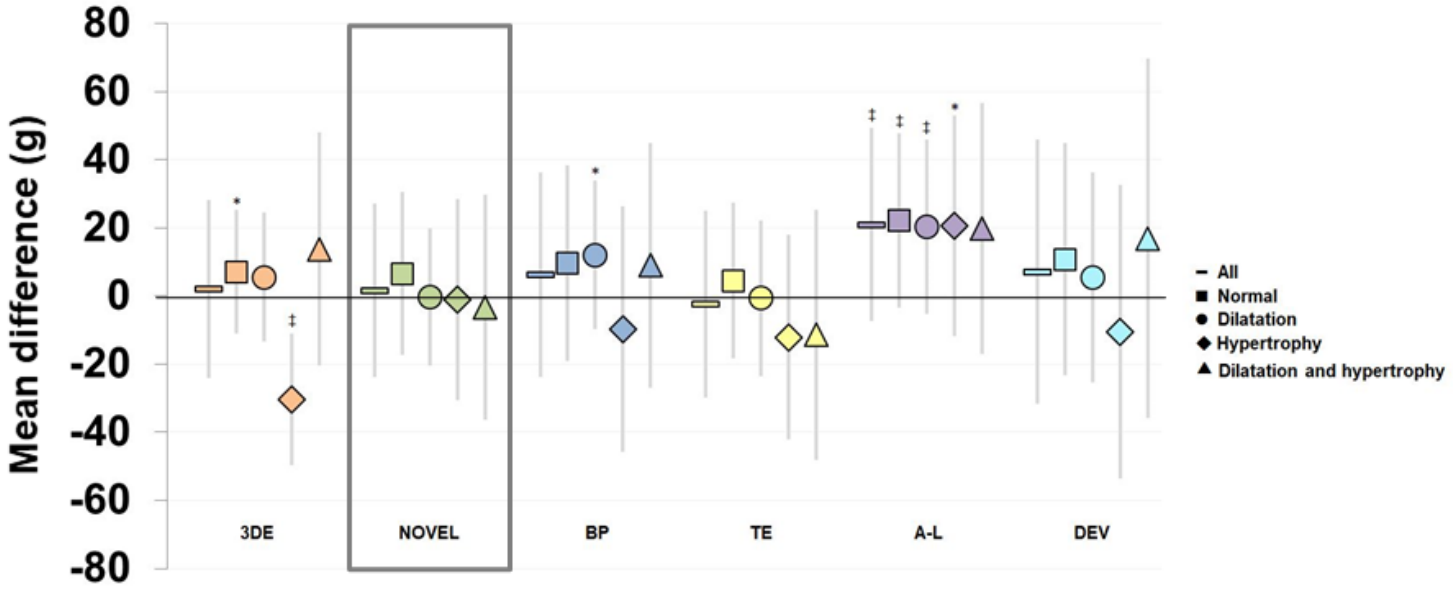


Figure 5

Agreement of left ventricular mass by echocardiography and cardiac magnetic resonance at baseline - stratified by geometry Mean differences (g) between echocardiography and cardiac magnetic resonance, positive value indicates overestimation by echocardiography. Longitudinal grey solid line is standard deviation. * p<0.05 † p<0.01 ‡ p<0.001 3DE three-dimensional echocardiography, BP biplane model, TE Truncated Ellipsoid, A-L Area-Length, DEV cube formula, Devereux correction

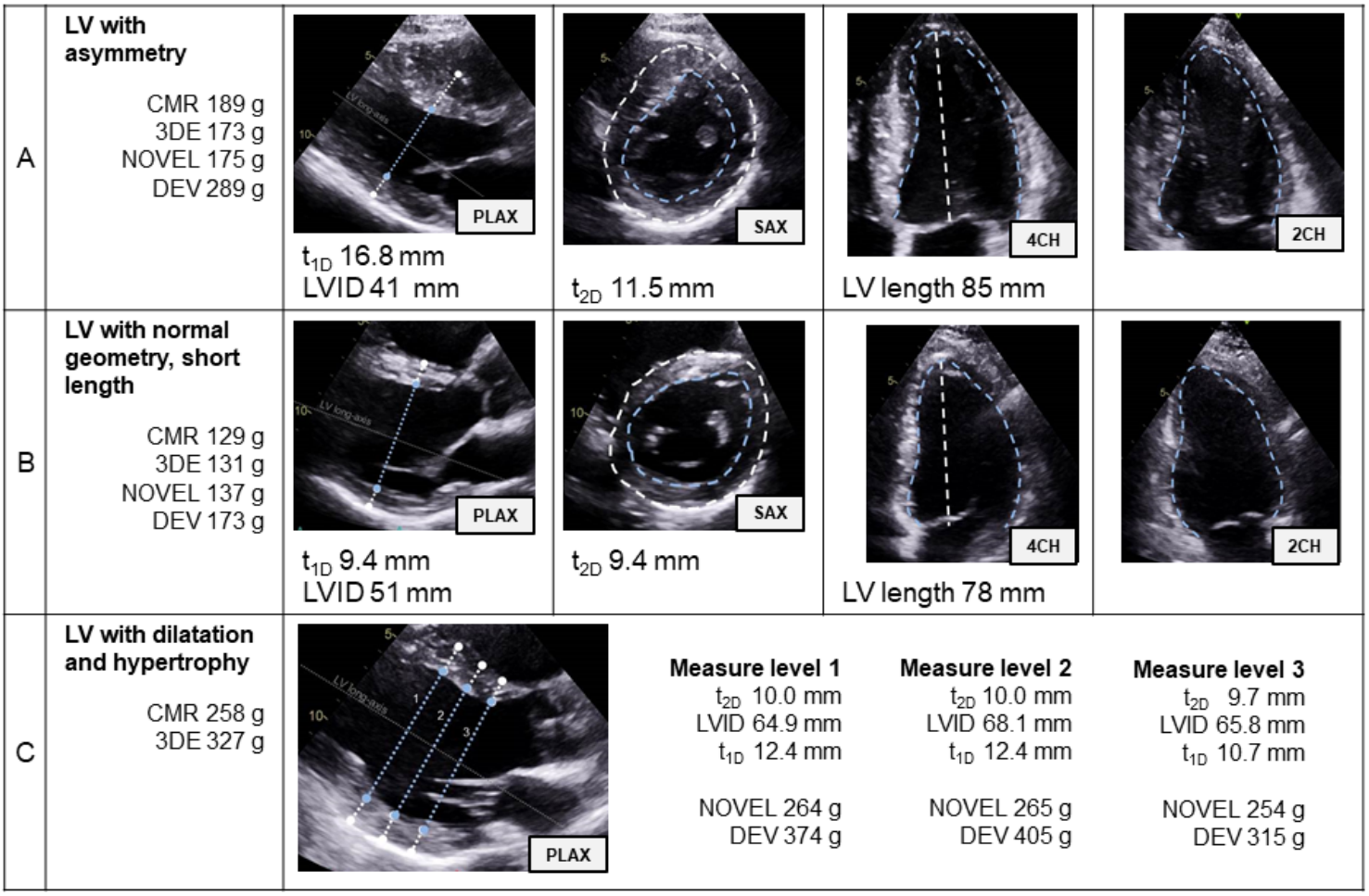


Figure 6

Examples of miscalculation by linear measurements A) Hypertrophic cardiomyopathy, asymmetry B) Normal geometry, short LV length C) Aortic regurgitation, dilatation and hypertrophy LV left ventricle, CMR cardiac magnetic resonance, 3DE three-dimensional echocardiography, DEV cube, Devereux correction, PLAX parasternal long-axis, 1D one-dimensional, t1D mean wall thickness PLAX, LVID left ventricular internal diameter, SAX short-axis, 2D two-dimensional, t2D mean wall thickness SAX, 4CH four-chamber view, 2CH two-chamber view

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarydatanovelmethod.pdf