



Research article

Agreement of 2D transthoracic echocardiography with cardiovascular magnetic resonance imaging after ST-elevation myocardial infarction



Tom Hendriks^a, Lawien Al Ali^a, Carlijn G. Maagdenberg^a, Joost P. van Melle^a,
Yoran M. Hummel^a, Matthijs Oudkerk^b, Dirk J. van Veldhuisen^a, Robin Nijveldt^{c,1},
Iwan C.C. van der Horst^d, Erik Lipsic^a, Pim van der Harst^{a,b,*}

^a University of Groningen, University Medical Center Groningen, Department of Cardiology, Groningen, PO box 30.001, 9700 RB, the Netherlands

^b University of Groningen, University Medical Center Groningen, Center for Medical Imaging, Groningen, PO box 30.001, 9700 RB, the Netherlands

^c VU University Medical Center, Department of Cardiology, Amsterdam, PO Box 7057, 1007 MB, the Netherlands

^d University of Groningen, University Medical Center Groningen, Department of Critical Care, Groningen, PO box 30.001, 9700 RB, the Netherlands

ARTICLE INFO

Keywords:

Magnetic resonance imaging
2D transthoracic echocardiography
Myocardial infarction
Left ventricular function

ABSTRACT

Background: This study was designed to investigate the agreement of 2D transthoracic echocardiography (2D TTE) with cardiovascular magnetic resonance imaging (CMR) in a contemporary population of ST-elevation myocardial infarction (STEMI) patients.

Methods: In this subanalysis of the GIPS-III trial, a randomized controlled trial investigating the administration of metformin in STEMI patients to prevent reperfusion injury, we studied 259 patients who underwent same-day CMR and 2D TTE assessments four months after hospitalization for a first STEMI. Bland-Altman analyses were performed to assess agreement between LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LV ejection fraction (LVEF), and LV mass measurements. Sensitivity and specificity of 2D TTE to detect categories of LVEF ($\leq 35\%$, $35\text{--}50\%$, $\geq 50\%$) was determined. Linear regression of absolute differences in measurements between imaging modalities was used to investigate whether patient characteristics impact measurement bias.

Results: Pairwise difference (bias) and 95% limits of agreement between CMR and 2D TTE measurements were +84 (37, 147) ml for LVEDV, +39 (6, 85) ml for LVESV, $-1.1 \pm 13.5\%$ for LVEF, and -75 (-154, -14) g for LV mass. Sensitivity and specificity of 2D TTE to detect subjects with moderately depressed LVEF (35–50%) as measured by CMR were 52% and 88% respectively. We observed a significant effect of enzymatic infarct size on bias between 2D TTE and CMR in measuring LVESV and LVEF ($P = 0.029$, $P = 0.001$ respectively), of age and sex on bias between 2D TTE and CMR in measuring LV mass ($P = 0.027$, $P < 0.001$) and LVEDV ($P = 0.001$, $P = 0.039$), and of heart rate on bias between 2D TTE and CMR in LV volume measurements ($P = 0.004$, $P = 0.016$).

Conclusions: Wide limits of agreement, underestimation of LV volumes and overestimation of LV mass was observed when comparing 2D TTE to CMR. Enzymatic infarct size, age, sex, and heart rate are potential sources of bias between imaging modalities.

1. Introduction

Assessment of left ventricular (LV) structure and function after ST-

elevation myocardial infarction (STEMI) is key in identifying patients at high risk of further cardiovascular events [1,2]. Not only reduced LV ejection fraction (LVEF), but also increased LV mass and abnormal

Abbreviations: 2D, two-dimensional; 3D, three-dimensional; CMR, cardiac magnetic resonance imaging; ICD, implantable cardioverter defibrillator; LV, left ventricular; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; STEMI, ST-elevation myocardial infarction; TTE, transthoracic echocardiography

* Corresponding author at: HPC AB 43, P.O. Box 30.001, 9700 RB, Groningen, the Netherlands.

E-mail addresses: t.hendriks@umcg.nl (T. Hendriks), l.al.ali@umcg.nl (L. Al Ali), c.g.maagdenberg@umcg.nl (C.G. Maagdenberg), j.p.van.melle@umcg.nl (J.P. van Melle), y.m.hummel@umcg.nl (Y.M. Hummel), m.oudkerk@umcg.nl (M. Oudkerk), d.j.van.veldhuisen@umcg.nl (D.J. van Veldhuisen), robin@nijveldt.net (R. Nijveldt), i.c.c.van.der.horst@umcg.nl (I.C.C. van der Horst), e.lipsic@umcg.nl (E. Lipsic), p.van.der.harst@umcg.nl (P. van der Harst).

¹ Present address: Radboudumc, Department of Cardiology, Nijmegen, the Netherlands.

<https://doi.org/10.1016/j.ejrad.2019.02.039>

Received 14 November 2018; Received in revised form 18 February 2019; Accepted 27 February 2019

0720-048X/© 2019 Elsevier B.V. All rights reserved.

geometry pose an increased risk for morbidity and mortality after STEMI [3]. Although cardiovascular magnetic resonance imaging (CMR) is considered the gold standard imaging modality for assessment of cardiac structure and function [4], it currently has its disadvantages in terms of availability, time-consumption, and costs. 2D transthoracic echocardiography (2D TTE) is a widely available, bedside, time- and cost-effective alternative for CMR, and standard clinical care in patients hospitalized for STEMI [1,2].

A meta-analysis on studies investigating the agreement between CMR and 2D TTE in the assessment of LV volumes and LVEF in patients and healthy volunteers show a large variation in bias and limits of agreement [5]. The individual studies have also lacked power to investigate whether patient characteristics might influence bias between imaging modalities. LV mass measurements are generally overlooked and have only been studied in subsets of patients [6,7]. We aimed to study the diagnostic accuracy of 2D TTE measurements compared with CMR in a large cohort of STEMI patients, and to investigate the potential effect of patient characteristics on bias between these imaging modalities.

2. Material and methods

2.1. Study population and design

We studied 259 patients included in the Glycometabolic Intervention as adjunct to Primary percutaneous intervention in ST elevation myocardial infarction (GIPS-III) trial with available CMR and 2D TTE assessments at four months after hospitalization for STEMI. This study is a subanalysis of the GIPS-III trial, a single-center, randomized, placebo-controlled trial, recruiting 380 consecutive patients presenting with a first STEMI between January 1, 2011 and May 26, 2013. Details on the GIPS-III trial have been reported previously [8,9]. In brief, 380 patients were randomized to take either 500 mg metformin or placebo twice daily during a period of four months. Written informed consent was obtained in all participants. One patient withdrew informed consent, leaving 379 patients in the final study. Major exclusion criteria were known diabetes mellitus (as patients with diabetes mellitus already received metformin and could therefore not be randomized), previous myocardial infarction, contraindications for CMR, the need for coronary artery bypass graft surgery, and severe renal dysfunction. The sample size of the study was determined for the primary efficacy measure, which was LVEF as measured by CMR at four months after the index event. Because no significant effect of metformin on LVEF was observed, and elaborate data collection including echocardiograms were obtained in most patients, the study was deemed suitable for further imaging substudies.

2.2. Imaging procedures

CMR is considered the reference standard. CMR was performed on a 3.0 T whole-body scanner (Achieva, Philips), using a phased array cardiac receiver coil. During repeated breath-holds, electrocardiogram-gated steady state free precession (SSFP) cine images were acquired in contiguous short-axis slices of 1 cm covering the entire LV. CMR scans (N = 271) were assessed in an independent core laboratory by two experienced observers, using QMass (Medis, Leiden, the Netherlands). Endo- and epicardial borders were outlined in the end-systolic and end-diastolic phases. LV end-diastolic volume (LVEDV), end-systolic volume (LVESV), and LV mass were measured in addition to LVEF, which was the primary outcome measure of the GIPS-III study. Cohort-specific CMR characteristics have been described and compared with reference values previously [10]. LVESV, LVEDV, LVEF, and LV mass were determined using the Simpson method of disk summation. LV mass was determined at the end-diastolic phase, excluding papillary muscles. Infarct size was defined as fraction of LV mass showing hyper-enhancement on late gadolinium enhancement series, determined using

the full width at half maximum (FWHM) technique [11].

2D TTE is considered the index test. 2D TTE was performed on the same day as the CMR assessment, in left decubital position, using a Vivid 7 echo system (General Electric, Horton, Norway). Post-processing analyses were performed in an independent core laboratory (Groningen Imaging Core Laboratory, Groningen, the Netherlands) by four experienced observers, on an Echopac BT 10 (General Electric, Horton, Norway). LVEDV, LVESV, and LVEF were determined using the biplane summation of disks method (modified Simpson's rule), which is the recommended method for 2D TTE volume calculations by the American Society of Echocardiography and the European Association of Cardiovascular Imaging [12]. The M-mode approach was not pursued, to avoid oblique sections of the ventricle. LV mass was estimated using the 2D linear dimension method [12,13].

Observers conducting CMR and 2D TTE post-processing analyses were blinded to all patient data, analyses were performed in accordance to contemporary guidelines [12,14].

2.3. Statistical analysis

Differences between CMR and 2D TTE measurements were tested for significance using a Wilcoxon matched-pairs signed-rank test. Bland-Altman analyses were used to assess limits of agreement between CMR and 2D TTE measurements [15]. Pairwise differences between CMR and 2D TTE-derived LVEDV, LVESV, and LV mass measurements were not normally distributed ($P < 0.05$), as assessed by the Shapiro-Wilk test. The assumption of a normal distribution of pairwise differences between CMR and 2D TTE-derived LVEF measurements could not be disproven ($P \geq 0.05$) with the Shapiro-Wilk test. Bias and limits of agreement between LVEF measurements were assessed using the mean and 95% confidence interval of the differences, bias and limits of agreement between LVEDV, LVESV, and LV mass measurements were assessed using the median and 2.5th and 97.5th percentiles of the differences. The correlation between 2D TTE and CMR LVEF measurements was quantified by calculating Pearson's coefficient. We determined sensitivity, specificity, and positive and negative predicting value of 2D TTE to identify clinically relevant LVEF categories ($\leq 35\%$, $35\text{--}50\%$, $\geq 50\%$) as measured with CMR. We performed univariate and multivariable linear regression analyses of the absolute pairwise difference between CMR and 2D TTE measurements (CMR – 2D TTE), including the mean of the two measurements, age, and sex as covariates, to assess the effect of potential confounders or sources of bias between imaging modalities. In addition to age and sex, variables with significance level (P-value) < 0.10 in univariate analyses were included in multivariable analysis. A P-value of 0.05 was considered significant, results were reported with standardized beta (Std. β), standardized error (SE) and P-value. Analyses were conducted with STATA/IC version 13.0 (StataCorp LP, College Station, Texas, USA).

3. Results

3.1. Patient characteristics

A total of 299 patients (79%) participating in the GIPS-III trial underwent 2D TTE assessment, image quality was insufficient to determine LV mass in 9 subjects and to determine LV volumes in 38 subjects. CMR was performed in 275 patients (73%), image quality was insufficient to determine LV mass in 8 subjects and to determine LV volumes in 4 subjects. CMR and 2D TTE measurements were available in 259 patients (61%), of which LV mass measurements in both imaging modalities were available in 255 patients and LV volume measurements in 236 patients. In-hospital clinical, angiographic and biochemical characteristics, as well as medication at discharge, are presented in Table 1. Median infarct size was 7.2% (2.6, 13.7) of LV mass.

Table 1
Patient characteristics during hospital admission for STEMI.

Characteristic	CMR and 2D TTE available (N = 259)	No CMR or 2D TTE available (N = 120)	P-value
Randomization treatment	130 (50.2)	61 (50.8)	0.91
Age, yrs	57.6 (11.6)	61.3 (11.4)	0.004
Sex, % female	52 (20.1)	43 (35.8)	< 0.001
Body mass index, kg/m ²	26.9 (3.5)	27.1 (4.4)	0.56
Race/ethnicity, % Caucasian	246 (95.0)	119 (99.2)	0.088
Hypertension	70 (27.0)	42 (35.0)	0.11
Dyslipidemia	158 (61.0)	81 (67.5)	0.22
Current smoking	131 (50.6)	78 (65.0)	0.009
Systolic blood pressure, mmHg	132.6 (21.8)	138.2 (26.1)	0.031
Diastolic blood pressure, mmHg	84.2 (14.4)	84.7 (15.1)	0.72
Heart rate, bpm	75.5 (15.9)	76.1 (17.3)	0.76
Single vessel disease	186 (71.8)	72 (60.0)	0.022
Infarct-related artery			0.48
LAD	105 (40.5)	41 (34.2)	
LCX	43 (16.6)	21 (17.5)	
RCA	111 (42.9)	58 (48.3)	
Infarct-related artery TIMI flow 0 pre-PCI	149 (57.5)	59 (49.2)	0.13
Infarct-related artery TIMI flow < 3 post-PCI	17 (6.6)	17 (14.2)	0.016
Myocardial blush grade 0-1	23 (8.9)	16 (13.3)	0.18
HbA1c	5.8 (5.6, 6.0)	5.8 (5.6, 6.1)	0.19
LDL cholesterol, mmol/L	3.9 (1.0)	3.8 (1.1)	0.72
eGFR, ml/min	97.4 (15.0)	94.3 (16.5)	0.068
Peak CK-MB, U/L	166 (78, 328)	122 (53, 310)	0.15
Peak Troponin T, ng/L	3121 (1304, 6365)	2084 (769, 5528)	0.099
Medication at discharge			
Aspirin	255 (98.5)	112 (93.3)	0.008
Statin	259 (100)	118 (98.3)	0.037
Beta-blocker	248 (95.8)	114 (95)	0.74
ACE-inhibitor or Angiotensin II receptor blocker	206 (79.5)	95 (79.2)	0.93
Aldosterone receptor antagonist	26 (10)	12 (10)	0.99
Diuretic	3 (1.2)	9 (7.5)	0.001

CMR, cardiovascular magnetic resonance imaging; 2D TTE, 2-dimensional transthoracic echocardiography; IQR, interquartile range; PCI, percutaneous coronary intervention; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction; HbA1c, glycated hemoglobin; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; CK, creatine kinase.

Data are expressed as mean (SD), median (IQR), or number (percentage).

3.2. Differences between CMR and 2D TTE

Differences between median values of same-day CMR and 2D TTE measurements were significant for all investigated variables. Median LVEDV was 189 ml (165, 226) measured by CMR, and 103 ml (88, 126) measured by 2D TTE ($P < 0.001$). Median LVESV was 86 ml (66, 107) measured by CMR, and 45 ml (37, 57) measured by 2D TTE ($P < 0.001$). Median LVEF was 55.4% (49.5, 59.7) measured by CMR, and 56.4% (50.5, 61.3) measured by 2D TTE ($P = 0.004$). Median LV mass was 102 g (86, 116) measured by CMR and 176 g (149, 201) measured by 2D TTE ($P < 0.001$). Correlations between CMR and 2D TTE were very strong for LVESV measurements ($r = 0.84$), and strong for LVEDV ($r = 0.75$), LVEF ($r = 0.67$), and LV mass ($r = 0.68$) measurements. Scatter plots to demonstrate correlations are presented in Fig. 1 and Bland-Altman diagrams are presented in Fig. 2. Pairwise difference (bias) and 95% limits of agreement between CMR and 2D TTE were +84 (37, 147) ml for LVEDV, +39 (6, 85) ml for LVESV, -1.1 (-14.7, 12.5) % for LVEF, and -75 (-154, -14) g for LV mass. We observed a sensitivity of 25% and a specificity of 99% for 2D TTE to detect subjects with severely depressed LVEF ($\leq 35\%$) as measured by CMR ($N = 8$), resulting in a positive predictive value of 40% and a negative predictive value of 97% (Table 2). In multivariable linear regression analyses, we observed a significant effect of enzymatic infarct size on bias in LVESV and LVEF measurements (Table 3), suggesting lower LVESV and higher LVEF measurements in 2D TTE ($P = 0.029$ and $P = 0.001$ respectively). Age and sex were associated with bias in LVEDV and LV mass measurements, suggesting higher LVEDV and LV mass measurements in 2D TTE compared to CMR. We also observed a significant effect of heart rate at hospital admission on bias in LV volume measurements; a higher heart rate at admission was associated

with relatively larger LVEDV and LVESV as measured with 2D TTE ($P = 0.006$ and $P = 0.012$ respectively). Systolic blood pressure was significantly associated with bias in LV mass measurements, indicating lower LV mass measurements with 2D TTE with increasing systolic blood pressure ($P = 0.024$).

4. Discussion

In same-day 2D TTE and CMR assessments of a large STEMI cohort, we observed a substantial underestimation of LV volumes and overestimation of LV mass in 2D TTE compared to CMR. Bias in LVEF measurements was small, but with a large range of agreement. We observed a low sensitivity of 2D TTE to identify subjects with $LVEF \leq 35\%$ and $LVEF < 50\%$, as measured with CMR. Enzymatic infarct size, age, heart rate, and sex appeared to be sources of bias between 2D TTE and CMR measurements. As image acquisition and post-processing was performed in adherence to clinical recommendations [12,14], we believe the observed differences are universal in character.

In our study population, LV volumes were substantially underestimated by 2D TTE when compared to CMR. This corresponds with the results of a large meta-analysis of imaging studies including both patients and healthy controls ($N = 1579$), in which LV volumes were underestimated (mean bias + 33 ml in LVEDV and + 16 ml in LVESV) to a lesser extent [5]. One large study including STEMI patients ($N = 150$) investigated the agreement between 2D TTE and CMR in the assessment of LV volumes and LVEF, and found a slightly smaller bias in LV volumes compared with our study (+ 54 ml in LVEDV and + 26 ml in LVESV) but with a similar range of agreement [16]. The observed bias in LVEF was similar compared to our presented study, but with a

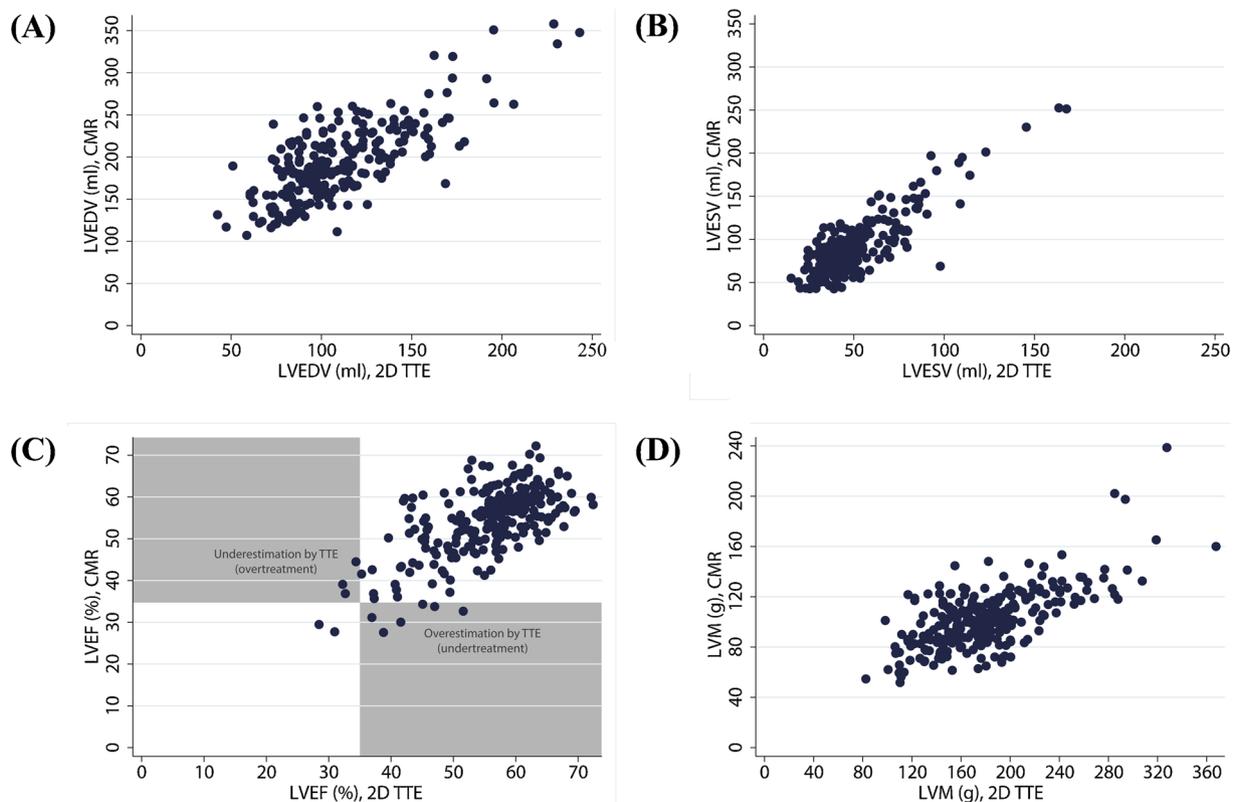


Fig. 1. Scatter plots demonstrating linear correlations between CMR-derived measurements (y-axis) and 2D TTE-derived measurements (x-axis) of (A) LVEDV, (B) LVESV, (C) LVEF, and (D) LV mass.

CMR, cardiovascular magnetic resonance imaging; 2D TTE, 2-dimensional transthoracic echocardiography; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; LV, left ventricular.

roughly 10% wider range in limits of agreement. The use of 3-dimensional (3D) TTE appears to lower the absolute bias between TTE and CMR in estimating LV volumes but does not significantly improve the ranges of agreement [5,17]. In everyday clinical practice, limits of agreement might be wider than in a highly controlled core laboratory setting. For clinicians, it is important to stay aware that results from post-processing of imaging assessments provide an estimation of the reality.

To further understand the observed differences, we believe we are the first to study the effect of potential confounders or sources of bias between 2D TTE and CMR measurements by applying linear regression analyses to find determinants of bias. We found that larger enzymatic infarct size (peak Troponin T) was associated with bias between 2D TTE and CMR-derived measurements of LVESV and LVEF, possibly resulting in an underestimation of LVESV and overestimation of LVEF by 2D TTE in patients with a large infarct size. This could partly explain why we observed a low sensitivity (52%) to detect LVEF < 50% using 2D TTE and an even lower sensitivity (25%) to detect LVEF ≤ 35%, although this was only based on 8 patients. This resulted in a positive predictive value of 40% for 2D TTE to predict LVEF ≤ 35%, and a positive predictive value of 54% to predict LVEF < 50%. An accurate LVEF measurement is highly important as it is frequently used to determine clinical indications, e.g. for implantable cardioverter defibrillator (ICD) implantation (LVEF ≤ 35%), heart failure pharmacotherapy (LVEF ≤ 40%), or classification of heart failure patients in the new category of heart failure with mid-range ejection fraction (HFmrEF, 40–49%) [18–20]. In a cohort of heart failure patients with mean LVEF of 30%, limits of agreement between 2D TTE and CMR were considerably wider (44%) compared with this study [21]. A previous study investigating 35 subjects from which 25 were patients diagnosed with dilated cardiomyopathy observed that 11 (44%) differed in LVEF class (≤ 35%, 35–55%, > 50%) when comparing biplane 2D TTE to CMR

[22]. Another study found prognostic benefit of CMR over 2D TTE when using LVEF measurements to determine clinical indication for ICD implantation [23]. These results suggest that the Simpson's biplane summation of disk method to determine LVEF in 2D TTE post-processing is more inaccurate in lower ranges of LVEF. Possible explanations are that the biplane method only visualizes part of the circumference of the left ventricle, possibly not accounting well enough for regional wall motion abnormalities, and that imaging planes are difficult to recognize in diseased ventricles. These results support the use of CMR in patients with large myocardial infarctions for clinical decision-making around ICD implantation and pharmacologic treatment, and for accurate classification of heart failure categories in clinical trials. An alternative would be to define imaging modality specific thresholds for treatment, which might be set higher in case of a more accurate CMR assessment.

Contrary to LV volumes, we found a large overestimation of LV mass, as determined by the linear dimension method on 2D TTE. Few studies have investigated the agreement of 2D TTE with CMR in assessing LV mass. It has been studied in patients with cardiomyopathy (N = 104) and patients with hypertension (N = 40), which both observed a bias of approximately +30%, similar to our results [6,7]. Both the 2D TTE linear dimension method and the SSFP-CMR short axis segmentation method have been validated against ex-vivo LV mass measurements of human hearts [13,24]. Important to note is that the validation study for CMR was performed using the Automatic Thresholding with Manual Trimming (ATMT) method which included trabecularization and papillary muscle mass [24]. CMR measurements of LV mass in the GIPS-III study excluded trabecularization and papillary muscle mass, possibly leading to underestimation of LV mass. The linear dimension method is commonly used in clinical practice, as recommended by the American Society of Echocardiography [12]. The main advantages of the linear method are that it is fast, has demonstrated prognostic value, and that reference values are well defined. The

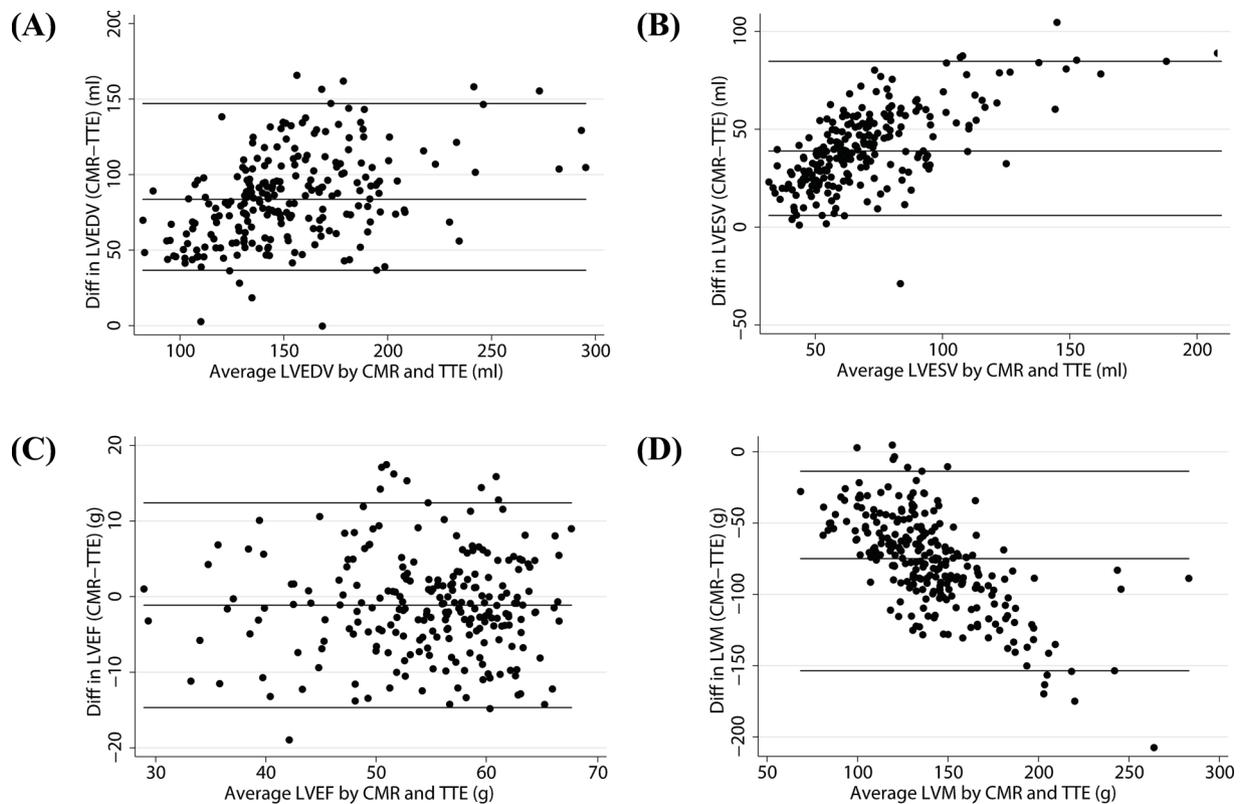


Fig. 2. Bland-Altman diagrams demonstrating bias and 95% limits of agreement in mean values of (A) LVEDV, (B) LVESV, (C) LVEF, and (D) LV mass, as measured by CMR and 2D TTE.

LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; LV, left ventricular; CMR, cardiovascular magnetic resonance imaging; 2D TTE, 2-dimensional transthoracic echocardiography.

Table 2

Sensitivity and specificity analyses of 2D TTE-derived LVEF.

	LVEF category (CMR)	LVEF category (TTE)			Total
		≤ 35%	35-50%	≥ 50%	
	≤ 35%	2 (25%)	5 (62.5%)	1 (12.5%)	8 (100%)
	35-50%	3 (5.8%)	27 (51.9%)	22 (42.3%)	52 (100%)
	≥ 50%	0 (0%)	18 (10.2%)	158 (89.8%)	176 (100%)
Total		5	50	181	236
Sensitivity		25%	52%	90%	
Specificity		99%	88%	62%	
Positive predictive value		40%	54%	87%	
Negative predictive value		97%	87%	67%	

2D TTE, 2-dimensional transthoracic echocardiography; CMR, cardiovascular magnetic resonance imaging; LVEF, left ventricular ejection fraction.

main disadvantage is that the linear method is based on the simplified assumption of the LV as a prolate ellipsoid of revolution, and does not account well for geometric variation [25]. STEMI survivors are known to experience geometric changes of the LV leading to a more spherical shape, which could account for some of the overestimation [26]. We believe that effort should be made to level measurement differences between imaging modalities in order to detect abnormalities at generalized thresholds. Improving the accuracy and reproducibility of TTE in estimating LV mass can be achieved by the more laborious manual or semiautomated delineation of endo- and epicardial borders, and by using contrast-enhanced 2D TTE or 3D TTE, of which the latter has been validated against CMR in a large cohort [27,28].

We observed a very strong association between female sex and bias between 2D TTE and CMR in LV mass measurements. Females are known to have smaller LV dimensions and a lower mass to volume ratio (or relative wall thickness) [29]. This could imply that the linear

dimension method does not account well for differences in LV geometry between genders, although the original discovery cohort did include more females than males [13]. Systolic blood pressure has also been linked to geometric (concentric) remodeling [30,31]. Future considerations could be to improve the linear dimension technique by studying a wider range of patients with and without LV hypertrophy in both sexes.

Interestingly, body mass index was not associated with bias in LV mass, LV volumes, or LVEF, although it is known to negatively affect TTE image quality [32]. Even though it affects reliability of measurements due to reducing visibility of endo- and epicardial borders, it appears to not lead to a structural under- or overestimation of 2D TTE measurements.

In clinical practice, LVEF remains widely used as a biomarker for risk stratification. However, it is only moderately reproducible because of limitations such as its reliance on geometric assumptions to

determine LV volumes and dependency on loading conditions and heart rate [33]. Myocardial deformation parameters such as strain and strain rate provide added value in predicting adverse outcome after myocardial infarction and should be considered in the future as an alternative or addition to the use of LVEF as major risk stratification parameter [34]. Other CMR-specific parameters that could provide important prognostic information after STEMI include myocardial salvage index, microvascular obstruction, and myocardial hemorrhage [35]. Future studies will have to determine which imaging parameters can best discriminate between patients needing regular care and high-risk patients requiring intensive monitoring and treatment.

4.1. Limitations

Results could have been influenced by exclusion criteria of the GIPS-III study such as previous STEMI or known diabetes. In this substudy, we excluded patients who did not undergo CMR and/or 2D TTE assessment. Excluded subjects were older, more often female, and had a smaller infarct size, resulting in a selection bias and limiting generalizability. LV mass measurements were missing in 2%, and LV volume measurements were missing in 9% of the included subjects. Median infarct size (7% of LV mass) was relatively small, which might have affected the results. Subjects generally had a well preserved LVEF, only 8 subjects (3%) had a clinical indication for ICD implantation (LVEF \leq 35% as measured with CMR).

5. Conclusions

Our findings confirm that LV volumes are substantially underestimated and LV mass is overestimated by 2D TTE compared to CMR, with wide ranges of agreement even in the presence of reasonable correlations. Our data suggests that age, gender, heart rate, and infarct size are sources of bias between imaging modalities. 2D TTE appears to have a low sensitivity to detect depressed LVEF, and increasing enzymatic infarct size leads to overestimation of 2D TTE measurements.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Acknowledgement

The GIPS-III trial was supported by ZonMw, the Netherlands Organization for Health Research and Development, The Hague, the Netherlands [grant number 95103007].

References

- P.T. O'Gara, F.G. Kushner, D.D. Ascheim, et al., ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, *Circulation* 127 (2013) 529–555.
- B. Ibanez, S. James, S. Agewall, et al., ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC), *Eur. Heart J.* 2017 (2017).
- A. Verma, A. Meris, H. Skali, et al., Prognostic implications of left ventricular mass and geometry following myocardial infarction: the VALIANT (VALsartan in Acute myocardial iNfarctiOn) echocardiographic study, *JACC Cardiovasc. Imaging* 1 (2008) 582–591.
- K. Alfakih, S. Reid, T. Jones, M. Sivananthan, Assessment of ventricular function and mass by cardiac magnetic resonance imaging, *Eur. Radiol.* 14 (2004) 1813–1822.
- M. Rigoli, S. Anandabaskaran, J.P. Christiansen, G.A. Whalley, Bias associated with left ventricular quantification by multimodality imaging: a systematic review and meta-analysis, *Open Heart* 3 (2016) e000388-2015-000388. eCollection 2016.
- K. Kusunose, D.H. Kwon, H. Motoki, S.D. Flamm, T.H. Marwick, Comparison of three-dimensional echocardiographic findings to those of magnetic resonance imaging for determination of left ventricular mass in patients with ischemic and non-ischemic cardiomyopathy, *Am. J. Cardiol.* 112 (2013) 604–611.
- L. Perdrix, N. Mansencal, B. Cochetex, et al., How to calculate left ventricular mass in routine practice? An echocardiographic versus cardiac magnetic resonance study, *Arch. Cardiovasc. Dis.* 104 (2011) 343–351.
- C.P. Lexis, I.C. van der Horst, E. Lipsic, et al., Metformin in non-diabetic patients presenting with ST elevation myocardial infarction: rationale and design of the glycometabolic intervention as adjunct to primary percutaneous intervention in ST elevation myocardial infarction (GIPS)-III trial, *Cardiovasc. Drugs Ther.* 26 (2012) 417–426.
- C.P. Lexis, I.C. van der Horst, E. Lipsic, et al., Effect of metformin on left ventricular function after acute myocardial infarction in patients without diabetes: the GIPS-III randomized clinical trial, *JAMA* 311 (2014) 1526–1535.
- T. Hendriks, M.H.T. Hartman, P.J.J. Vlaar, et al., Predictors of left ventricular remodeling after ST-elevation myocardial infarction, *Int. J. Cardiovasc. Imaging* 33 (2017) 1415–1423.
- A.S. Flett, J. Hasleton, C. Cook, et al., Evaluation of techniques for the quantification of myocardial scar of differing etiology using cardiac magnetic resonance, *JACC Cardiovasc. Imaging* 4 (2011) 150–156.
- R.M. Lang, L.P. Badano, V. Mor-Avi, et al., Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American society of echocardiography and the European association of cardiovascular imaging, *J. Am. Soc. Echocardiogr.* 28 (2015) 1–39 e14.
- R.B. Devereux, D.R. Alonso, E.M. Lutas, et al., Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings, *Am. J. Cardiol.* 57 (1986) 450–458.
- J. Schulz-Menger, D.A. Bluemke, J. Bremerich, et al., Standardized image interpretation and post processing in cardiovascular magnetic resonance: society for Cardiovascular Magnetic Resonance (SCMR) board of trustees task force on standardized post processing, *J. Cardiovasc. Magn. Reson.* 15 (2013) 35-429X-15-35.
- J.M. Bland, D.G. Altman, Statistical methods for assessing agreement between two methods of clinical measurement, *Lancet* 1 (1986) 307–310.
- N. Mistry, S. Halvorsen, P. Hoffmann, et al., Assessment of left ventricular function with magnetic resonance imaging vs. echocardiography, contrast echocardiography, and single-photon emission computed tomography in patients with recent ST-elevation myocardial infarction, *Eur. J. Echocardiogr.* 11 (2010) 793–800.
- J. Greupner, E. Zimmermann, A. Grohmann, et al., Head-to-head comparison of left ventricular function assessment with 64-row computed tomography, biplane left cineventriculography, and both 2- and 3-dimensional transthoracic echocardiography: comparison with magnetic resonance imaging as the reference standard, *J. Am. Coll. Cardiol.* 59 (2012) 1897–1907.
- S.M. Al-Khatib, W.G. Stevenson, M.J. Ackerman, et al., AHA/ACC/HRS Guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society, *Circulation* (2017) 2017.
- S.G. Priori, C. Blomstrom-Lundqvist, A. Mazzanti, et al., ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), *Eur. Heart J.* 2015 (36) (2015) 2793–2867.
- P. Ponikowski, A.A. Voors, S.D. Anker, et al., ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC, *Eur. J. Heart Fail.* 2016 (18) (2016) 891–975.
- N.G. Bellenger, M.I. Burgess, S.G. Ray, et al., Comparison of left ventricular ejection fraction and volumes in heart failure by echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance: are they interchangeable? *Eur. Heart J.* 21 (2000) 1387–1396.
- M.L. Chuang, M.G. Hibberd, C.J. Salton, et al., Importance of imaging method over imaging modality in noninvasive determination of left ventricular volumes and ejection fraction: assessment by two- and three-dimensional echocardiography and magnetic resonance imaging, *J. Am. Coll. Cardiol.* 35 (2000) 477–484.
- G. Pontone, A.I. Guaricci, D. Andreini, et al., Prognostic benefit of cardiac magnetic resonance over transthoracic echocardiography for the assessment of ischemic and nonischemic dilated cardiomyopathy patients referred for the evaluation of primary prevention implantable cardioverter-defibrillator therapy, *Circ. Cardiovasc. Imaging* 9 (2016) e004956.
- N.J. Farber, S.T. Reddy, M. Doyle, et al., Ex vivo cardiovascular magnetic resonance measurements of right and left ventricular mass compared with direct mass measurement in excised hearts after transplantation: a first human SSFP comparison, *J. Cardiovasc. Magn. Reson.* 16 (2014) 74-014-0074-0.
- A.C. Armstrong, S. Gidding, O. Gjesdal, C. Wu, D.A. Bluemke, J.A. Lima, LV mass assessed by echocardiography and CMR, cardiovascular outcomes, and medical practice, *JACC Cardiovasc. Imaging* 5 (2012) 837–848.
- J.N. Cohn, R. Ferrari, N. Sharpe, Cardiac remodeling—concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. Behalf of an International Forum on Cardiac Remodeling, *J. Am. Coll. Cardiol.* 35 (2000) 569–582.
- J.D. Kasprzak, B. Paelinck, F.J. Ten Cate, et al., Comparison of native and contrast-enhanced harmonic echocardiography for visualization of left ventricular endocardial border, *Am. J. Cardiol.* 83 (1999) 211–217.
- M. Takeuchi, T. Nishikage, V. Mor-Avi, et al., Measurement of left ventricular mass by real-time three-dimensional echocardiography: validation against magnetic resonance and comparison with two-dimensional and m-mode measurements, *J. Am.*

- Soc. Echocardiogr. 21 (2008) 1001–1005.
- [29] S.E. Petersen, N. Aung, M.M. Sanghvi, et al., Reference ranges for cardiac structure and function using cardiovascular magnetic resonance (CMR) in Caucasians from the UK Biobank population cohort, *J. Cardiovasc. Magn. Reson.* 19 (2017) 18-017-0327-9.
- [30] S.R. Heckbert, W. Post, G.D. Pearson, et al., Traditional cardiovascular risk factors in relation to left ventricular mass, volume, and systolic function by cardiac magnetic resonance imaging: the Multiethnic Study of Atherosclerosis, *J. Am. Coll. Cardiol.* 48 (2006) 2285–2292.
- [31] S. Garg, J.A. de Lemos, C. Ayers, et al., Association of a 4-tiered classification of LV hypertrophy with adverse CV outcomes in the general population, *JACC Cardiovasc. Imaging* 8 (2015) 1034–1041.
- [32] S.D. Siadecki, S.E. Frasure, R.E. Lewis, T. Saul, High body mass index is strongly correlated with decreased image quality in focused bedside echocardiography, *J. Emerg. Med.* 50 (2016) 295–301.
- [33] M. Cikes, S.D. Solomon, Beyond ejection fraction: an integrative approach for assessment of cardiac structure and function in heart failure, *Eur. Heart J.* 37 (2016) 1642–1650.
- [34] C.L. Hung, A. Verma, H. Uno, et al., Longitudinal and circumferential strain rate, left ventricular remodeling, and prognosis after myocardial infarction, *J. Am. Coll. Cardiol.* 56 (2010) 1812–1822.
- [35] G. Pontone, A.I. Guaricci, D. Andreini, et al., Prognostic stratification of patients with ST-segment-elevation myocardial infarction (PROSPECT): a cardiac magnetic resonance study, *Circ. Cardiovasc. Imaging* 10 (2017), <https://doi.org/10.1161/CIRCIMAGING.117.006428>.