Comparative Assessments of Left and Right Ventricular Function by Two-Dimensional, Contrast Enhanced and Three-Dimensional Echocardiography with Gated Heart Pool Scans in Patients Following Myocardial Infarction

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Multiple noninvasive imaging modalities are available to measure biventricular function, although limited studies have assessed agreement between modalities in assessing left and right ventricular ejection fraction (LVEF & RVEF) in the same cohort of patients. In this study we prospectively compared the agreement of 2-dimensional echocardiography (2DE), contrast enhanced 2DE, 3-dimensional echocardiography (3DE), and gated heart pool scan (GHPS) measures of LVEF and RVEF in patients with acute ST-elevation myocardial infarction. We recruited 95 consecutive ST-elevation myocardial infarction patients (mean age 61.4 ± 12.0, male: 79.5%) admitted to a major tertiary hospital between July 2016 and May 2018. Despite minimal inter- and intra-observer variability (coefficient of variance < 5% in both categories), substantial discrepancies exist between modalities with Pearson's correlation coefficients ranging from 0.64 to 0.91 for LVEF measurements, and 0.27 to 0.86 for RVEF measurements. Bland-Altman plots demonstrated no systematic bias between modalities. GHPS and 3DE offered the closest agreement for both LVEF and RVEF, demonstrating the greatest correlation coefficient (r = 0.91 and 0.86 respectively), lowest mean absolute differences (4% and 3% respectively), and narrowest Bland-Altman limits of agreement (19% and 18% respectively). Greater than 10% of 2DE and contrast enhanced 2DE scans discordantly showed LVEF values >40% for patients whose LVEF was measured as ≤ 40% by 3DE or GHPS. In conclusion, substantial variation exists between modalities when assessing LVEF and RVEF, although we demonstrate that 3DE and GHPS have the closest agreement. This variability should be considered in clinical management of patients, and modalities should not be used interchangeably in sequential patient follow-up. **© 2020 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2020;134:14−23)**

Left ventricular ejection fraction (LVEF) is an established and critical predictor of arrhythmic risk and overall prognosis, and is a crucial parameter used to direct management decisions for a variety of cardiac conditions.[1−6] Similarly, impairment of right ventricular ejection fraction (RVEF) has emerged as an important prognostic determinant[7] despite the traditional view that depressed right-sided cardiac function was of limited consequence.[8] It follows that modern cardiovascular practice is heavily reliant on the accurate, reproducible and accessible measurement of biventricular volumes and function. Multiple noninvasive imaging modalities exist for the assessment of left and right ventricular (LV and RV) ejection fraction (EF), each with their own relative strengths and weaknesses.[9−14] These modalities include two- and three-dimensional echocardiography (2DE and 3DE), contrast-enhanced 2 dimensional echocardiography (C2DE), cardiac magnetic resonance imaging (CMR), and radionucleotide based techniques such as gated heart pool scans (GHPS). Ultimately the choice of a technique will be based on convenience, cost, availability and local practice and as such it is important to gain an appreciation for the interchangeability and agreement of results across each modality. In this study we prospectively compared the agreement of 2DE, C2DE, 3DE, and GHPS measures of both LVEF and RVEF, in patients with acute ST-elevation myocardial infarction (STEMI).

Methods

Our study included 95 STEMI patients from Westmead Hospital, a major tertiary institution in Sydney, Australia. Patients were prospectively enrolled between July 2016 and

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See page 21 for disclosure information.

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May 2018 during inpatient admission for treatment of STEMI. STEMI was diagnosed on the basis of standard clinical and electrocardiographic criteria[15] and all patients were treated with percutaneous revascularisation and guideline directed medical therapy.[16] The study group comprised of consecutive patients who underwent both GHPS and transthoracic echocardiogram (TTE) following revascularisation for STEMI with both tests being performed before hospital discharge. TTE involved acquisition of 2DE, C2DE, and 3DE data sets. Patients with incomplete data sets (n = 7) or scans of poor image quality for RV assessment (n = 29) were excluded from final statistical analyses (Figure 1).

Informed consent was obtained from all participants before inclusion in the study. The study protocol conformed to the ethical guidelines of the 1964 Declaration of Helsinki and was approved by the Human Research Ethics Committee of the Western Sydney Local Health District (HREC reference number: LNR/16/WMEAD/135).

Detailed patient demographics and clinical characteristics were collected by research staff directly from patients or through hospital medical records. A history of known ischaemic heart disease (previous percutaneous coronary intervention, coronary artery bypass surgery, or coronary disease for medical management) and cardiac risk factors (hypertension, hyperlipidaemia, diabetes mellitus, and current or ex-smoker) were recorded for each patient. The ECG localization of infarct along with culprit artery on angiography was also documented.

Patients underwent a comprehensive TTE with acquisition of 2DE, C2DE, and 3DE datasets according to protocols listed in the following. All TTEs were performed using a General Electric Vivid E95 scanner (GE Vingmed Ultrasound A/S, Horten, Norway), with all images stored on a central server and analyzed offline using dedicated software (GE Echopac version BT13; General Electric, Horton, Norway for 2DE and LV 3DE; Tomtec Arena 2.30.02, Tomtec Imaging Systems GMBH, Unterschleissheim, Germany for RV 3DE measurements). 3D data sets were acquired using the matrix array transducer available with the E95 ultrasound system. Established guideline-based criteria were used for measurements of LVEF and RVEF.[17] Data was independently reviewed by a cardiology fellow blinded to patient details, with separate measurements of LV and RV parameters performed. A subset of scans was reviewed by a second cardiology fellow for assessment of interobserver variability, and again by the original investigator at a later date for assessment of intra-observer variability.

For determination of LV volumes and EF, apical 4 chamber (A4C) and apical 2 chamber (A2C) views were acquired. LV end diastolic and end systolic volumes were measured using the blood-tissue interfaces, with measurements performed offline using Echopac software. Volume calculations were performed using the modified biplane method of disks summation (modified Simpson's rule).[17]

RV systolic function was evaluated following acquisition of a RV-focused view. RV volumes were obtained using the area-length method, a technique which assumes an ellipsoid or modified pyramidal approximation of RV geometry,[18] and RVEF was calculated.

The C2DE dataset was obtained by acquiring A4C and A2C views following intravenous administration of an echocardiographic contrast agent (Definity, Lantheus Medical Imaging, Massachusetts). This was performed immediately after completion of the study. Activated contrast was delivered intravenously in 0.5 to 1 ml boluses followed by a 5 to 10 ml normal saline flush. LVEF of the contrast enhanced images was subsequently calculated offline using the modified Simpson's rule.

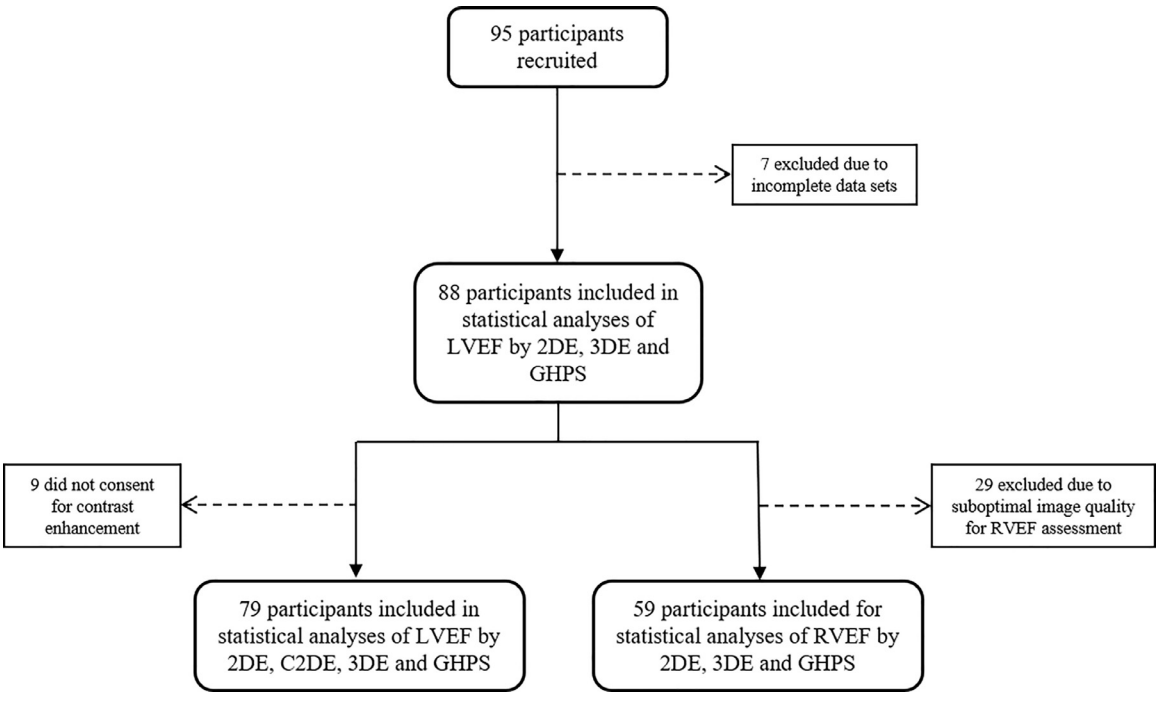

Figure 1. Flowchart of study population. 2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; C2DE = contrast enhanced 2-dimensional echocardiography; GHPS = gated heart pool scan; LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction.

C2DE was not used for assessment of right ventricular function given the lack of validation for contrast enhancement in this setting.[19]

3DE imaging was obtained with multi-beat full-volume datasets and maximized frame rates (frame rates<12 Hz excluded from analyses). 3D LVEF was calculated in a semi-automated fashion using the Echopac software package (Figure 2). Endocardial borders were automatically detected after user identification of the LV apex and centre of the mitral annulus on the A4C view at end-diastole. Detected borders could be manually edited as necessary. End-systolic volumes, end-diastolic volumes and 3D LVEF were then computed. 3D RVEF was calculated in a semi-automated fashion using the Tomtec software package (Figure 2). First, the fiducial markers were placed to identify the LV. The LV apex and centre of the mitral annulus were selected at end-diastole in the A4C and A2C views. In the apical 3 chamber view, the aortic annulus was identified. In the RV focused A4C view, the RV apex and centre of the tricuspid annulus were selected. In the short axis view the anterior and posterior insertion points of the RV free wall were identified. The software then automatically reconstructed the RV endocardial surface, with manual editing performed as required. RV volumes and EF were then computed.

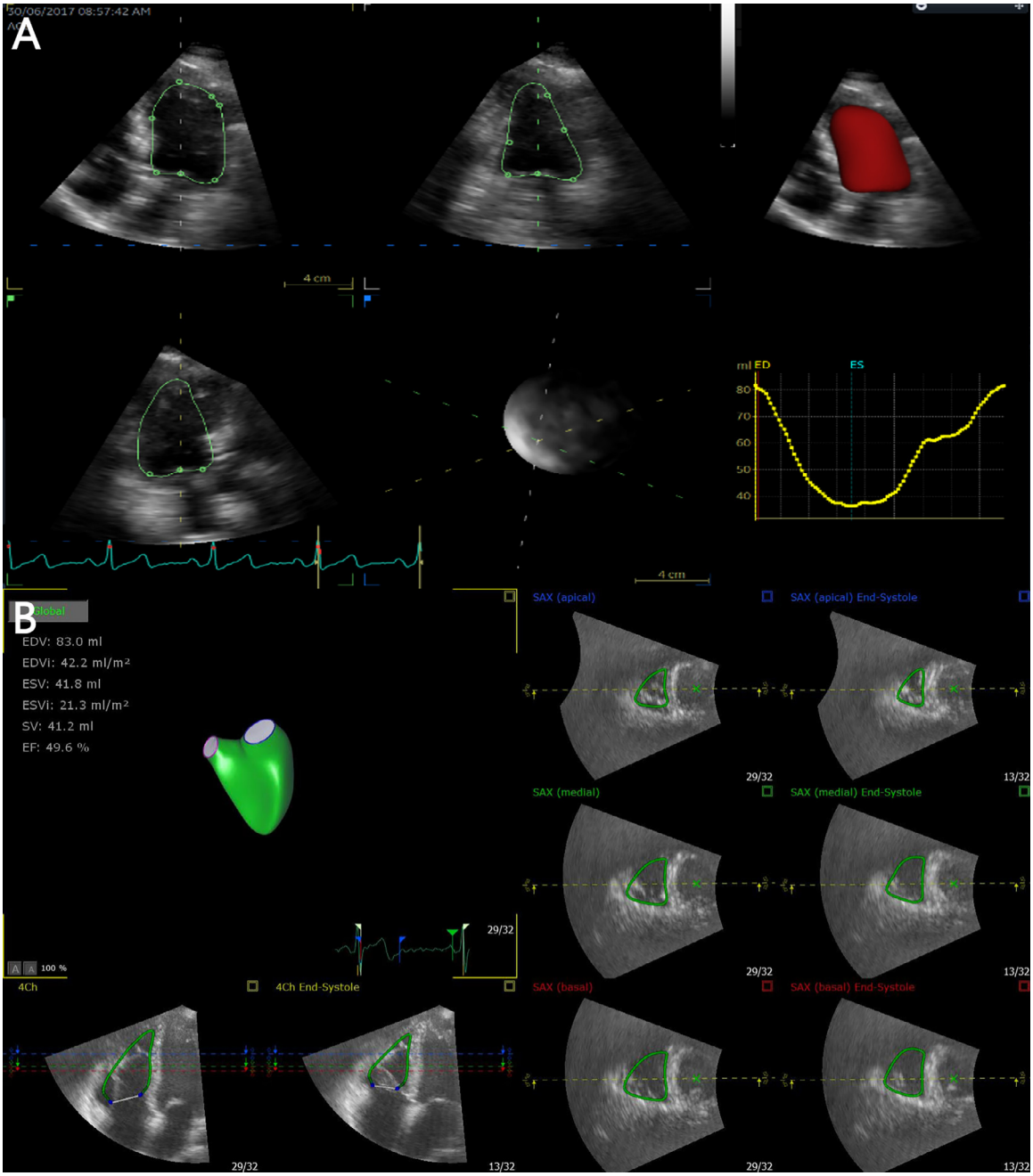

Figure 2. Three dimensional transthoracic echocardiograms with volumetric reconstruction of ventricular cavities (*A*) Left ventricular ejection fraction quantification using Echopac software (*B*) Right ventricular ejection fraction quantification using Tomtec software.

All patients underwent a gated heart pool scan with acquisition of dynamic first pass ventriculography and equilibrium gated planar images. Supine planar imaging was acquired after labelling of red blood cells with a modified in vivo/in vitro method.[20,21] Stannous pyrophosphate, 0.7 mg, was administered intravenously before red cell labeling with 800 to 900 MBq^{99m} technetium pertechnetate. Dynamic first pass acquisition was used to define the right ventricle. Dynamic first pass right anterior oblique ventriculography and gated equilibrium planar left lateral, anterior and modified left anterior oblique views were acquired with a HIRES collimator. Caudal tilt was used to improve separation of the ventricles. ECG gating was performed using R wave triggering with 16 frames per RR interval, and the RR tolerance was set to 10% to 20%. All scans were performed using a Siemens Symbia T gamma camera (Siemens Medical Solutions, Pennsylvania) with ESoft Cardiac Bloodpool acquisition protocol. Images were stored on a central server. An experienced nuclear medicine physician reviewed manually created ventricular and background regions of interest (Figure 3). Following established guideline-based criteria,[20] the cine loop of the equilibrium gated images was used to quality control the regions of interests and assist with the definition of valvular planes in end diastole and systole. Dedicated software (IDL, Harris Geospatial, Colorado) on a Siemens E-Soft workstation was used to calculate LVEF and RVEF from the time activity curve.

Intra-observer variability was determined by having the original investigator, blinded to previous measurements, repeat measurements on a third of total patients (n = 31) on 2 separate occasions, at least 2 weeks apart. The standard deviation (SD) and coefficient of variation was calculated using these 3 measurements. Interobserver variability was calculated by having a second observer perform LVEF measurements in this same subgroup of patients, blinded to previous measurements.

Statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Corporation, New York). Continuous data were summarized by the mean ± SD and categorical data by frequencies and percentages. For each pairwise comparison of LVEF and RVEF, Pearson's correlation coefficient (r) was used to quantify the strength of linear association between modalities. Bland-Altman plots were used to illustrate each pairwise agreement, showing the systematic bias and limits of agreement (mean difference ± 2 $SD_{diff,}$ where SD_{diff} is the SD of differences). A sample size of 30 subjects has 80% power to detect a clinically significant difference in EF of at least 5% between modalities provided $SD_{diff} \leq 6.6\%$. Our sample size of 88 subjects has 80% power to detect a 2% mean difference if $SD_{diff} \leq 6.6\%$.

Results

A total of 95 consecutive STEMI patients were recruited for the study. Of these, 7 patients were excluded due to datasets lacking either 3DE (n = 3) or GHPS (n = 4); thus, LV assessment by 2DE, 3DE, and GHPS was possible in 88 patients. Of these, 79 patients also had C2DE (9 patients did not consent for contrast enhancement). For RV assessment, 59 patients had complete datasets of sufficient image quality (2DE, 3DE, and GHPS) and were included in statistical analyses.

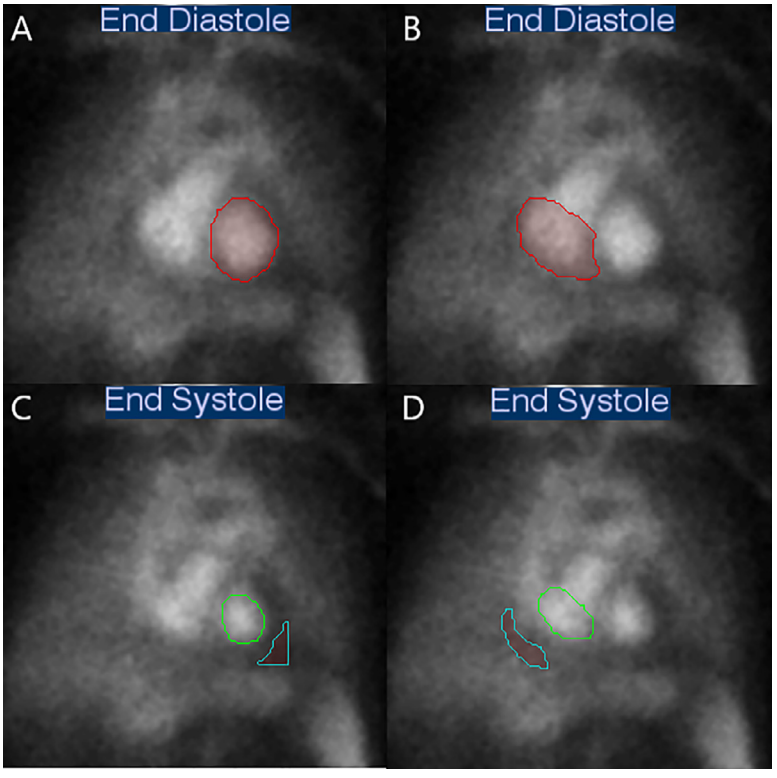

Figure 3. Left anterior oblique equilibrium gated image for left ventricle and right ventricle analysis. Left ventricular region of interest in end diastole (*A*) and end systole (*C*) Right ventricular region of interest in end diastole (*B*) and end systole (*D*).

Table 1 shows the clinical and demographic characteristics of analyzed patients. The mean age of patients was 61 ±12 years and 80% were men. TTE or GHPS was performed within a mean of 3.5 days from the time of STEMI. The mean duration between TTE and GHPS was less than a day, with a third of patients having had both scans on the same day. STEMI was anatomically categorized based on ECG localization of ST elevation according to standard criteria,[15] with most patients having had anterior (leads V_1-V_6; 46%) or inferior (leads II, III, aVF; 44%) infarctions, and a small proportion with posterior (leads V_7-V_9; 7%) or lateral (leads I, aVL; 3%) infarctions. The culprit coronary artery on angiography was most commonly the left anterior descending, followed by the left circumflex, right and finally the ramus intermedius.

LV and RV end-systolic and end-diastolic volumes (ESV and EDV) along with calculated EFs for modalities are listed in Table 2. Given planar GHPS does not assess intracardiac volumes, no values are listed. Similarly given RV volumes were not assessed in the C2DE dataset, no values are listed. EDV of both ventricles tended to be higher when measured by 3DE, with 3DE LVEDV mean of 114 ml compared with 2DE LVEDV of 107 ml, and 3DE RVEDV mean of 49 ml compared with 2DE RVEDV of 30 ml. Similarly, the mean ESV of both ventricles were also higher in 3DE data sets, with 3DE LVESV of 62 ml compared with 2DE LVESV of 57 ml, and 3DE RVESV of 28 ml compared with 2DE RVESV of 15 ml. Overall mean LVEF measurements were similar across modalities, with LVEF of 49%, 50%, 47%, and 48% for 2DE, C2DE, 3DE, and GHPS, and RVEF of 47%, 44%, and 45% for 2DE, 3DE, and GHPS.

When assessing agreement by Pearson's correlation coefficient (r), 3DE and GHPS had the closest correlation for both LVEF and RVEF (r = 0.91 and 0.86 respectively). This agreement was also evident by these modalities having had the lowest mean absolute differences (4% for LVEF and 3% for RVEF) and narrowest Bland-Altman limits of agreement (19 for LVEF and 18 for RVEF). The poorest correlations were between 2DE measures of RVEF with both 3DE RVEF and GHPS RVEF (r = 0.27 and 0.32), an unsurprising result given the lack of validation in assessing RVEF by 2DE. These measures also had the highest mean absolute differences (8% for both pairs) and widest Bland-Altman limits of agreement (39 for both pairs). The remainder of modalities had correlation coefficients ranging from 0.73 to 0.80, mean absolute differences from 5% to 7% and Bland-Altman limit of agreement ranges from 24 to 33, as shown in Table 3 and Figures 4 and 5.

Modalities were compared in their agreement for identifying patients with LVEF ≤ 40%, a cut-off that has therapeutic relevance following STEMI (Table 4). The majority of scans demonstrated concordance to measure LVEF > 40% regardless of which imaging modality was used. However, head-to-head comparisons showed discordance in the important estimation of LVEF ≤ 40. This was particularly notable in comparisons of 2DE or C2DE with 3DE or GHPS in which discordance was identified in up to 18% of all scans. In these comparisons, the majority of discordance arose from 2DE or C2DE giving LVEF > 40%, whereas the GHPS or 3DE measured LVEFs on the same patient as ≤ 40%. 3DE and GHPS also displayed some degree of discordance, with 11% of scans showing disagreement in identifying LVEFs ≤ 40%. In this case however there was less bias in disagreement, with both modalities identifying 5 scans each in which LVEF was underestimated as compared with the other modality.

Intra- and inter-observer variability as assessed by the SD and coefficient of variance is displayed in Table 5, and all lay within 5% for assessment of both LVEF and RVEF across all modalities.

Table 1
Clinical and demographic profile of ST elevation myocardial infarction patients; results are presented as mean ± standard deviation or as frequency and percentage

Variable	LVEF (n = 88)	RVEF (n = 59)
Age (years)	61.4 ± 12.0	60.8 ± 11.8
Men	70 (80%)	47 (80%)
Body mass index (kg/m^2)	28.2 ± 5.1	27.9 ± 4.4
Duration between STEMI and TTE (days)	2.9 ± 1.5	2.8 ± 1.5
Duration between STEMI and GHPS (days)	3.4 ± 1.3	3.4 ± 1.5
Duration between TTE and GHPS (days)	0.5 ± 1.8	0.6 ± 1.9
ECG localisation of infarction		
Anterior (ST elevation in leads V_1-V_6)	40 (46%)	27 (46%)
Inferior (ST elevation in leads II, III, aVF)	39 (44%)	26 (44%)
Posterior (ST elevation in leads V_7-V_9)	6 (7%)	4 (7%)
Lateral (ST elevation in leads I, aVL)	3 (3%)	2 (3%)
Culprit coronary artery		
Left anterior descending	43 (49%)	28 (48%)
Left circumflex	31 (35%)	10 (17%)
Right	13 (15%)	21 (36%)
Ramus intermedius	1 (1.1%)	0 (0%)
Atherosclerotic risk factors		
Prior history of ischaemic heart disease	18 (20%)	10 (17%)
Hypertension	52 (59%)	36 (61%)
Hyperlipidaemia	35 (40%)	24 (41%)
Diabetes mellitus	28 (32%)	21 (36%)
Current or ex-smoker	44 (50%)	31 (55%)

ECG = electrocardiogram; GHPS = gated heart pool scan; LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction; STEMI = ST elevation myocardial infarction; TTE = transthoracic echocardiogram.

Table 2
Mean end diastolic volume, end systolic volume and ejection fraction between imaging modalities; results are presented as mean ± standard deviation

Ventricle	Imaging modality	EDV (ml)	ESV (ml)	EF (%)
Left	3DE	114 ± 48	62 ± 38	47 ± 10
	GHPS	-	-	48 ± 11
	2DE	107 ± 64	57 ± 51	49 ± 10
	C2DE	104 ± 34	53 ± 23	50 ± 9
Right	3DE	49 ± 20	28 ± 14	44 ± 8
	GHPS	-	-	45 ± 9
	2DE	30 ± 14	15 ± 7	47 ± 9

2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; C2DE = contrast enhanced 2-dimensional echocardiography; GHPS = gated heart pool scan; LVEDV = left ventricular end diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end systolic volume; RVEDV = right ventricular end diastolic volume; RVEF = right ventricular ejection fraction; RVESV = right ventricular end systolic volume.

Table 3
Agreement of left and right ventricular ejection fraction measurements between modalities

Ventricle	Imaging Modality A	Imaging Modality B	Correlation (r) between A and B	Mean absolute difference (A−B)	Standard deviation of difference (A−B)	Width of Bland-Altman LOA
Left	3DE	GHPS	0.91	4	4.7	18.9
	3DE	2DE	0.80	5	6.4	25.4
	3DE	C2DE	0.73	6	6.6	26.6
	GHPS	2DE	0.73	6	7.9	31.6
	GHPS	C2DE	0.64	7	8.3	33.2
	2DE	C2DE	0.80	5	6.1	24.3
Right	3DE	GHPS	0.86	3	4.5	17.8
	3DE	2DE	0.27	8	9.8	39.3
	GHPS	2DE	0.32	8	9.9	39.6

2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; C2DE = contrast enhanced 2-dimensional echocardiography; GHPS = gated heart pool scan; LOA = limit of agreement; LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction.

Discussion

Quantification of biventricular EF has numerous prognostic and therapeutic implications, particularly post-myocardial infarction. In this study we compared 2DE, C2DE, 3DE, and GHPS for determination of biventricular EF in a population of patients post-STEMI. The salient findings from our study were:

(1) Despite minimal interobserver and intraobserver differences, substantial variation exists in all modalities for measurement of both LVEF and RVEF.

(2) In head-to-head comparisons, 3DE and GHPS had the best agreement for measurement of both LVEF and RVEF.

(3) 2DE and C2DE had the greatest discordance in identifying patients with LVEF $\leq$ 40% as measured by 3DE and GHPS.

(4) 2DE measures of RVEF correlated extremely poorly with both GHPS and 3DE measures of RVEF.

Previous studies have assessed variations in EF as measured by different imaging modalities,[22−25] however few have assessed agreement of both LVEF and RVEF in the same cohort of patients. Furthermore, this is the first study to our knowledge to assess agreement of biventricular EF across imaging modalities in the post-STEMI population, a group of patients in which predischarge assessment of EF may facilitate appropriate therapy or follow-up care.[26]

Despite minimal inter- and intra-observer variability, we found substantial differences in LVEF and RVEF measurements across the spectrum of studied modalities. Bland-Altman analyses showed no systematic bias in overestimation or underestimation of biventricular EFs by each of these modalities. Although it is feasible that variations in measured EFs may have occurred due to TTE and GHPS not occurring simultaneously, the mean duration between these scans was only 0.5 $\pm$ 1.8 days, with a third of patients having had both scans on the same day. Thus, it is unlikely that intervening medical therapy or altered haemodynamic profiles could be solely accountable for variability between modalities.

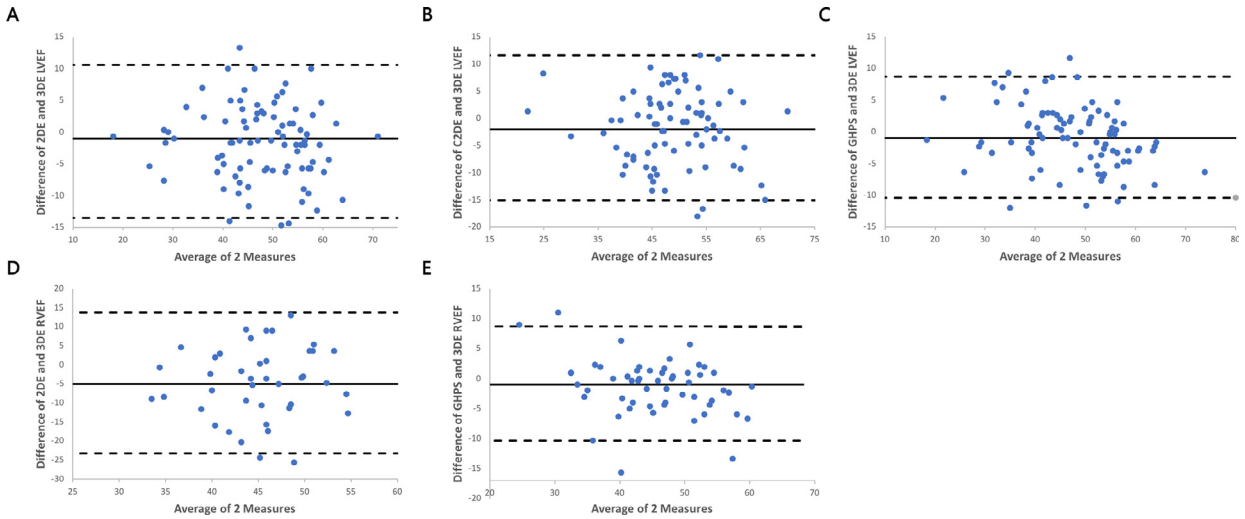

Figure 4. Bland-Altman plots for left and right ventricular ejection fractions. (*A*) 2DE and C2DE LVEF (*B*) C2DE and 3DE LVEF (*C*) GHPS and 3D LVEF (*D*) 2DE and 3DE RVEF (*E*) GHPS and 3DE RVEF. 2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; C2DE = contrast enhanced 2-dimensional echocardiography; GHPS = gated heart pool scan; LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction.

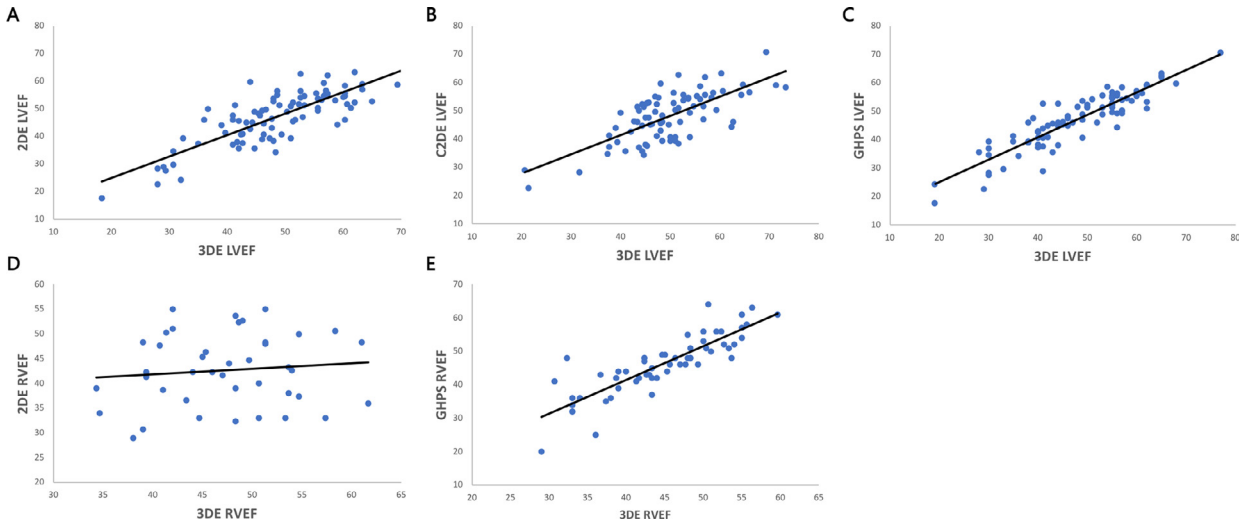

Figure 5. Correlation scatter plots for left and right ventricular ejection fractions. (*A*) 2DE and 3DE LVEF LVEF (*B*) C2DE and 3DE LVEF (*C*) GHPS and 3D LVEF (*D*) 2DE and 3DE RVEF (*E*) GHPS and 3DE RVEF. 2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; C2DE = contrast enhanced 2-dimensional echocardiography; GHPS = gated heart pool scan; LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction.

Excluding comparisons involving 2DE RVEF which are discussed separately, correlation coefficients varied from 0.60 to 0.90 and mean absolute differences varied from 3% to 7%. Although a variation of LVEF or RVEF within 3% to 7% may be considered clinically acceptable in some settings, we found substantial discordance between modalities when assessing for LVEF ≤ 40%, with up to 18% of patients having had disagreement in LVEFs ≤ 40% in head-to-head comparisons of modalities. LVEF ≤ 40% is a cut-off that can have therapeutic implications for patients following myocardial infarction,[27] and thus confidence in imaging modalities when lower LVEFs are reported is paramount. Of particular note was comparisons of 2DE or C2DE with 3DE or GHPS in which discordance was identified in 16% to 18% of all scans. In these comparisons, the majority of discordance arose from 2DE or C2DE overestimating LVEF when in the same patients, EF was measured as ≤ 40% by GHPS or 3DE. In routine clinical practice, an incorrect measurement in which an LVEF of ≤ 40% is not identified may have significant impact on recommended management in post-STEMI patients. Moreover, this highlights that for sequential follow-up, different modalities cannot be used interchangeably.

Interestingly, the addition of echocardiographic contrast did not substantially improve correlation of biplane LVEF with 3DE and GHPS (r values of 0.64 & 0.73 for C2DE vs GHPS & 2DE vs GHPS, and 0.73 & 0.80 for C2DE vs 3DE & 2DE vs 3DE respectively). On review of our contrast studies, we found a proportion of studies with acoustic shadowing, resulting in basal dropout of the contrast agent, thus resulting in inaccurate tracing of endocardial borders (Supplemental figure 1). This is a documented phenomenon, generally occurring in the presence of high concentrations of contrast agent,[17] and results in underestimation of LV volumes as compared with other modalities. Moreover, contrast was used even when 2DE endocardial definition was good, suggesting no added benefit in performing contrast echocardiography routinely in all patients.

When evaluating RVEF, 2DE performed extremely poorly compared with 3DE and GHPS, with correlation coefficients of 0.27 and 0.32 respectively. This is likely due to the inaccuracy of all 2DE methods of RV volumetric assessment, including the area-length method employed in this study.[28] For this application, 3DE is far superior and has been shown to be more accurate and reproducible than 2DE in measurement of RVEF compared with CMR.[29] In our study we also found that 3DE measures of RVEF had good agreement with GHPS (r = 0.88).

Of all head-to-head comparisons, GHPS and 3DE offered the most agreement for both LVEF and RVEF,

Table 4
Agreement and disagreement for left ventricular ejection fraction cut-off at 40% between modalities; results are presented as frequency and percentage

Imaging modality A	Imaging modality B	LVEF ≤ 40% for both A and B	LVEF > 40% for both A and B	LVEF ≤ 40% for A, LVEF > 40% for B	LVEF > 40% for A, LVEF ≤ 40% for B	Disagreement between A and B
3DE	GHPS	15 (17%)	63 (71.6%)	5 (5.7%)	5 (5.7%)	10 (11.4%)
3DE	2DE	10 (11.3%)	64 (72.7%)	10 (11.4%)	4 (4.5%)	14 (15.9%)
3DE	C2DE	6 (7.6%)	60 (75.9%)	10 (12.7%)	3 (3.8%)	13 (16.5%)
GHPS	2DE	11 (12.5%)	63 (71.6%)	11 (12.5%)	3 (3.4%)	14 (15.9%)
GHPS	C2DE	6 (7.6%)	59 (74.7%)	12 (15.2%)	2 (2.5%)	14 (17.7%)s

2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; C2DE = contrast enhanced 2-dimensional echocardiography; GHPS = gated heart pool scan; LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction.

Table 5
Intra- and inter-observer variability between modalities

Ventricle	Imaging modality	Intra-observer			Inter-observer			
		Mean EF (%)	Standard deviation	Coefficient of variance (%)	Mean EF observer 1 (%)	Mean EF observer 2 (%)	Standard deviation	Coefficient of variance (%)
Left	3DE	47.1	1.6	3.4	47.5	47.9	2.2	4.7
	2DE	48.6	1.5	3.1	47.1	47.4	1.2	2.6
	C2DE	49.7	2.0	4.0	49.7	49.8	0.6	1.2
Right	3DE	44.5	1.6	3.6	43.2	43.1	1.8	4.1
	2DE	47.1	1.63	3.5	45	45.1	2.2	4.9

2DE = 2-dimensional echocardiography; 3DE = 3-dimensional echocardiography; C2DE = contrast enhanced 2-dimensional echocardiography; GHPS = gated heart pool scan; LVEF = left ventricular ejection fraction; RVEF = right ventricular ejection fraction.

demonstrating the greatest correlation coefficient (r = 0.91 and 0.86 respectively), lowest mean absolute differences (4% and 3% respectively) and narrowest Bland-Altman limit of agreement ranges (19% and 18% respectively). 3DE is increasingly available and comparable to CMR for measurement of LV[30] and RV[29] volumes, and in this study, we have shown that there is a strong correlation between 3DE and GHPS assessments of biventricular EFs.

Predischarge assessment of LVEF following STEMI is a class 1 recommendation by the American College of Cardiology,[16] and in this study we show that despite the availability of multiple techniques to assess biventricular EF, significant discordance amongst modalities may exist. The choice of modality will ultimately be directed by physician preference, patient factors and local expertise; however, we found that 3DE may provide more reliable measures of both LVEF and RVEF as compared with 2DE and C2DE. If a 3DE dataset cannot be acquired due to lack of availability or suboptimal image quality, we have shown GHPS can provide comparable assessments of biventricular systolic function.

Some limitations should be acknowledged. CMR is considered the gold standard for cardiac volumetric assessment,[9] however is expensive, relatively inaccessible and was not used in this study. Given that there was no reference standard available, agreement between modalities was assessed by statistical measures. Secondly, despite ultrasonography contrast agents having been shown to improve correlation of LVEF with CMR,[23,31] we found C2DE did not substantially improve correlation with GHPS and 3DE as compared with non-contrast 2DE. This may in part be related to the technical issue in a subset of scans in which excess contrast agent resulted in acoustic shadowing, affecting accurate delineation of endocardial borders. The infusion method of contrast administration[32] rather than bolus technique may have reduced this error. Finally, due to the relatively small sample size of STEMI patients, our results need further validation in larger studies.

In conclusion, although LVEF is a widely reported parameter and the lynchpin for many treatment decisions especially in STEMI patients, there is substantial variability in its measurement using different imaging modalities. Variability was noted across a spectrum of measurements, with discordance noted in lower as well as higher LVEF values (defined as an LVEF cut-off of 40%). In the absence of routine access to CMR, our results suggest 3DE and GHPS offer the closest agreement with one another, with a mean absolute difference of 4% and 3% for LVEF and RVEF measurements respectively. 2DE and C2DE did not provide as comparable measures to GHPS for EF assessment (mean absolute differences from 6% to 8%). Given the increasing availability of 3DE, this modality should be considered for routine clinical evaluation, particularly given that it is easily accessible, reproducible, radiation-free, and a relatively cheap alternative to GHPS for the measurement of LVEF and RVEF in suitable patients.

Authors Contribution

Dinesh Selvakumar: Formal analysis, Investigation, Writing-original draft, Writing-Review & Editing, Visualisation, Project Administration. Paula Brown: Investigation. Paul Geenty: Investigation. Robert Barnett: Investigation. Catherine AB Saunders: Investigation, Writing-original draft, Writing-Review & Editing. Mikhail Altman: Methodology, Writing-Review & Editing. Liza Thomas: Conceptualisation, Methodology, Writing-Original Draft, Writing-Review & Editing, Supervision, Funding Acquisition.

Disclosures

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this study.

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Supplementary materials

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