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Statistical agreement of left ventricle measurements using cardiac magnetic resonance and 2D echocardiography in ischemic heart failure

Authors' Contribution:

- A** Study Design
- B** Data Collection
- C** Statistical Analysis
- D** Data Interpretation
- E** Manuscript Preparation
- F** Literature Search
- G** Funds Collection

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Summary

Background:

The aim of this study was to compare cardiac magnetic resonance imaging (CMR) with 2-dimensional echocardiography (2D echo) in the assessment of left ventricle (LV) function parameters and mass in patients with ischemic heart disease and severely depressed LV function. Although 2D echo is commonly used to assess LV indices, CMR is the state-of-the-art technique. Agreement between these 2 methods in these patients has not been well established.

Material/Methods:

LV indexed end systolic and diastolic volumes (EDVi and ESVi), indexed mass (LVMi) and ejection fraction (EF) were assessed in 67 patients (12 women), using 2D echo and CMR.

Results:

According to statistical analysis (Bland-Altman), 2D echo underestimated LV EDV and ESV and overestimated EF and LVMi compared to CMR. The highest correlation between 2D echo and CMR was found for EDVi ($R^2=0.73$, $p<0.0001$) and ESVi ($R^2=0.69$, $p<0.0001$) and the lowest for EF ($R^2=0.21$, $p=0.001$) and LVMi ($R^2=0.20$, $p=0.002$). The maximal differences between 2D echo and CMR were found for highest measurements of LV volumes and mass, and for lowest EF values.

Conclusions:

There is moderate to strong correlation between CMR and 2D echo in the assessment of LV function parameters and mass in patients with ischemic heart failure. Between-method agreement depends on the degree of LV dysfunction. The results of assessment of the severely damaged LV obtained by the use of 2D echo should be interpreted with caution.

Key words:

cardiac magnetic resonance imaging • two-dimensional echocardiography • end-stage ischemic heart failure

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BACKGROUND

Systolic left ventricle (LV) function is a basic factor influencing prognosis and decision-making in patients with ischemic heart failure [1,2]. Invasive and non-invasive techniques are used to evaluate cardiac function in the course of ischemic disease. Cardiac magnetic resonance imaging (CMR) is the non-invasive, state-of-the-art technique in the assessment of cardiac function, owing to its excellent soft-tissue contrast, good blood-to-myocardium contrast and sufficient spatial/temporal resolution for cardiac imaging [3,4]. However, in routine clinical settings, transthoracic two-dimensional echocardiography (2D echo) is the most widely available technique and the method of choice from the economic point of view [5]. Despite the many comparisons between CMR and 2D echo in the evaluation of LV function existing in the literature, the data on the agreement of both methods in patients with ischemic heart disease are inconclusive [6–9]. Some authors suggest that CMR and 2D echo were not interchangeable in the assessment of cardiac function [6]. According to others, CMR was the preferred technique, owing to its three-dimensional approach and superior image quality [10]. In recent years, many authors have found better agreement between CMR, two-dimensional and, especially, three-dimensional echocardiography in the assessment of cardiac function [11–14]. However, the results in patients with heart failure are still ambiguous [15,16]. It is also unclear if the between-method agreement depends on the degree of LV dysfunction [14]. The aim of our study was to compare CMR with 2D echo in the assessment of LV volumes, LV mass and ejection fraction (EF) in patients with ischemic heart disease and severely depressed LV function.

MATERIAL AND METHODS

The study group consisted of consecutive patients admitted to the cardiology or cardiac surgery departments of our hospital with clinically significant congestive heart failure and low EF, as reported by their referring physicians. The cause of heart failure in all the patients was multi-vessel coronary artery disease with a history of myocardial infarction. The patients were referred for clinically indicated CMR and 2D echo as part of their evaluation. The exclusion criteria were arrhythmia and/or contraindications to CMR (cardiac pacemakers, ferromagnetic implants or claustrophobia). Patients with clinically significant aortic valve disease, mitral stenosis and non-ischemic mitral regurgitation were excluded from the analysis. After taking the exclusion criteria into consideration, the study group consisted of 67 patients (55 men and 12 women). The patients' data are summarized in Table 1. The mean period of time between CMR and 2D echo was 5±2 days. The study was approved by the local ethics committee and written informed consent was obtained from all participating patients.

CMR protocol

CMR studies were performed using a 1.0T MR Unit (Magnetom Harmony, Siemens) with the following technical parameters: magnetic gradients amplitude: 40 mT, slew rate 200 mT/m/s, dedicated four-element phase-array receiver coil. Examination protocol consisted of an SE/T1-weighted sequence, 'dark blood' images in the axial plane and a Balanced Steady State Free Precession cine

Table 1. Patients' characteristics.

Demographic features	
Age (years)	58.1±13.1
Male, n (%)	55 (82.1)
NYHA class, n (%)	
I–II	54 (77.1)
III–IV	16 (22.9)
History of myocardial infarction, n (%)	
Anterior wall	53 (78.6)
Lateral wall	14 (20.0)
Inferior wall	20 (28.6)
Mitral regurgitation severity, n (%)	
Trivial or +1	38 (54.3)
2	22 (31.4)
3	8 (11.4)
4	2 (2.9)
Echocardiography	
EDVi (ml/m ²)	118.5±29.9*
ESVi (ml/m ²)	80.3±29.9*
EF (%)	28.9±4.6*
LVMi (g/m ²)	194.4±52.9*
Wall motion score index (1/1)	2.23±0.2
Cardiac magnetic resonance	
EDVi (ml/m ²)	159.9±47.8
ESVi (ml/m ²)	124.2±43.9
EF (%)	23.5±7.0
LVMi (g/m ²)	107±24.4

Values are presented as mean ± standard deviation for quantitative variables and crude value and percentages (in brackets) for qualitative variables. EDVi – end-diastolic volume index; ESVi – end-systolic volume index; EF – ejection fraction; LVMi – left ventricle mass index; * p<0.001 for 2D echo vs. CMR comparison.

ECG gated sequence. MRI scans were performed while the patients were holding their breath. The imaging parameters were: 19 temporal phases per slice, 24 segments, voxel size 2.1×2.1×8 mm, repetition time 3.0–3.6 ms, echo time 1.2–1.4 ms, flip angle 67°, number of averages 1. To cover the entire left ventricle, slices of 8mm with no interslice gap were planned in short-axis view, perpendicular to the long axis on a four-chamber and a two-chamber view.

The parameters of systolic left ventricle function – LV end-diastolic and end-systolic volume indexes (EDVi and ESVi), EF and LV mass index (LVMi) – were assessed by means of a dedicated workstation (Leonardo, Siemens), using cardiac MRI software (Argus, Siemens). Endocardial and epicardial contours were manually drawn on short-axis images

Table 2. Correlation between the investigated measures in 2D echo and CMR.

Parameter	EDVi (ml/m ²)	ESVi (ml/m ²)	EF (%)	LVMi (g/m ²)
Coefficient of correlation	0.86 (95% CI 0.77; 0.91)	0.83 (95% CI 0.74; 0.89)	0.45 (95% CI 0.24; 0.62)	0.45 (95% CI 0.18; 0.65)
Coefficient of determination	0.73	0.69	0.21	0.2
Concordance correlation coefficient	0.41 (95% CI 0.31; 0.51)	0.46 (95% CI 0.35; 0.56)	0.28 (95% CI 0.14; 0.41)	0.12 (95% CI 0.04; 0.20)
Linear regression equation*	y=-5.60+1.56x	y=4.10+1.34x	y=4.17+0.66x	y=71.76+0.21x
p	<0.0001	<0.0001	0.0001	0.002

*'y' denotes CMR value and 'x' denotes 2D echo value, 'p' denotes statistical significance of linear correlation coefficient; CMR – cardiac magnetic resonance; 2D echo – two dimensional echocardiography; EDVi – end-diastolic volume index; ESVi – end-systolic volume index; EF – ejection fraction; LVMi – left ventricle mass index.

by 2 operators (K.G. and P.U.), who were unaware of the 2D echo results. Papillary muscles and endocardial trabeculations were excluded from LV mass. To correct through-plane motion, basal slices with an incomplete muscular ring were partially contoured.

To compare first and second measurements of 1 observer (intra-observer variability) and to compare the first and the second measurements of 2 independent investigators (inter-observer variability), interclass correlation coefficients were calculated. The results showed almost complete between-measurement correlation with substantial intra-observer agreement (ICC=0.984±0.998), and strong between-measurement correlation with good inter-observer agreement (ICC=0.828±0.995).

2D echo protocol

2D echo exams were performed by 1 operator (J.B.), using a Sonos 7500 scanner coupled with a 2.5 MHz sector transducer (Philips Medical System). EDVi, ESVi and EF were obtained by the biplane Simpson's method. Calculation of the LV mass was performed using the area-length method [17]. To obtain a wall motion score index, the LV was divided into 16 segments as recommended by the American Society of Echocardiography, and a score was assigned to each segment (1 = normal; 2 = hypokinesis; 3 = severe hypokinesis; 4 = akinesis; 5 = dyskinesis) (18). All the segment scores were then added and divided by the number of segments analyzed.

Statistical analysis

The values are presented as means and standard deviation for quantitative variables and percentages for qualitative variables. The normality of the quantitative data was confirmed with the Shapiro-Wilk W test. The logarithmic transformation of all non-normally distributed data enabled the standard approach to be used. The between-group comparison was evaluated using Student's t-test. The correlation between the continuous measures investigated in the 2D echo and CMR was evaluated using Pearson's correlation coefficient and the coefficient of determination (R^2). The relationship between variables was then assessed with a linear regression analysis and concordance correlation coefficients (CCC) were used to evaluate agreement [19]. The between-method comparison included a Bland-Altman analysis where the difference $CMR_{value} - 2D\ echo_{value}$ was plotted

against the mean $(CMR_{value} + 2D\ echo_{value}) / 2$ [20]. In the between-method agreement assessment, a linear regression equation was used to evaluate whether the differences were dependent on the magnitude of measurements. The results of the statistical tests were considered as statistically significant, with $p < 0.05$. The statistical analysis was performed by means of MedCalc 11.1.1.0 (MedCalc, Belgium).

RESULTS

The comparison of left ventricular measures with the use of 2D echo and CMR revealed that ESVi and EDVi were statistically significantly higher, but EF and LVMi were statistically significantly lower by CMR compared to 2D echo ($p < 0.001$ for all). The linear regression analysis revealed a moderate to strong correlation between the 2D echo and CMR measurements. These results are summarized in Table 2. The highest values of the coefficients of determination were found in relation to EDVi ($R^2=0.73$) and ESVi ($R^2=0.69$), and the lowest for EF ($R^2=0.21$) and LVMi ($R^2=0.20$). The coefficients of concordance were also the highest for ESVi (CCC=0.46) and EDVi (CCC=0.41) and the lowest for LVMi (CCC=0.12). The linear regression analysis for the 2D echo and CMR measurements of LV parameters is shown in Figure 1. The Bland-Altman analysis revealed that both LV volumes were statistically significantly underestimated in the 2D echo as compared to the CMR. The effect was seen for all values of EDVi and ESVi. Figure 2A shows the Bland-Altman analysis for EDVi. The mean difference between the CMR and 2D echo was +43.7 ml/m² (95% CI +37.0; +50.5). The lower limit of agreement was -10.8 ml/m² (95% CI -22.4; +0.9) and the upper limit was +98.2 ml/m² (95% CI +88.6; +109.9). Figure 2B shows the Bland-Altman plot for ESVi. The mean difference between the CMR and 2D echo was +41.4 ml/m² (95% CI +35.2; +42.7), with a lower limit of agreement of -8.9 ml/m² (95% CI -19.6; +1.9) and an upper limit of +91.7 ml/m² (95% CI +81.0; +102.5). The between-method agreement for EF is shown in Figure 2C. The mean difference between CMR and 2D echo was -5.7% (95% CI -7.1; -4.2), with the lower limit of agreement equal to -17.4% (95% CI -19.9; -14.9) and an upper limit of +6.0% (95% CI +3.6; +8.5). For EF average values less than 35%, which corresponds to the actual low EF, the 2D echo overestimated the measure, as compared to the CMR. The Bland-Altman analysis also revealed that for the total range of values, LVMi was statistically significantly overestimated in the 2D echo as compared to the

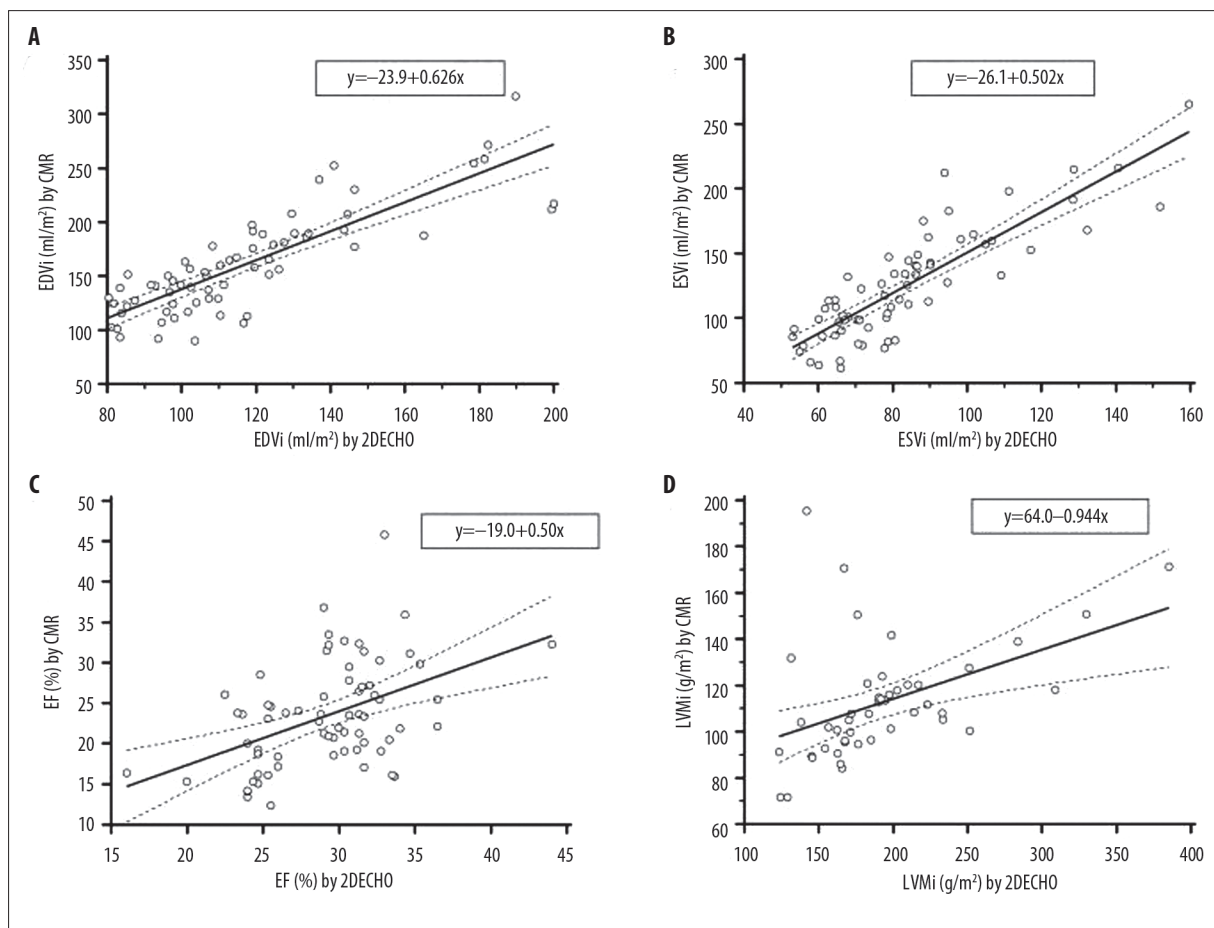


Figure 1. Linear regression analysis for two dimensional echocardiography (2D ECHO) and cardiac magnetic resonance imaging (CMR) of the investigated parameters of left ventricle: (A) end-diastolic volume index (EDVi); (B) end-systolic volume index (ESVi); (C) ejection fraction (EF); (D) left ventricle mass index (LVMI).

CMR (Figure 2D). The mean difference between methods was -79.9 g/m^2 (95% CI -94.1 ; -65.8), the lower limit was -173.4 g/m^2 (95% CI -197.7 ; -149.0) and the upper limit was $+13.5 \text{ g/m}^2$ (95% CI -10.9 ; $+37.8$).

The results of the Bland-Altman regression analysis are summarized in Table 3 and presented in Figure 2. There were noticeable proportional errors; in relation to EDVi, ESVi and LVMI the highest between-method differences were found for the highest measurements and in relation to EF for the lowest values. The results confirmed that the agreement between the 2D echo and CMR were highly dependent on the magnitude of the measurements and that stronger decline in LV function results in higher differences between methods.

DISCUSSION

The aim of the study was to compare CMR and 2D echo in the evaluation of left ventricle function, volumes and mass in patients with severely depressed LV function caused by ischemic heart disease. There are only a few papers comparing these 2 diagnostic modalities in this specific population [10,13,14]. Our results suggest a moderate to strong correlation between 2D echo and CMR measurements. We found that this correlation was highly dependent on the degree of LV dysfunction for all of the parameters analyzed.

Comparison of LV volumes and EF in CMR and 2D echo

We report a strong correlation between 2D echo and CMR in the evaluation of LV volumes. Our results of the Bland-Altman analysis revealed that LV volumes were significantly underestimated by the 2D echo, as compared to the CMR. These results are similar to those obtained in other studies. According to Bellenger et al. the 2D echo underestimated LV volumes (mean difference: EDV: 95 ml; ESV: 133 ml) and the limit of agreement was wider than in our study [6]. Gardner et al. reported that the 2D echo underestimated EDVi by 69 ml/m^2 and ESVi by 35 ml/m^2 [14]. The source of this discrepancy is the different techniques used by these 2 cardiac imaging methods. 2D ECHO is a real-time imaging modality, with better temporal resolution than CMR, which was an advantage in our population with ischemic wall motion abnormalities [12]. On the other hand, CMR has better spatial and contrast resolution, which is especially important in cases with thin LV wall due to ischemia, as in our study [15]. The 2D technique of the evaluation of LV function in ECHO is the source of error from foreshortened views and inaccurate geometric modeling [21]. However, multislice CMR technique, based on the analysis of the stack of short-axis images, is also difficult in patients with aneurysmal LV dilatation, due to poor endocardial definition near the apex, as the result of partial-volume effect [9].

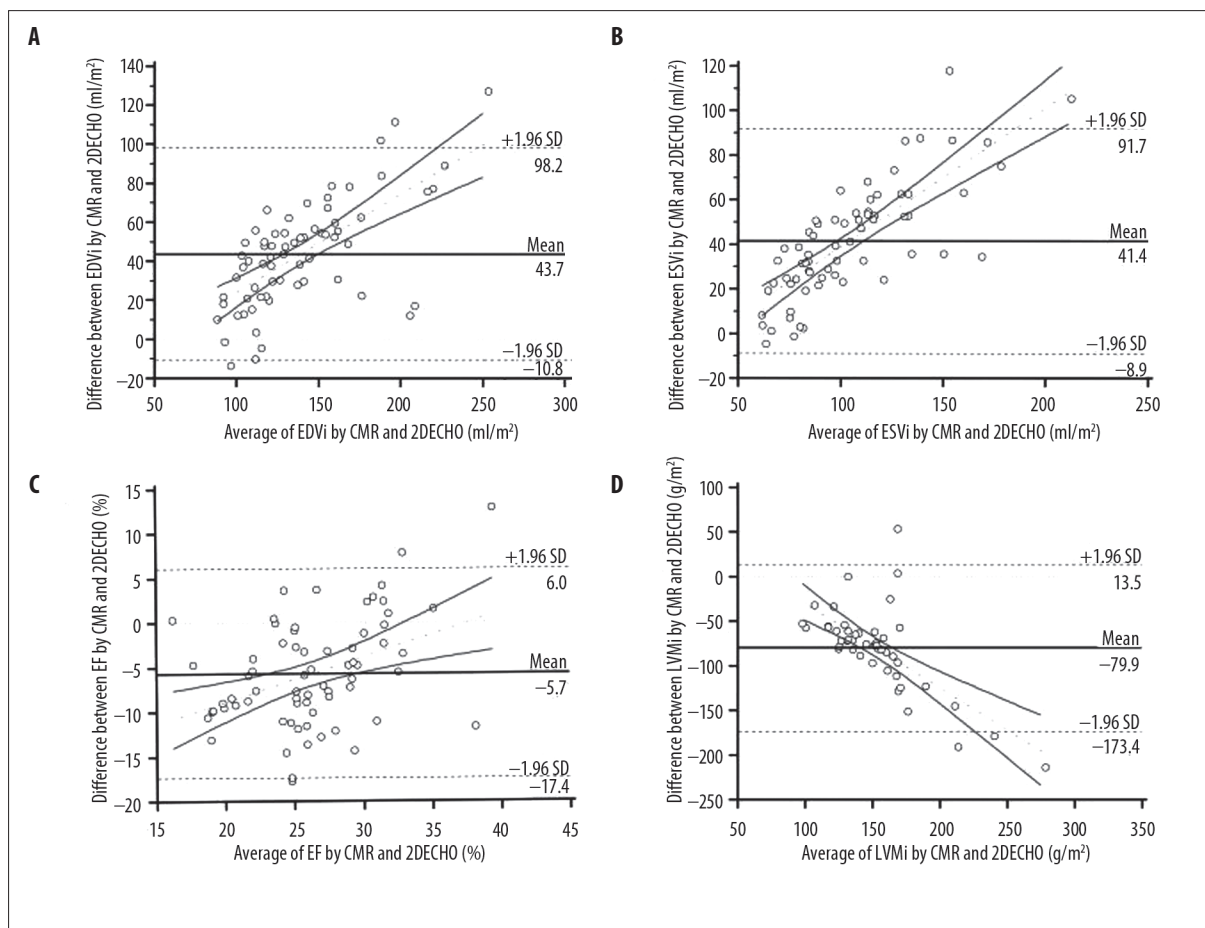


Figure 2. Bland-Altman plot with regression analysis for two dimensional echocardiography (2D ECHO) and cardiac magnetic resonance imaging (CMR) of the investigated parameters of left ventricle: (A) end-diastolic volume index (EDVi); (B) end-systolic volume index (ESVi); (C) ejection fraction (EF); (D) left ventricle mass index (LVMI).

Table 3. Regression analysis for the Bland-Altman method comparison.

Parameters	Regression equation	'p' for the intercept	'p' for the slope
EDVi (ml/m ²)	$y = -23.9 + 0.626x$	0.0009	<0.0001
ESVi (ml/m ²)	$y = -26.1 + 0.502x$	0.012	<0.0001
EF (%)	$y = -19.0 + 0.50x$	<0.0001	0.0008
LVMI (g/m ²)	$y = 64.0 - 0.944x$	0.011	<0.0001

EDVi – end-diastolic volume index, ESVi – end-systolic volume index, EF – ejection fraction, LVMI – left ventricle mass index.

The agreement between 3DECHO and CMR in the literature seems to be better. In a single-centre study carried out by Sugeng et al, the 3DECHO only slightly underestimated LV volumes (5–6 ml, 95% limit of agreement) [13]. However, in a multi-centre validation paper by Mor-Avi et al, the 2D echo-derived volumes, as compared to the CMR, showed significant negative biases – (–29% for EDV and –27% for ESV) [16].

In our study, the correlation between the CMR and 2D echo in EF ($R^2=0.21$) was weaker than for LV volumes, but was still statistically significant. The mean difference between

the CMR and the 2D echo was –5.7%. These values are consistent with those described in the literature. The 2D echo overestimates EF by 10%, according to Nowosielski [22] and by 4% according to Gardner [14]. Sugeng et al reported an agreement between CMR and 3DECHO at a level of 8% [13]. EF evaluation in CMR and 2D echo depends on the accuracy of LV ESV and EDV measurements. Even small differences in volume measurements may result in increased error of LV EF estimates [8]. In our study, LV function and mass in the 2D echo were calculated using the Simpson rule [17]. According to Bellenger, this method is the most accurate for volumetric LV quantification as

compared to the CMR [9]. However, this method is less reliable when the geometrical model does not correspond to the true ventricular cavity anatomy in patients with LV ischemic remodeling, as in our study.

The CMR software we used did not allow for the correction of the LV contours on the long axis, which was a source of error. To correct through-plane motion, basal slices with an incomplete muscular ring of less than 75% were only partially contoured. According to Kirschbaum et al, the addition of the long-axis to the short-axis contours during the CMR post-processing limits the extent of the volume at the base of the heart, and reduces inter-study variability [23]. We found that tracing LV contours in CMR in the regions of LV apex in patients with LV aneurysm was difficult due to the low contrast resolution between blood pool and muscle. We assume that regional wall-motion and wall thickness abnormalities due to ischemia impact the accuracy of endocardial contouring in both CMR and 2D ECHO, which could be a source of the discrepancy between the 2 methods. As we examined the population with severe LV dysfunction, the differences between the 2 methods became larger compared to other studies.

Comparison of LV mass in CMR and 2D echo

In our study, the correlation between the CMR and 2D echo for cardiac mass measurements was moderate. LVMI was significantly overestimated in 2D echo as compared to CMR. We have described a significant discrepancy between these 2 methods in calculating LV mass ($R^2=0.20$). The well-recognized formula used in 2D ECHO to calculate LV mass relies on a geometric assumption of uniform chamber size and shape [18]. LV mass cannot be measured properly in heavily dilated hearts by means of 2D echo because they do not fit the pyramidal scan volume. Previous authors have highlighted the fact that the accuracy of LV mass measurements in 2D echo is limited due to difficulties in obtaining anatomically corrected apical views [24–26]. This may result in the foreshortening of the LV long axis, especially in patients with a dilated LV. In a study carried out on 83 patients (33 of them with wall motion abnormalities), Pouleur et al. found a reasonably good correlation between echocardiography and CMR. However, only 14% of the patients in that study had an EF of 36% [12]. In a study covering 25 patients, Chuang et al. reported a bias of 16g between the 2D echo and the CMR [25]. Caiani et al. found that 2D echo underestimated LV mass comparing to CMR [26]. He postulated the need for further investigations of patients with LV dilatation and aneurysms.

The agreement between the 2D echo and the CMR relied on the number of imaging planes. Taking into account slice thickness and interslice distance, LV mass can be obtained by multiplication of volume with the specific density of the myocardium [7]. However, we examined a population of patients after myocardial infarction, with a large area of myocardial scar, which has a different specific density than healthy myocardium. This could affect the accuracy of LV mass calculation in our study.

To decrease the measurement error, endocardial contouring of CMR short axis images in our study was performed by a single operator. Papillary muscles and LV myocardial trabeculae were included into the LV volume, which increases

measurement reproducibility; however, this can overestimate LV volumes and decrease LV mass [27–30].

A medium-field CMR unit was used in this study (1.0 T). In the literature, we were unable to find any comparison between this type of scanner and the commonly used 1.5 T CMR systems in the assessment of LV function. The decreased field strength, which could decrease the signal-to-noise ratio, may be a study limitation. Furthermore, the 8mm slice thickness could result in partial volume effects.

Differences between CMR and 2D echo by degree of the LV dysfunction

We found that the agreement between CMR and 2D echo in the evaluation of the LV volumes was highly dependent on the magnitude of the measurements. The highest between-method difference was found for the highest volumes. We find this result to be clinically important, taking into account the fact that the 2D echo underestimates LV volumes in comparison to the CMR. This means that, in patients with severe ischemic LV dilatation and aneurysm, LV volume as measured by 2D echo should be analyzed with special caution, as the difference between the 2 methods could be at its highest. Similarly, if the severely damaged LV was examined using 2D echo, the latter overestimates EF proportionately with greater degree of LV damage. Again, this result is clinically important. In patients with the most severe ischemic LV dysfunction, the EF may be even lower than a value obtained using the 2D echo [31].

A similar relationship was found for LV mass. There were noticeable proportional errors between both methods, depending on the LVMI. The increase in the mass of LV correlated well with the increase of LV dysfunction and we found that the agreement between the 2D echo and CMR was highly dependent on the degree of LV dysfunction – the highest differences existed in patients with the highest LV myocardial mass.

This problem is not really recognized in the literature. We were able to find only a few studies analyzing the correlation between CMR and 2D echo on the basis of the degree of LV dysfunction. Gardner et al. found that the differences between the 2 methods in the measurement of LV volumes increased with lower EF values, with a threshold of 46%. However, inter-modality differences were not statistically dependent on the EF subgroup [14,32]. In an article comparing CMR and 2D echo in patients with acute MI, Nowosielski suggested that slight myocardial impairment (EF >55%) might be difficult to detect by 2D echo; thus, correlation between transesophageal echocardiography and CMR might be more significant in a more severely injured myocardium [22]. Contrary to this, in a multi-centre study validating the 3D echo *vs.* the CMR, Mor-Avi et al. found a good agreement between the CMR and the 3D echo in the measurement of EF and LV volumes in patients with an EF more than 35% [16]. With the exception of works by Bellenger (the mean EF by CMR was 30%) and Mor-Avi (a wide range of EF with the lowest values starting from 20%), LV function was only moderately impaired in the other papers published (mean EF from 45% to 55%) [9,16]. Moreover, the population described with ischemic heart failure was also smaller than ours.

Our study has several limitations. The size of evaluated sample is limited, and it might require more data to confirm our results. For a comprehensive study, an experimental invasive validation would be important, and the lack of such validation is a limitation of our results.

CONCLUSIONS

There is moderate to strong correlation between CMR and 2D echo in the assessment of LV function parameters and mass in patients with severe ischemic left ventricular dysfunction. Unfortunately, between-method agreement strongly depends on the degree of LV dysfunction. Differences in LV indices are higher in patients with more severe LV dysfunction. The results of assessment of the severely damaged LV obtained by the use of 2D echo should be interpreted with caution.

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