




## Original Article



# Comparison of Left Ventricular Volumes Measured by 3DE, SPECT and CMR

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### Conflict of Interest

The authors have no financial conflicts of interest.

## ABSTRACT

**BACKGROUND:** Information regarding left ventricular (LV) volume and left ventricular ejection fraction (LVEF) has major diagnostic and prognostic value when assessing patients after ST-elevation myocardial infarction (STEMI). We aimed to investigate the agreement between measurement of LV volumes and LVEF by three-dimensional echocardiography (3DE), single-photon emission computed tomography (SPECT) and cardiac magnetic resonance (CMR) imaging in patients in a stable phase after STEMI.

**METHODS:** Fifteen patients underwent examinations by 3DE, SPECT and CMR three months after STEMI.

**RESULTS:** There was a significant bias in end-diastolic volume (EDV) measured by 3DE (−64 mL,  $p < 0.001$ ) and SPECT (−55 mL,  $p < 0.001$ ) compared with that measured by CMR. This was also the case for end-systolic volume (ESV) measured by 3DE (−36 mL,  $p < 0.001$ ) and SPECT (−28 mL,  $p < 0.001$ ). No significant differences were found between 3DE and SPECT for EDV or ESV. However, LVEF did not differ between the three methods. The agreement between all three methods was moderate (intra-class correlation coefficient [ICC] = 0.44) for LV volume and good for LVEF (ICC = 0.72).

**CONCLUSIONS:** LV volumes assessed by 3DE did not differ from SPECT, and despite larger LV volumes by CMR, measurements of LVEF showed good agreement between all three methods.

**Keywords:** Left ventricular function; Myocardial infarction; Three-dimensional echocardiography; Magnetic resonance imaging; Single-photon emission-computed tomography

## INTRODUCTION

It has been shown that increased cardiac volume after a myocardial infarction (MI) is associated with increased mortality<sup>(1,2)</sup> and that the left ventricular ejection fraction (LVEF) is an important determination of survival in patients following MI.<sup>(3,4)</sup> Therefore, information regarding the left ventricular (LV) volume and LVEF after an MI is of great importance for determining the prognosis of patients. Moreover, increased prognostic information can guide further treatment and secondary preventative measures.<sup>(5,7)</sup> LV volume and LVEF can be measured using several techniques, including three-dimensional echocardiography (3DE),

single-photon emission computed tomography (SPECT) and cardiac magnetic resonance imaging (CMR) depending on the availability of equipment and expert knowledge. CMR is considered the “gold” standard for measuring LV volume and LVEF,<sup>8,42</sup> but because all three methods (3DE, SPECT and CMR) are used, both in clinical practice and in research, we sought to determine the level of agreement between them. Previous studies have compared pairs of the above-mentioned methods.<sup>13-18</sup> To the best of our knowledge only one study has compared all three methods with regard to these variables.<sup>19</sup> That study used the radionuclide thallium and included only patients with a relatively well-preserved LVEF ( $49\% \pm 13\%$ ). The aim of the present study was to assess the level of agreement between 3DE and SPECT as well as CMR measurements of LV volume and LVEF in patients with prior ST-elevation myocardial infarction (STEMI).

## METHODS

### Study population

The study population was recruited via a randomized study on patients with a first-time acute STEMI treated with percutaneous coronary intervention, performed at the Karolinska University Hospital.<sup>20</sup> From this study population of 89 patients, 15 patients completed interpretable examinations on the same day with 3DE, SPECT and CMR and were included in the present study. Their mean age was  $63 \pm 9$  years (mean  $\pm$  SD), range 43–79 years, including two women. Their mean height was  $177 \pm 6$  cm and mean weight  $86 \pm 9$  kg. The STEMI was caused by occlusion of the left anterior descending artery in seven (47%) of the patients, the right coronary artery in six (40%) and in the left circumflex artery in two (13%).

Written informed consent was given by all patients included in the study, which was approved by the local hospital radiation protection committee and by the Regional Ethics Review Board in Stockholm.

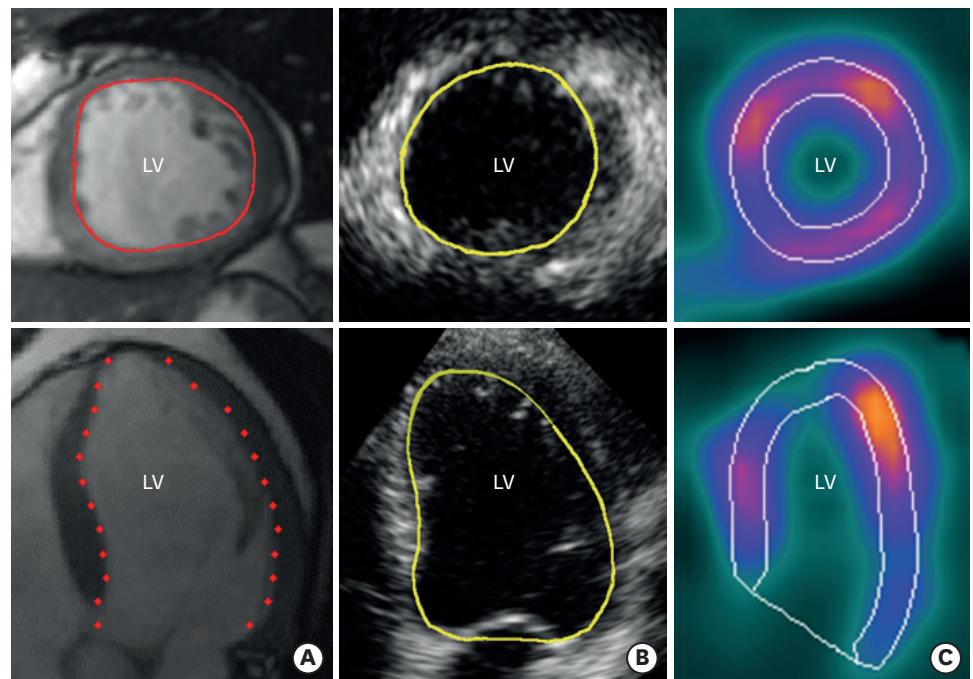
### Data collection and analysis

All 15 patients underwent examinations by 3DE, SPECT and CMR on the same day, 90 ( $\pm 10$ ) days post infarction. Data acquisition and analyses were performed blinded to all other data by experts in each field. The intra- and inter-observer reliability was studied in 10 randomly selected patients. The volume calculations for these patients were performed twice by the same observer, and once by a second observer. The two observers were blinded to each other's findings. Examples of endocardial tracings by all three modalities are presented in **Figure 1**.

### 3DE

Transthoracic 3DE examinations were performed by an experienced sonographer using a commercial ultrasound scanner (Philips iE33, Philips Medical Systems, Andover, MA, USA). The images were obtained using a 3DE transducer (X3-1, Philips) with the patient in the left lateral decubitus position. The images were acquired from the apical transducer position through four or seven consecutive cardiac cycles during breath-hold, generating a full-volume pyramidal data set with an average frame rate of 21/s.

The 3DE data were analysed offline using the semi-automatic software QLab 8.1 (Philips). The long-axis and rotational angle of two orthogonal planes were adjusted to yield a four-chamber view and a two-chamber view. The end-diastolic (first frame) and end-systolic (smallest cavity) frames were identified and five points were then manually placed in the



**Figure 1.** Examples of short-axis (top) and long axis (bottom) cut planes with endocardial tracings in images acquired by CMR (A), 3DE (B) and SPECT (C) demonstrating the difference in the ability to identify LV trabeculations. All images are acquired from the same study patient. Traces are somewhat enhanced to increase readability. 3DE: three-dimensional echocardiography, CMR: cardiac magnetic resonance imaging, LV: left ventricle, SPECT: single-photon emission computed tomography.

two frames adjacent to the lateral, medial, anterior and inferior part of the mitral valve annulus and one point in the apex. Subsequently, the endocardial surface was outlined using an automated contour-detection algorithm. The surface was examined in multiple sagittal and transverse planes and was manually adjusted as necessary. The LV outflow tract (LVOT) was excluded from the volume calculations, but papillary muscles and trabeculations were included in the LV volumes when visible. The volume enclosed by the generated surface was computed by the program, yielding the EDV and ESV for each data set. LVEF was calculated using the standard formula.

### SPECT

Patients received an injection of 600 Mbq of  $^{99m}\text{Tc}$  sestamibi (Cardiolite<sup>®</sup>, Lantheus MI UK Ltd) intravenously at rest. The patients had not eaten or drunk any caffeine-containing beverages for 4 h prior to the injection. ECG-gated images were acquired 1–4 h after the injection using a dual-head gamma camera (DST-XL, Sopa Medical Vision, Bue Cedex, France). The patients were placed in the supine position and imaged in steps of  $5.6^\circ$  using a  $64 \times 64$  matrix, with a typical size of  $5 \times 5$  mm and a slice thickness of 5 mm. A 20% energy window and 140 keV photo peak were used. Images were gated at eight frames per cardiac cycle using an R-wave trigger, and 60 s per projection over a  $180^\circ$  orbit. Total acquisition time was 16 min. No attenuation or scatter correction was applied. The frame rate of the gated images varied with the heart rate of the subjects. The heart rate during SPECT was not recorded, however using the heart rate data from the 3DE studies the average frame rate was estimated to 8.1 /s.

The SPECT images were reconstructed and analysed offline on a Vision workstation (IBM RS/6000) using the automated and commercially available software program Quantitative

Gated SPECT (QGS; Cedars-Sinai Health System, Los Angeles, CA, USA). Reconstruction was performed with a filtered back-projection using a Wiener filter with a power of 4.5. The reconstructed voxel size was  $3 \times 3 \times 3$  mm.

Papillary muscles were included in the LV volume. The LVOT was excluded from the LV volume, since it is not visible with the SPECT technique.

### CMR

The CMR studies were performed using a 1.5 Tesla CMR system (Signa Excite Twin Speed, General Electric Healthcare, Waukesha, WI, USA) and a phased-array radiofrequency receiver (8-channel) cardiac coil. ECG-gated images were acquired during end-expiratory breath holding. The image protocol included scout images, localization of the short axis and then coverage of the whole LV with retrospectively gated cine steady-state free precession images. Ten to 12 short-axis views and 2-, 3- and 4-chamber views were obtained. The following scanner parameters were used: echo time (TE) 1.58 ms, repetition time (TR) 3.61 ms, flip angle  $60^\circ$ , 25 phases, 8-mm slice, matrix  $226 \times 226$ . All CMR images were analysed offline using semi-automatic freely available segmentation software (Segment V.1.8 R1405).<sup>21)</sup> In the short-axis images, end-systolic volume (ESV) and end-diastolic volume (EDV) were measured in the phase that had the largest and smallest LV volumes, respectively. The LVOT, papillary muscles and trabeculations were included in the LV. The basal short axis slice was identified by simultaneously observing long axis views of the LV while performing the tracings, specifically the three chamber view where the LVOT is visible.

### Statistical analysis

To evaluate the agreement between the three methods, Bland–Altman plots were generated. One-way repeated-measures analysis of variance (ANOVA) was used to determine whether there were any systematic differences between the methods. An intra-class correlation coefficient (ICC) was calculated to evaluate the agreement between the methods for measurement of LV volume and LVEF. The strength of agreement was assessed according to guidelines proposed by Landis and Koch,<sup>22)</sup> which define agreement as poor (ICC < 0.20), fair (ICC 0.21–0.40), moderate (ICC 0.41–0.60), good (ICC 0.61–0.80), or very good (ICC > 0.80). Linear regression analysis was performed to evaluate the correlation between LV volumes and LVEF assessed by CMR and SPECT and CMR and 3DE. No linear regression was performed between SPECT and 3DE, because neither of these methods is considered gold standard. The correlation coefficient  $\beta$  was used for the linear regression analysis. The following guidelines proposed by Chan<sup>23)</sup> were used to assess the strength of the linear relationship: poor ( $\beta < 0.3$ ), fair ( $\beta 0.3–0.5$ ), moderately strong ( $\beta 0.6–0.8$ ), and very strong ( $\beta \geq 0.8$ ). To study the intra-/inter-observer reliability, the ICC and the coefficient of variation (CV) were calculated. One-way repeated-measures ANOVA was also used to analyse whether there were any systematic differences between the measurements. The level of significance was set at  $p < 0.05$ . Statistical analysis was performed using Statistica (Statsoft Inc., version 9.0–10.0, Tulsa, OK, USA) and IBM SPSS Statistics Version 24 (IBM Corp., Armonk, NY, USA).

## RESULTS

LV volumes and LVEF measured by 3DE, SPECT and CMR are presented in **Table 1**. **Figures 2–4** show the agreement between the three methods for measurements of ESV, EDV and LVEF.

**Table 1.** LV volumes and LVEF for each method, presented as mean  $\pm$  SD (n = 15)

	CMR	SPECT	3DE
EDV (mL)	191 $\pm$ 42	137 $\pm$ 41*	127 $\pm$ 26*†
ESV (mL)	105 $\pm$ 40	77 $\pm$ 36*	68 $\pm$ 22*†
EF (%)	47 $\pm$ 11	46 $\pm$ 12	47 $\pm$ 8

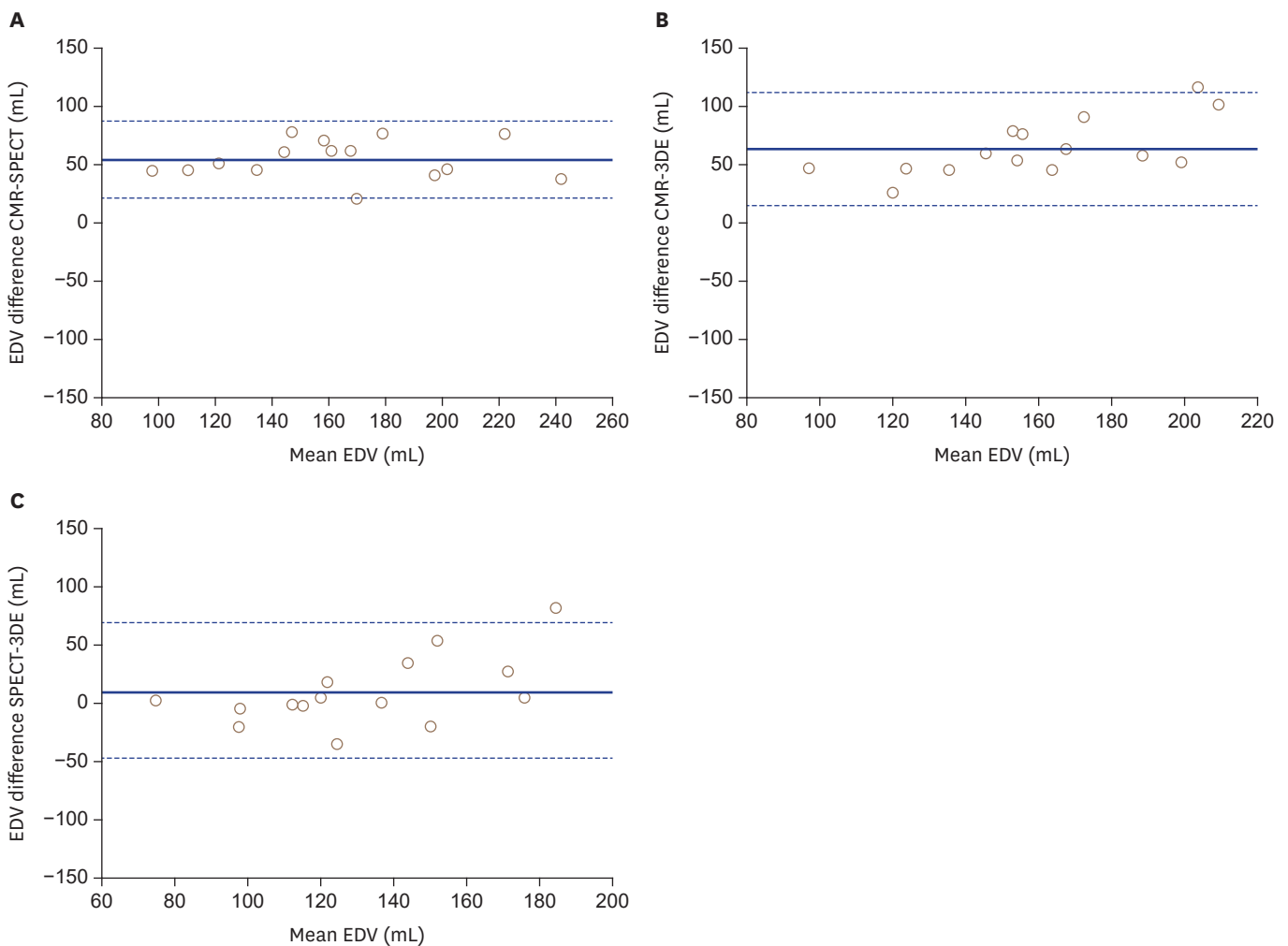
3DE: three-dimensional echocardiography, CMR: cardiac magnetic resonance, EDV: end-diastolic volume, EF: ejection fraction, ESV: end-systolic volume, LV: left ventricular, LVEF: left ventricular ejection fraction, SPECT: single-photon emission computed tomography.

\*p < 0.001 for SPECT and 3DE versus CMR; †p > 0.1 for 3DE versus SPECT.

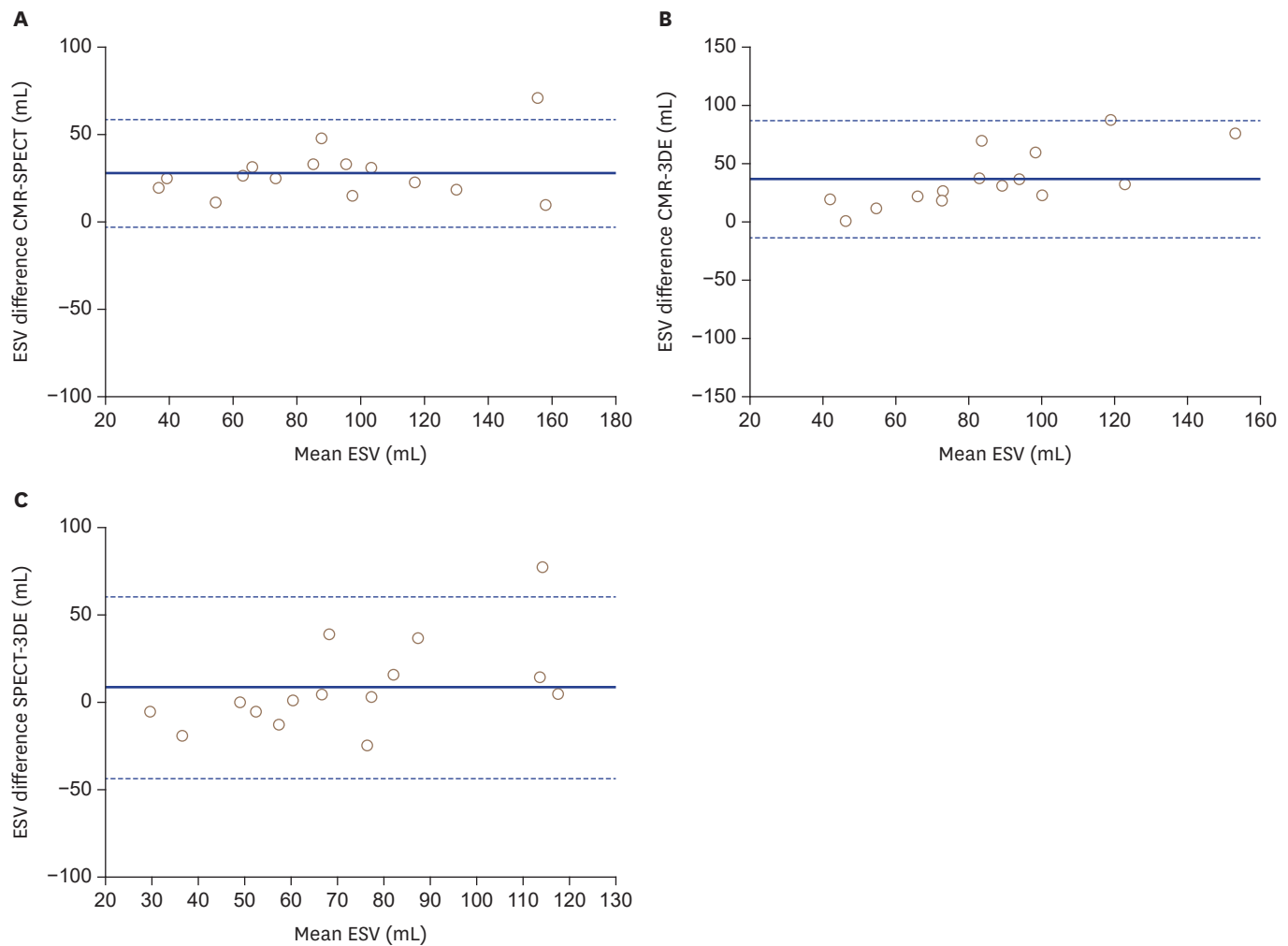
### End-diastolic volumes

EDV measured by the three methods differed significantly (p < 0.001). Both SPECT and 3DE underestimated EDV (55  $\pm$  33 mL, p < 0.001 and 64  $\pm$  47 mL, p < 0.001, respectively), compared with CMR (**Figure 2A, B**). No significant difference was demonstrated between SPECT and 3DE (9  $\pm$  55 mL, p = 0.23) (**Figure 2C**).

The agreement was good between SPECT and 3DE (ICC = 0.66) and moderate between CMR and SPECT (ICC = 0.49). Agreement between all three methods was moderate (ICC = 0.43).



**Figure 2.** Bland–Altman plot of agreement between CMR and SPECT (A), CMR and 3DE (B) and SPECT and 3DE (C) for measurement of EDV. The solid line represents the mean difference, and the dashed lines represent the 95% confidence interval. 3DE: three-dimensional echocardiography, CMR: cardiac magnetic resonance imaging, EDV: end-diastolic volume, SPECT: single-photon emission computed tomography.



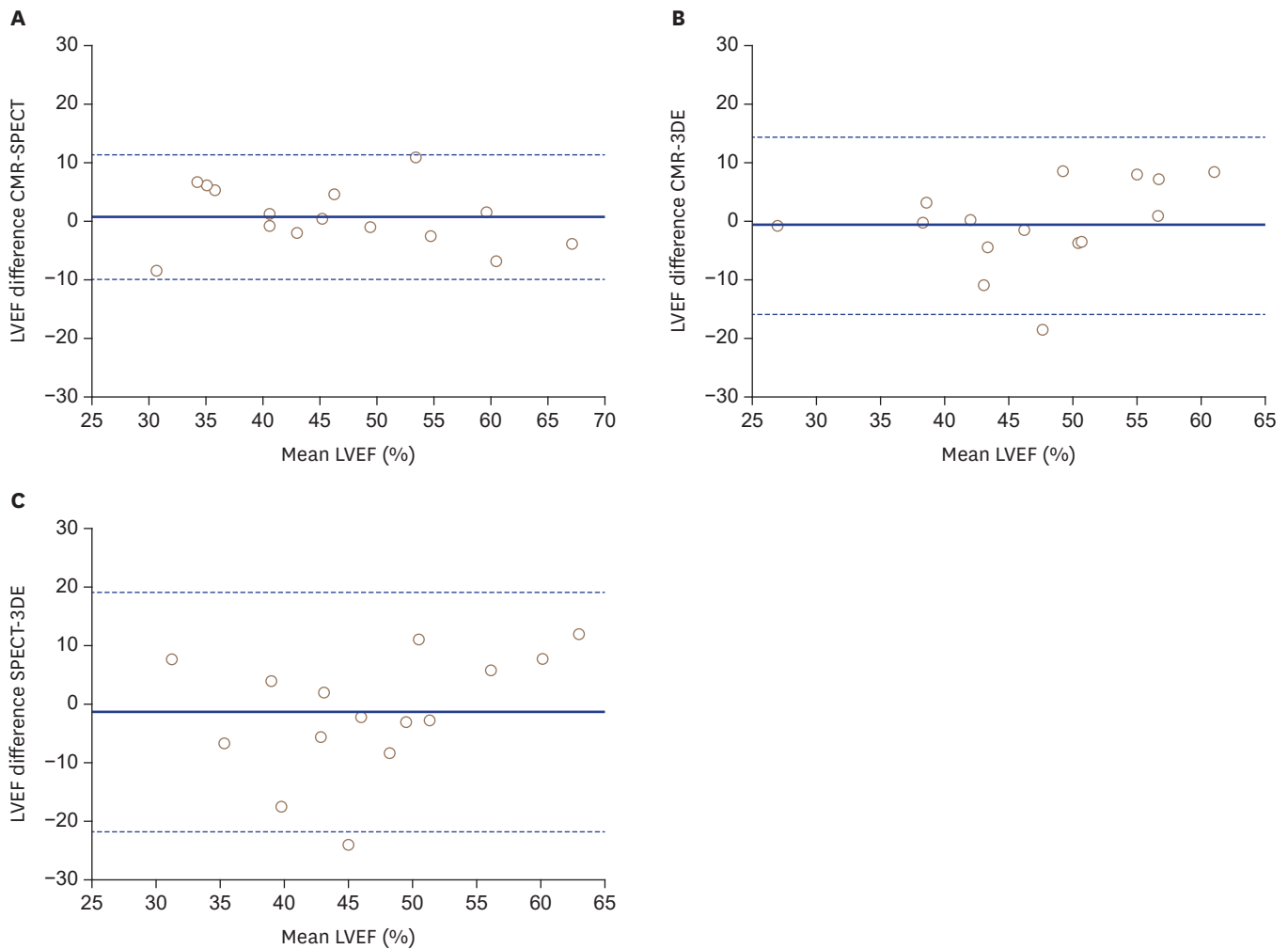
**Figure 3.** Bland–Altman plot of agreement between CMR and SPECT (A), CMR and 3DE (B) and SPECT and 3DE (C) for measurement of ESV. The solid line represents the mean difference, and the dashed lines represent the 95% confidence interval. 3DE: three-dimensional echocardiography, CMR: cardiac magnetic resonance imaging, ESV: end-systolic volume, SPECT: single-photon emission computed tomography.

and that between CMR and 3DE was fair (ICC = 0.28). The linear regression analysis showed that for EDV, the correlations between CMR and SPECT and between CMR and 3DE were very strong ( $\beta = 0.92$ ,  $p < 0.001$ , and  $\beta = 0.84$ ,  $p < 0.001$ , respectively).

### End-systolic volumes

There was a significant difference between the three methods ( $p < 0.001$ ) for measurement of ESV. Both SPECT and 3DE underestimated ESV ( $28 \pm 30$  mL,  $p < 0.001$  and  $36 \pm 49$  mL,  $p < 0.001$ , respectively), compared with CMR (**Figure 3A, B**). No significant difference was demonstrated between SPECT and 3DE ( $9 \pm 51$  mL,  $p = 0.22$ ) (**Figure 3C**). The agreement between CMR and SPECT and between SPECT and 3DE was good (ICC = 0.73 and 0.62, respectively), and that between CMR and 3DE was moderate (ICC = 0.44). The agreement between all three methods was moderate (ICC = 0.60). The linear regression analysis showed very strong correlations between CMR and SPECT and between CMR and 3DE ( $\beta = 0.93$ ,  $p < 0.001$ , and  $\beta = 0.82$ ,  $p < 0.001$ , respectively).





**Figure 4.** Bland-Altman plot of agreement between CMR and SPECT (A), CMR and 3DE (B) and SPECT and 3DE (C) for measurement of LVEF. The solid line represents the mean difference, and the dashed lines represent the 95% confidence interval. 3DE: three-dimensional echocardiography, CMR: cardiac magnetic resonance imaging, LVEF: left ventricular ejection fraction, SPECT: single-photon emission computed tomography.

### Left ventricular ejection fraction

There was no significant difference between the LVEF measured by the three methods ( $p = 0.82$ ) (Figure. 4A-C). The mean difference between CMR and SPECT for LVEF was  $0.75 \pm 10\%$ , that between CMR and 3DE was  $-0.56 \pm 15\%$ , and between SPECT and 3DE was  $-1.3 \pm 20\%$ . The agreement was very good between CMR and SPECT (ICC = 0.89), good between CMR and 3DE and between all three methods (ICC = 0.71 and 0.72, respectively), moderate between SPECT and 3DE (ICC = 0.51). The linear regression analysis showed that the agreement for LVEF was very strong between CMR and SPECT ( $\beta = 0.90$ ,  $p < 0.001$ ) and moderately strong between CMR and 3DE ( $\beta = 0.72$ ,  $p = 0.003$ ).

### Intra-/inter-observer reliability

#### 3DE

There was no significant difference in the intra-observer reliability of measurements of ESV ( $p = 0.73$ ). However, there was a significant difference between the inter-observer reliability of ESV measurements ( $p = 0.04$ ). No significant difference was observed between the intra- and inter-observer reliability of measurements of EDV ( $p = 0.54$  and  $0.10$ , respectively) or

**Table 2.** Intra- and inter-observer reliability for 3DE, SPECT and CMR

	Intra-observer		Inter-observer	
	ICC	CV (%)	ICC	CV (%)
<b>3DE</b>				
ESV	0.95	7.44	0.54	26.6
EDV	0.92	7.34	0.66	14.2
EF	0.86	8.27	0.55	15.3
<b>SPECT</b>				
ESV	1.00	2.0	1.00	1.76
EDV	1.00	1.46	1.00	1.57
EF	1.00	1.55	1.00	1.20
<b>CMR</b>				
ESV	1.00	2.91	0.99	3.60
EDV	0.99	1.62	0.99	1.96
EF	0.99	2.96	0.99	2.90

3DE: three-dimensional echocardiography, CMR: cardiac magnetic resonance imaging, CV: coefficient of variation, EDV: end-diastolic volume, ESV: end-systolic volume, ICC: intra-class correlation, LVEF: left ventricular ejection fraction, SPECT: single-photon emission computed tomography.

LVEF ( $p = 0.40$  and  $0.13$ , respectively). The intra-/inter-observer reliability of 3DE as assessed by ICC and CV is shown in **Table 2**. The intra-observer reliability was very good for all the studied variables (ICC =  $0.86$ – $0.95$ ) and the CVs ranged from  $7.3\%$  to  $8.3\%$ . Inter-observer reliability was good for EDV (ICC =  $0.70$ ), and moderate for ESV and LVEF (ICC =  $0.54$  and  $0.41$ , respectively). The CVs ranged from  $14\%$  to  $27\%$ .

#### SPECT

There was no significant difference between the intra- and inter-observer reliability of measurements of ESV ( $p = 0.37$  and  $0.32$ ), EDV ( $p = 0.35$  and  $0.86$ ) or LVEF ( $p = 0.39$  and  $0.10$ ), respectively. The ICC and CV for SPECT for intra-/inter-observer reliability are shown in **Table 2**. Both intra- and inter-observer reliability was very good for all the studied variables (ICC =  $0.88$ – $1.00$ ). The CV ranged from  $1.5\%$  to  $2.0\%$  for intra-observer reliability and from  $1.2\%$  to  $1.8\%$  for inter-observer reliability.

#### CMR

There was no significant difference between the intra- and inter-observer reliability of measurements of ESV ( $p = 0.83$  and  $0.81$ , respectively), EDV ( $p = 0.58$  and  $0.58$ , respectively) or LVEF ( $p = 0.56$  and  $0.60$ , respectively). The ICC and CV for intra-/inter-observer reliability of CMR are shown in **Table 2**. Both intra- and inter-observer reliability were very good for all the studied variables (ICC =  $0.99$ – $1.00$ ). For intra-observer reliability, the CV ranged from  $1.6\%$  to  $3.0\%$ , while that for inter-observer reliability ranged from  $2.0\%$  to  $3.6\%$ .

## DISCUSSION

This study showed that in post-STEMI patients, there was a significant difference between the three imaging methods for measurements of LV volumes, but not for LVEF. Both 3DE and SPECT underestimated the LV volumes compared with CMR. Although the degree of underestimation was somewhat less by SPECT, there was no significant difference between LV volumes assessed by SPECT and 3DE.

Underestimation of LV volumes by 3DE and SPECT compared with CMR has been reported previously.<sup>16)17)19)24)25)</sup> One explanation for the underestimation of volume by SPECT is that the



LVOT is not included in the calculation with SPECT, whereas with CMR, the LVOT is normally included in the LV volume. Also, the higher image resolution of CMR allows for better visualization of the border between endocardial trabeculations and the LV cavity.<sup>17)24)26)27)</sup> Previous studies have concluded that the underestimation of LV volumes by SPECT compared with CMR is greater in patients with smaller LV volumes, because of problems with spatial resolution and scatter.<sup>19)</sup> No such pattern could be seen in this study; however, the number of patients included in our study may not be adequate to detect such a difference.

Similarly, the underestimation by 3DE could be explained by differences in image quality and in the volume calculations. The trabeculations are not always included in the 3DE volume calculations, because the spatial resolution is inadequate to allow differentiation of the myocardium from smaller trabeculations. In this study, the LVOT was not included in the 3DE volume calculations, but, when visible, trabeculations and papillary muscles were included. As seen in **Figure 1** trabeculations are more discernible in the CMR image than in the other two modalities. One of the problems with using 3DE clinically is that the image quality is dependent on the patient's body composition, the acoustic window and on the experience of the operator.<sup>28)</sup> One way to increase the spatial resolution in 3DE images is by using contrast agents, thereby improving delineation of the endocardial border.<sup>16)29)30)</sup> Studies comparing measurement of LV volumes by 3DE and CMR have shown that volume measurements are equivalent to those measured by CMR when they are calculated from contrast-enhanced 3DE, whereas LV volumes acquired from non-contrast-enhanced 3DE are slightly underestimated compared with CMR.<sup>29)31)</sup> Clearly, the image quality is a major factor in the observed differences in acquired volumes.

In a study by Chan et al.<sup>19)</sup>, the degree of underestimation of LV volumes compared with CMR was less severe with 3DE than with SPECT, whereas in this study the underestimation was greater with 3DE than with SPECT. One reason for this could be the use of different analysis software, since they performed volumetric analysis using software that includes LVOT in the contour tracing.

The high reproducibility of measurements in SPECT was most likely because we used the automatic software QGS, leading to a reduced risk of subjective analysis. Similar findings regarding intra-/inter-observer reliability in SPECT have been reported in other studies.<sup>19)</sup> The weaker inter-observer reliability for 3DE was probably because the analysis was semi-automatic, which increased the risk of subjective influence. In other studies, the inter-observer reliability for 3DE has been slightly better than that observed in our study.<sup>19)32)</sup> One reason for the poorer inter-observer reliability for 3DE in our study could be the factors discussed above, i.e., that the technique is operator dependent and that we analysed a smaller number of subjects.

For CMR, the results in our study are in line with those of other studies. Bellenger et al.<sup>33)</sup> reported very good intra-/inter-observer reliability for measurements of LV volume and LVEF ( $r = 0.95-0.99$ ). Another study by Sonesson et al.<sup>34)</sup> also found the intra-/inter-observer reliability for LV volumes and LVEF to be good (CV = 6% and 3%, respectively). Despite the volume calculations in CMR involving manual delineation using a semi-automatic software program, the intra- and inter-observer reliability seem to be similar to those for SPECT, where an automated software program is used to perform the volume calculations. This is likely because of the technique's high spatial resolution and the excellent contrast between blood and myocardium, which makes it easier to define the endocardial border.

Clearly the differences in LV volume determinations are not only caused by inherent differences between the imaging modalities. The specific analysis software used may also contribute to the discrepancies, which in turn may limit the generalization when other software is applied. One limitation with this study was that the study population was small. Some patients were excluded because of poor image quality in the echocardiographic study, and possibly a larger number of 3DE images would have been interpretable if a contrast agent had been used for the 3DE examination.

A strength of this study is that we used the radionuclide technetium, instead of thallium. Technetium-labeled substances have several advantages compared with thallium-labeled ones, including a shorter half-life (6 h compared to 72 h for thallium), which reduces the patient's radiation exposure. Technetium is also less likely to cause attenuation, because of its lower photon energy. Furthermore, thallium has been reported to have higher variability than technetium.<sup>9)</sup> Another strength with this study is that all three examinations were carried out on the same day, in order to minimize the risk for possible physiological day-to-day changes.

### Conclusion

Comparison of 3DE and SPECT with CMR showed that there is a significant difference between the methods for measurement of the LV volumes, and that both 3DE and SPECT underestimate the LV volumes compared with CMR. Despite the differences between the three methods for the measurement of LV volumes, the determination of LVEF showed good agreement between all three methods.

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