High-Definition Blood Flow Imaging Improves Quantification of LV volumes and Ejection Fraction

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ABSTRACT

Aims: The accuracy and reproducibility of echocardiography to quantify left ventricular ejection (LVEF) is limited due to image quality. High-definition blood flow imaging is a new technique which improves cavity delineation without the need for medication or intravenous access. We sought to examine the impact of high-definition blood flow imaging on accuracy and reproducibility of LV systolic function assessment.

Methods & Results: Prospective observational study of consecutive patients undergoing two dimensional (2D) and three dimensional (3D) echocardiography (TTE), high-definition blood flow imaging and cardiac magnetic resonance imaging (CMR) within 1 hour of each other. Left ventricular systolic function characterised by left ventricular systolic volumes (LVESV) and diastolic volumes (LVEDV) and LVEF were measured. Seventy-six patients were included. Correlation of 2D TTE with CMR was modest (r = 0.68) with a worse correlation in patients with 3 or more segments not visualised (r=0.58). High-definition blood flow imaging was feasible in all patients and the correlation of LVEF with CMR was excellent (r = 0.88). The difference between 2D, High-Definition Blood Flow and 3D TTE compared to CMR were 5±9%, 2±5% and 1±3% respectively. The proportion of patients where the grade of LV function was correctly classified improved from 72.3 % using 2D TTE to 92.8% using high-definition blood flow imaging. 3D TTE also had excellent correlation with CMR (r=0.97) however was only feasible in 72.4% of patients.

Conclusion: High-definition blood flow imaging is highly feasible and significantly improves the diagnostic accuracy and grading of LV function compared to 2D echocardiography.

KEY WORDS

Left Ventricle Ejection Fraction
Contrast
Cardiac Magnetic Resonance
Three-Dimensional
High-Definition Blood Flow
Echocardiography

BACKGROUND

Quantification of left ventricular systolic function is important for all cardiovascular diseases. Left ventricular ejection fraction (LVEF) is integral part of diagnosis and risk stratification of every area of cardiology and is required to determine appropriate heart failure therapies, timing of intervention in valve disease, guide chemotherapeutic options (1,2).

Two-Dimensional (2D) Echocardiography is the most widely available and used modality for assessment of LV systolic function. One of the main limitations of echocardiography remains accuracy in patients with poor endocardial definition. Ultrasound contrast enhancing agents have been shown to improve accuracy compared to cardiac magnetic resonance (CMR) and reduce variability (3). In addition, the improved diagnostic yield changes management and reduces additional downstream testing (4). Despite the large evidence base, contrast use in patients with sub-optimal image quality remains low due to the additional training and personnel required (5,6).

Three-dimensional (3D) echocardiography minimizes the geometric assumptions and foreshortening of the ventricle. Several studies have identified it is more accurate and reproducible than 2D (7). However, feasibility remains limited in patients with poor image quality.

Newer technologies have emerged with the potential to improve endocardial definition and thereby quantification of LVEF. High-definition blood flow imaging is a left ventricular cavity blood flow imaging technique which suppresses attenuation of the left ventricular cavity signal and enhances discrimination of blood flow of the left ventricular cavity from tissue. We sought to investigate whether the use of this blood flow imaging technique improves the accuracy and reproducibility of LVEF quantification compared to 2D echocardiography, 3D echocardiography and CMR.

METHODS

Study cohort

We performed a prospective, observational study of patients attending for clinically indicated CMR with a range of different cardiovascular pathologies. Patient underwent CMR followed by echocardiography within 1 hour of each other. All studies were performed between March and December 2022. All subjects gave written informed consent to participate in the study. The study was approved by the ethical committee of UK National Research Ethics Service (07/H0715/101).

Cardiac Magnetic Resonance

CMR was performed at 1.5 or 3 Tesla (Magnetom Avanto, Siemens Medical Solution) with 32 channel cardiac coil arrays. Left ventricular volumes and ejection fraction were assessed by cine steady-state free precession sequences and analysed using Circle CVI42 (Circle Cardiovascular Imaging Inc., Calgary, Canada) semi-automated software. At least 15 phases per cardiac cycle were acquired for LV functional analysis. ECG gating was either prospectively or retrospectively acquired depending on heart rate, presence of ectopics and rhythm regularity. Eight mm slice thickness with two mm slice gap was used to provide full LV volume coverage. All studies were performed by cardiologists with level III accreditation. The cardiologists were blinded to echocardiography results.

Echocardiography

Transthoracic echocardiography was performed by accredited echocardiographers using ARIETTA 850 DeepInsight ultrasound system (FUJIFILM Healthcare, Tokyo, Japan) with a 2.5 MHz 2D phased -array transducer and a 2.5MHz 3D phased-array transducer. The echocardiographers were blinded and unaware of the CMR result. 2D, High-Definition blood flow and 3D were performed sequentially. 2D echocardiography views, including apical four and two-chamber views were obtained with the patient in the left lateral decubitus position. Left ventricular volumes and LVEF were measured and calculated using Simpson's biplane method.

Four-chamber and 2 chamber views were obtained with using high-definition blood flow imaging (LVeFlow ,Fujifilm Healthcare, Tokyo, Japan) (Figure 1). The depth and sector size were adjusted to focus on the LV. The high-definition blood flow imaging preset "LV eFlow" was switched on. The region of interest was adjusted to include the whole LV cavity. The "LV eFlow" gain was adjusted to obtain optimal delineation of the LV endocardial border. In patients with slow flow in the apex (apical aneurysm, very poor LV systolic function) the velocity range was reduced. Left ventricular volumes and LVEF were measured using the high-definition blood flow images using Simpsons biplane method. 3D left ventricular volumes were obtained in the four-chamber view. Semi-automated analysis of 3D left ventricular volumes was performed on the machine using commercially- available software (TomTec Imaging Systems GmbH, Unterschleissheim, Germany).

Statistical analysis

Continuous variables are described as mean ± SD or as median [interquartile range], while categorical variables are described as percentages. Normal distribution was assessed by using the Shapiro-Wilk test. To compare variables, Student's t-test or Mann Whitney were used for continuous variables, as appropriate and chi-square test for categorical variables. Comparison of left ventricular volumes and LVEF between different imaging modalities was performed using regression analysis. Intraclass correlation was performed for inter-variability evaluation in a randomly selected subset of 10 patients. Bland-Altman plot analysis was performed for bias exclusion between different imaging methods. All tests were 2-sided and a p-value<0.05 was considered as statistically significant. SPSS statistics software version 25.0 (SPSS, Chicago, Illinois) & GraphPad Prism version 9 was used to perform statistical evaluation.

RESULTS

Study population

A total of 76 patients were included in this study. Baseline demographics are presented in table 1. The overall mean age was 57 ± 17.1 years old with 59.2% male and a median body surface area 1.9 m^2. The three main indications for cardiovascular imaging were ischemic heart disease (N=26,34.2%), dilated cardiomyopathy (N=16, 21.1%) and valvular heart disease assessment (13, 17.1%).

Using 2D echocardiography, two or more segments were not visualised in 20/76 (26.3%) patients. Median left ventricular end-diastolic volume (LVEDV) was 116 (90-175) mls using 2D

Simpson Biplane mode, 113 (94-159) mls using high definition blood flow imaging, 118 (95-173) using 3D echocardiography and 159 (132-213) mls using CMR. Median left ventricular end-systolic volume (LVESV) was 50 (35-84) mls, 42 (31-67) mls, 46 (35-78) mls and 104 (58-104) mls, respectively. For LVEF, median values obtained were 54 % (48-61%) , 62 % (55-69%) ml, 60 % (55-68%) ml and 60 % (54-67%) ml, respectively (table 2).

Correlation between 2D, 3D, High-Definition Blood Imaging and CMR

LV volumetric assessment by 2D Simpson biplane method was highly correlated with CMR volumes (LVEDV: r=0.89; LVESV: r=0.86) with moderate correlation with LVEF (r=0.68). The correlation worsened with increased numbers of poorly visualised segments increased (table 3). The correlation between 2D and CMR LVEF in patients where 3 or more myocardial segments were not well visualised (r= 0.58).

High-definition blood flow imaging was feasible in all patients. LV volumes using high-definition blood flow imaging also yielded a strong correlation with CMR (LVEDV: r=0.911; LVESV: r=0.973). There was higher correlation between high-definition blood flow imaging LVEF and CMR LVEF (r=0.88) than 2D Simpsons Biplane LVEF and CMR (r=0.68).

3D echocardiography was feasible in 55/76 (72.4%) of the cohort. The correlation between 3D left ventricular volumes and LVEF and CMR volumes and LVEF was excellent (LVEDV: r=0.915; LVESV: r=0.904; LVEF: r= 0.965).

Overall, 24/76 (31.6%) had an LVEF < 50%. High-definition blood flow imaging had a better correlation with CMR LVEF than 2D Simpsons method in patients with LVEF < 50%. The correlation between 2D Simpsons Biplane LVEF, High-definition blood flow imaging LVEF and 3D LVEF with CMR was 0.746, 0.868 and 0.964, respectively.

Differences in LVESV, LVEDV and LVEF between Modalities

Differences in LVESV, LVEDV and LVEF between 2D, 3D, High-Definition Blood flow imaging and CRM are presented in table 4. Echocardiography whether by 2D, high-definition imaging or 3D underestimated LV volumes compared to CMR. Overall, the LVEF difference between CMR and 2D Simpsons biplane was 5±9%, whereas the difference between CMR and 2D high definition blood flow imaging was 2±5%, see figure 2 and 3. In patients where all LV myocardial segments were visible, the LVEF difference between CMR and 2D Simpsons biplane was 8±9% and the difference between CMR and high definition blood flow imaging was 1±5%. In patients where one or more LV myocardial segments were not visible, the LVEF difference between CMR and 2D Simpsons biplane was 7±16% and the difference between CMR and high definition blood flow imaging was 2±7%.

On those that underwent 3D volumetric assessment, the difference from CMR was 1±3% (Table 4). When using CMR as the gold standard, the percentage of patients where the grade of LV function was correctly classified was 72.3 % using 2D echocardiography compared to 92.8% using high-definition blood flow imaging and 96.4% using 3D echocardiography, $p<0.005$.

Inter-observer variability was performed on a random sample of 10 patients (13%). Intraclass Correlation for LVEDV, LVESV and LVEF for 2D were 0.87, 0.87, 0.75. For High-Definition blood flow imaging, Intraclass Correlation for LVEDV, LVESV and LVEF were 0.94, 0.,94 and 0.90. For 3D, Intraclass Correlation for LVEDV, LVESV and LVEF were 0.99, 0.99, 0.93. Intra-observer variability showed intraclass Correlation for LVEDV, LVESV and LVEF for

2D were 0.94, 0.91, 0.71. For High-Definition blood flow imaging, Intraclass Correlation for LVEDV, LVESV and LVEF were 0.94, 0.91 and 0.88. For 3D, Intraclass Correlation for LVEDV, LVESV and LVEF were 0.99, 0.99,0.98.

DISCUSSION

This study shows a large proportion of patients with 2D echocardiography have > 2 segments poorly visualised and 2D has moderate correlation with CMR for estimation of LV volumes and LVEF. 3D echocardiography has a high correlation with CMR however could not be performed in around a fifth of patients. The use of high-definition blood flow imaging is highly feasible and improves the accuracy of quantification and grading of LVEF similar to CMR in both patients with preserved and impaired LV function.

2D echocardiography remains the most widely used modality for grading and quantification of LV systolic function. However, poor endocardial definition can occur in up to 20% of patients which significantly reduces accuracy, increases variability and leads to incorrect grading of LV function. Contrast enhancing agents significantly improve accuracy and grading of echocardiography compared to CMR with reduced variability (3). The use of contrast enhancing agents significantly impacts patient management by greater correct classification of LV function and identification of other pathology e.g thrombus and leads to less downstream testing (4). However, despite the wealth of evidence, there is large underuse of contrast enhancing agents in echocardiography (5). This relates to perceived barriers to implementation including extra training and staffing required with obtaining intravenous access and administering contrast (6). This is despite the use of contrast having shown to be cost effective. 3D echocardiography is not limited by the geometric assumptions and foreshortening that can lead to inaccuracies of 2D methods. 3D is more accurate and reproducible than 2D and is therefore the method of choice if feasible (7,8,9). However, this technique is still limited in patients with poor image quality. Therefore, a novel method to improve quantification of LV systolic function in patients with poor image quality may improve patient care.

High-definition blood flow imaging can detect lower blood flow signal than conventional power or colour Doppler mode. Power flow uses the principles of flow velocity imaging in a completely different way from conventional display. Flows are displayed as Doppler signal strength for each imaging pixel (or PW Doppler packet). The presence or absence of flow therefore forms the interface between blood and tissue. Because the precise flow velocity is not relevant to the final imaging display, the velocity bands can be extended lower, thus registering the weak signals near the myocardium which would normally be buried in myocardial clutter. Together, this results in improved spatial and temporal resolution at the blood pool / myocardial interface. Therefore, the imaging provides improved spatial and temporal resolution of the finer left ventricular blood flow. There is limited previous data evaluating the technology. Wu et al (10) found high-definition blood flow imaging was quicker to perform than using contrast echocardiography and provided similar quantification of LV volumes and LVEF. Ahmad et al (11) compared high-definition imaging to CMR and found a good correlation, however this analysis was limited to 18 patients with up to 3 month difference between the studies.

In this study, we have shown high-definition blood flow imaging is highly feasible and can be performed in all patients. Like 2D and 3D echo, high-definition blood flow under-estimated left volumes when compared to CMR. The reason for echocardiographic techniques underestimating volumes compared to CMR may relate to difficulty in differentiation of myocardium and trabeculae and therefore not including the trabeculae as part of the LV cavity (12). However, the technique improves accuracy. In particular, high-definition blood flow imaging improves correlation with CMR derived ejection fraction, reduces variability and improves grading of LV function. This is of particular clinical importance in patients where degree of LV impairment is important for decision making including device implantation, initiation of evidence-based heart failure therapies and monitoring during potentially cardiotoxic cancer therapies.

Although further research is needed, high definition imaging could provide a useful adjunct to the standard transthoracic echocardiogram to assess LV systolic function where standard two dimensional image quality precludes accurate assessment due to inability to visualise the endocardial borders well. The requirement for additional imaging with 3D echo or CMR will depend on the clinical scenario as they provide unique additional diagnostic information.

The limitations of this study are the single centre nature of the study. Contrast echocardiography was not performed as a comparator. We used CMR as the gold standard and showed the accuracy is comparable to CMR. Previous studies have shown limited uptake of contrast use in routine transthoracic echocardiography in clinical practice despite a wealth of evidence over several decades (5,6). High-definition blood flow imaging offers a simple method to improve quantification of LVEF where there are difficulties in implementing contrast echocardiography. We did not evaluate the use of high-definition blood flow imaging to evaluate LV thrombus or regional wall motion abnormalities and this should be evaluated in larger multi-centre studies. In addition, the technique should be evaluated with a greater proportion of patients with a wide range of LVEF including those with moderate or severely impaired LVEF. The software is only available on a single vendor at present. However, we hope as the technique develops other vendors may adopt this technology.

In conclusion, the use of high-definition blood flow imaging is feasible and improves the accuracy of LV ejection fraction quantification and grading of LV function compared to 2D echocardiography.

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Data Availability Statements

The data underlying this article will be shared on reasonable request to the corresponding author.

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TABLES

Table 1. Demographics.

	Number
Age (Years)	57 ± 17.1
Sex (Male)	45 (59.2%)
Body Surface Area (m^2)	1.9 (1.8 – 2.1)
Co-morbidities	
Diabetes	7 (9%)
Hypertension	13 (17.1%)
Chronic Renal Failure	7 (9.2%)
Cardiovascular Pathology	
Ischaemic Heart Disease	26 (34.2%)
Dilated Cardiomyopathy	16 (21.1%)
Hypertrophic Cardiomyopathy	7 (9.2%)
Valvular Heart Disease	13 (17.1%)
Infiltrative Heart Disease	2 (2.6%)
Other	12 (15.8%)

Table 2. Volumetric assessment by two dimensional echocardiography, high-definition blood flow imaging, three dimensional echocardiography and cardiac magnetic resonance.

	LVEDV (mls)	LVESV (mls)	LVEF (%)
Two-Dimensional Echocardiography	116 (90 - 175)	50 (35 - 84)	54 (48 – 61)
High-Definition Blood Flow Imaging	113 (94 – 159)	42 (31 – 67)	62 (55 – 69)
Three-Dimensional Echocardiography	118 (95 – 173)	46 (35 – 78)	60 (55 – 68)
Cardiac Magnetic Resonance	159 (132 – 213)	55 (45 – 83)	60 (54 – 67)

Left ventricular end-diastolic volume (LVEDV), Left ventricular end-systolic volume (LVESV), left ventricular ejection fraction (LVEF)

Table 3. Correlation between 2D echocardiography and high-definition blood flow imaging compared to cardiac magnetic resonance imaging adjusted for number of non-visible segments using 2D echocardiography.

	Two-Dimensional Echocardiography			High-Definition Blood Flow Imaging		
Non-visible Segments on Two-Dimensional Echocardiography	LVEDV	LVESV	LVEF	LVEDV	LVESV	LVEF
Overall	0.89	0.86	0.68	0.91	0.94	0.88
2 segments	0.91	0.90	0.64	0.89	0.94	0.87
≥3 segments	0.91	0.90	0.58	0.90	0.94	0.87

Left ventricular end-diastolic volume (LVEDV), Left ventricular end-systolic volume (LVESV), left ventricular ejection fraction (LVEF)

Table 4: Differences between echocardiographic and magnetic resonance imaging measurements

	Two-Dimensional Echocardiography	High-Definition Blood Flow Imaging	Three-Dimensional Imaging
End-diastolic volume (mls)	44±27	45±25	41±26
End-systolic volume (mls)	15±24	24±22	20±24
Ejection fraction (%)	5±9	2±5	1±3

FIGURE LEGENDS

Graphical Abstract

Figure 1. Example of High-Definition Blood Flow Imaging In Diastole and Systole.

Figure 2. Difference in LVEF between 2D, 3D, High-Definition Blood Imaging and CMR.

Figure 3. Bland Altman Plots comparing differences in LVEDV, LVESV and LVEF between 2D, High-Definition Blood Flow Imaging, 3D and CMR.

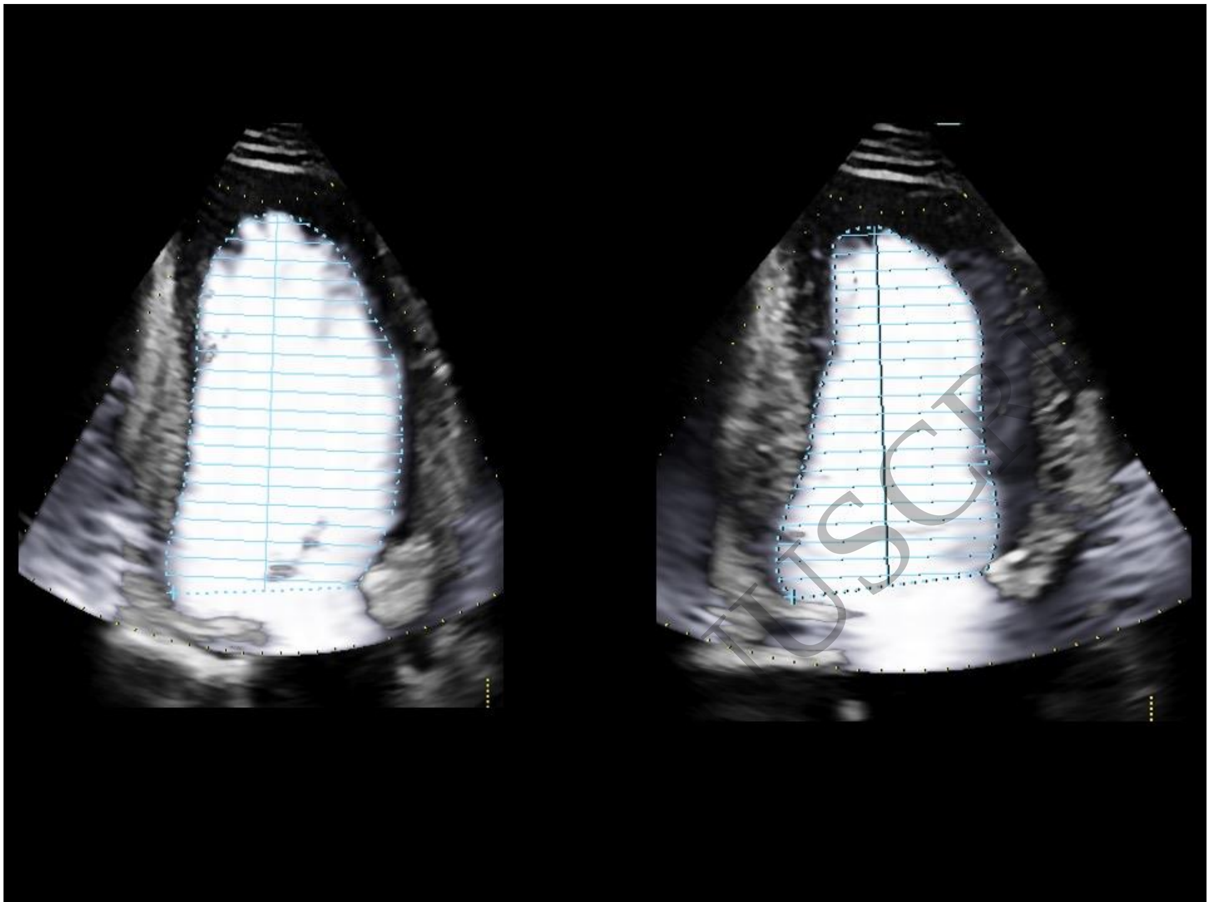

Figure 1
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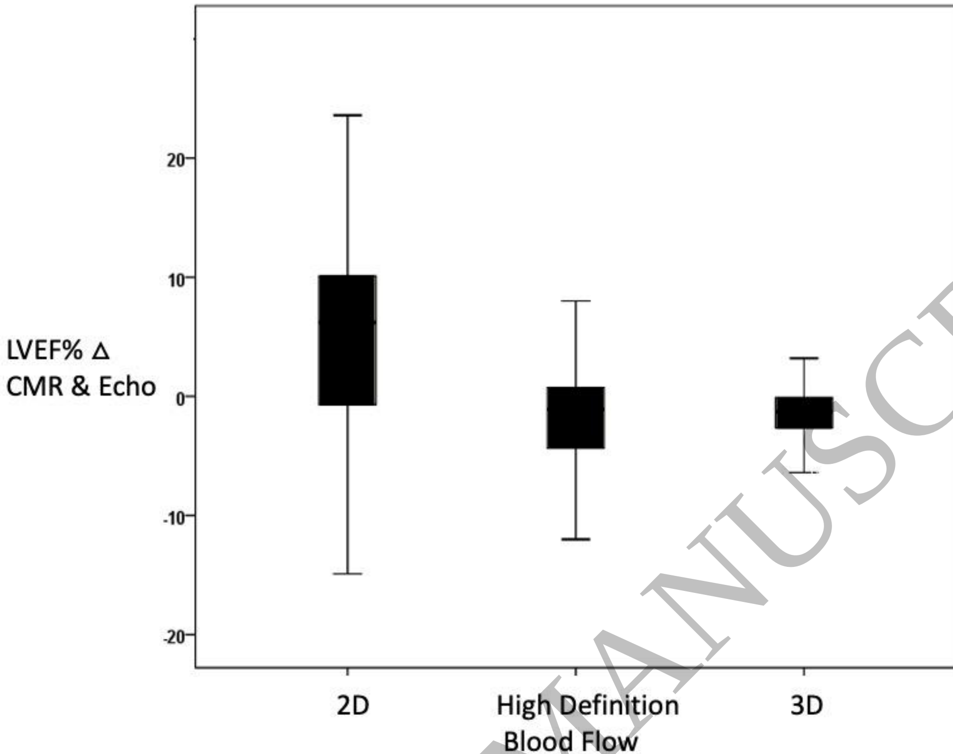

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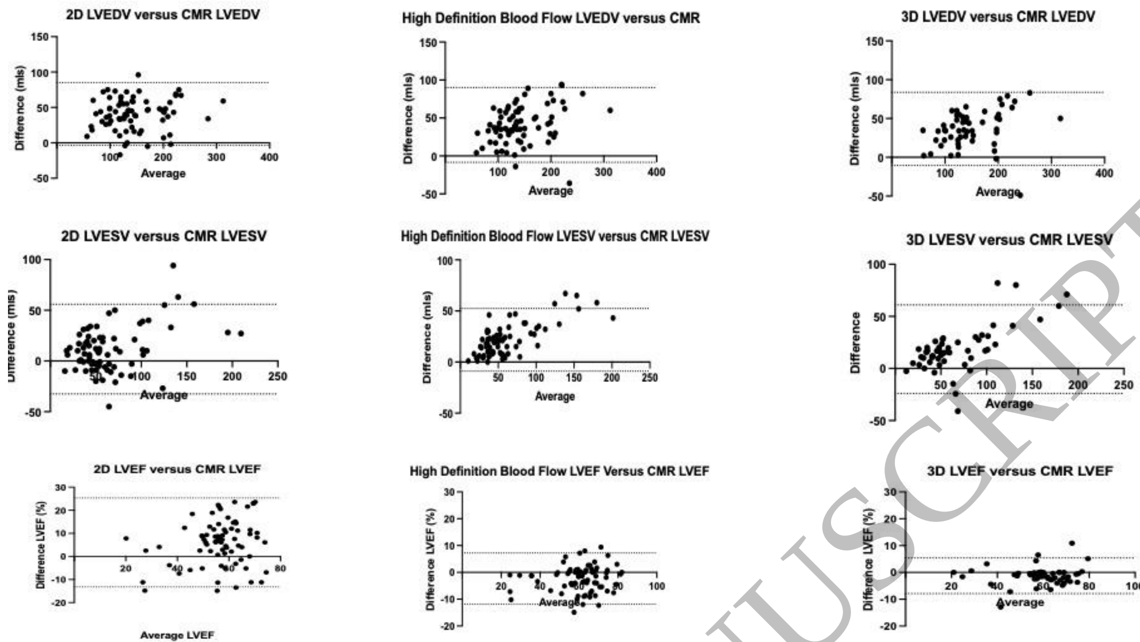

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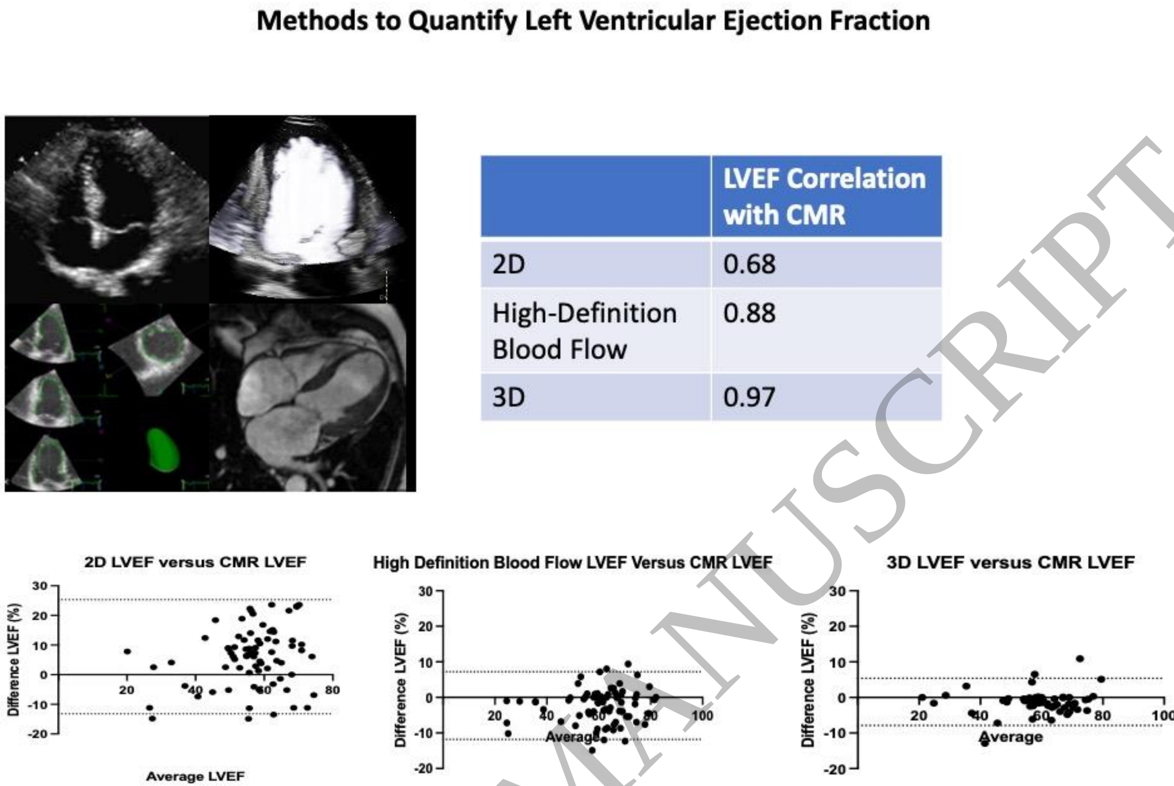

	LVEF Correlation with CMR
2D	0.68
High-Definition Blood Flow	0.88
3D	0.97

Graphical Abstract
159x119 mm (x DPI)