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ORIGINAL PAPER

Cardiovascular magnetic resonance of cardiac morphology and function: impact of different strategies of contour drawing and indexing

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Abstract

Background Cardiovascular magnetic resonance (CMR) is the gold standard for the quantitative assessment of cardiac volumes, mass and function. There are, however, various strategies for establishing endocardial borders, the cardiac phase used for measurements and the body dimensions used for indexing these results. The aim of the study was to assess the impact of different strategies on reference values.

Methods and results 362 healthy volunteers (190 men, mean age 51 ± 13 years) underwent a standard CMR protocol. Left ventricular end-diastolic (LV-EDV) and end-systolic (LV-ESV) volumes and LV mass (LV-M) were measured at end systole and end diastole in SSFP sequences using two methods, one of which included papillary muscles and trabecular tissue in the LV-M ("include" approach), while the other excluded this tissue ("exclude" approach). There was a strong correlation between the results for LV volumes and LV ejection fraction (LV-EF) between the "include" and the "exclude" approach, while the mean values were different: LV-EDV: 149.7 ± 32.5 ml vs 160.5 ± 35.0 ml, $p < 0.0001$; LV-ESV: 48.7 ± 14.5 ml vs 56.4 ± 16.7 ml, $p < 0.0001$; LV-EF: 67.7 ± 5.4% vs 65.1 ± 5.6%, $p < 0.0001$. When comparing end-systolic with end-diastolic data, values for LV-M were significantly higher in end systole irrespective of whether papillary muscles and trabecular tissues were included or not. Furthermore, LV-M missed overweight-induced LV hypertrophy when indexed to body surface area (BSA) instead of height.

Conclusion Quantitative assessment of LV volumes and mass with inclusion of papillary muscles and trabeculae to myocardial mass resulted in significantly different values, while indexing to BSA and not height may miss LV hypertrophy in terms of overweight.

Keywords Left ventricular function · Reference values · Cardiovascular magnetic resonance · Contour drawing · Indexing

Abbreviations

CMR	Cardiovascular magnetic resonance
LV	Left ventricular
RV	Right ventricular
LV-EDV	Left ventricular end-diastolic volume
LV-ESV	Left ventricular end-systolic volume
RV-EDV	Right ventricular enddiastolic volume
RV-ESV	Right ventricular endsystolic volume
LV-EF	Left ventricular ejection fraction
LV-M	LV mass
BSA	Body surface area
SSFP	Steady-state free precession
SD	Standard deviation
FIG	Figure

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00392-018-1371-7) contains supplementary material, which is available to authorized users.

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Background

The quantitative assessment of left (LV) and right (RV) ventricular volumes, mass and function plays a major role in the clinical phenotyping of patients with suspected cardiovascular disease. Cardiovascular magnetic resonance (CMR) has emerged as the non-invasive reference standard for the evaluation of cardiac function providing accurate and reproducible measurements of cardiac volumes and morphology [1–5] besides adding valuable information about perfusion, fibrosis, edema and risk stratification in cardiovascular disease [6–9]. The most recent set of recommendations of the Society of Cardiovascular Magnetic Resonance (SCMR) for standardized image interpretation and chamber quantification set focus on the delineation of the endocardial border and on the inclusion criteria for the basal slices derived from the short axis views. However, there is still no uniformly accepted convention on the inclusion of trabecular tissue and papillary muscles in the myocardial mass. There is general agreement that trabecular tissue is muscular tissue and thus should be included in the measurement of LV mass (LV-M) and excluded from LV volumes [10, 11]. Furthermore, validation studies of CMR also used the entire LV-M [3, 12, 13]. Omitting this tissue in fact has been shown to lead to significant underestimation of the LV-M in patients with LV hypertrophy [14, 15]. In clinical routine, however, this is often not implemented, mainly because, previously, analysis software did not have simple tools for the automatic or semi-automatic tracing of this tissue. Instead, frequently the simplified approach excluding papillary muscles and trabeculae from the myocardium is applied [11]. Based on improved algorithms, most commercially available software tools nowadays allow for an easy semi-automatic or automatic delineation of the subendocardial border [16].

LV-M is typically also measured during diastole, although during this phase trabecular tissue is much less compacted and thus more prone to partial-volume errors caused by the mixed presence of both, muscular tissue and blood.

Furthermore, values are most often indexed to body surface area (BSA), while several studies have shown an advantage of height-based indices [17, 18], which have also been found highly suitable for follow-up studies in obesity interventions [19–21].

Our study aimed to compare different methods for quantification of LV function and mass (with or without including trabecular tissue and papillary muscles in the LV-M, systolic vs diastolic measurement of LV-M, normalization to BSA vs height) in a population of healthy volunteers.

Methods

Study cohort

We enrolled consecutive participants in a prospective cohort study of a healthy population. Exclusion criteria were signs, symptoms or a history of any cardiac disease, including arterial hypertension, cardiovascular, cerebrovascular or non-cardiac diseases, as well as any regular medication except for contraceptives or vitamins. Screening included clinical history, physical examination, 12-lead electrocardiogram and a resting blood pressure. In all volunteers fasting glucose and HBA1c were assessed, while individuals with impaired glucose tolerance or manifest diabetes mellitus were excluded. Furthermore, in every participant a CMR stress test (first-pass perfusion with adenosine-induced vasodilation or stress function CMR during dobutamine) was performed to exclude significant coronary artery disease. All subjects gave written informed consent. The study was approved by the local institutional ethics committee in accordance with the Declaration of Helsinki.

Cardiovascular magnetic resonance acquisition protocol and image analysis

Standard CMR was performed on a 1.5T or 3T clinical MR scanner (Ingenia™, Philips Healthcare, Best, The Netherlands) equipped with a cardiac phased array receiver coil. All patients were examined in the supine position. A vector electrocardiogram was used for R-wave triggering. Short axis cine images covering the whole LV from base to apex (8 mm slice thickness, no gap between each slice), as well as cine long axis 2-, 3- and 4-chamber views were obtained by a standard steady-state free precession sequence (SSFP). Typical scan parameters were: repetition time (TR) 2.8 ms; echo time (TE) 1.4 ms; flip angle 60° (1.5T), 40° (3T); spatial resolution $1.7 \times 1.7 \times 8\ mm^3$ (1.5T), $1.9 \times 1.9 \times 8\ mm^3$ (3T); ≥ 35 phases per cardiac cycle with a breath-hold time of 7–10 s per image and prospective gating.

All CMR scans were analyzed using certified post-processing software (cvi^{42}, version 5.1.1, Circle Cardiovascular Imaging Inc., Calgary, Canada).

LV volumes

End diastole and end systole were defined by the phases with the largest and smallest area of the blood pool at a mid-ventricular level.

LV end-diastolic volumes (LV-EDV) and LV end-systolic volumes (LV-ESV) were derived from short axis slices and assessed in two ways:

1. In the standard approach (include), papillary muscles and trabeculae were included as myocardial tissue and, therefore, accounted as part of the myocardium for assessment of LV volumes ($LV\text{-}EDV_{include}$ and $LV\text{-}ESV_{include}$). For this, endocardial contours of papillary muscles and trabecular tissue were delineated by semi-automatic threshold selection and accounted for myocardial mass.
2. In the simplified approach (exclude), papillary muscles and trabeculae were regarded as LV blood volume and, therefore, excluded from the myocardium for measurement of $LV\text{-}EDV_{exclude}$ and $LV\text{-}ESV_{exclude}$.

In both techniques, LV volume was included up to the planes of the aortic and mitral valve. Long axis views were used to carefully exclude aortic or atrial blood.

LV ejection fraction (LV-EF) and LV stroke volume (LV-SV) were measured with both, the "include" and the "exclude" approach.

RV volumes

Corresponding to the LV, RV volumes were derived from short axis slices and defined by endocardial contour at end diastole and end systole as defined by the maximal and minimal area of the blood pool in a slice with a large representation of the RV cavity. The basal slice of the RV corroborated with the long axis views and the RV outflow tract was accounted for in the RV volume. Trabeculae and papillary muscles were excluded from RV volume.

LV mass

For LV-M assessment, the epicardial border was traced semi-automatically and manual correction was performed if necessary. LV-M was calculated for end diastole and end systole as follows:

$$\text{LV-M} = (\text{total epicardial volume} - \text{total endocardial volume}) \times 1.05\ \text{g/ml}.$$

Corresponding to volumes, LV-M was determined including papillary muscles and trabeculae as myocardial tissue (LV-$M_{include}$), while excluding them with the simplified approach (LV-$M_{exclude}$). Corresponding to the LV-EF measurements, reference views in the long axis were used to correctly identify basal myocardial tissue.

LV volumes, RV volumes and LV-M were indexed to height and to body BSA according to the Dubois formula [22]. An example for the assessment of LV and RV volumes and LV-M is given in Fig. 1.

Reproducibility

Inter- and intraobserver variability of the measurements of LV and RV function and LV-M were evaluated in 25 randomly selected subjects. For intraobserver variability, the same investigator performed the measurements twice within 4 weeks. For interobserver variability, two independent blinded investigators assessed the CMR examinations separately.

Statistical analysis

Statistical analysis was carried out using the software solution MedCalc (Version 13.1.2.0, MedCalc Software, Ostend, Belgium). Normal distribution was tested using the D´Agostino Pearson test. All data are given as mean ± standard deviation (SD). Continuous variables were compared by Student's *t* test when normally distributed. Otherwise, comparisons between different age-related or gender-related groups were made by Mann–Whitney *U* test. Measuring techniques were compared with Bland–Altman plots. Correlation was measured by the Spearman's coefficient of rank correlation. Inter- and intraobserver variability was assessed by correlation coefficient. Associations between morphological and functional parameters and age were assessed with linear regressions. Differences were regarded as statistically significant at $p < 0.05$.

Results

Study population

We enrolled 362 healthy volunteers (172 women and 190 men, mean age 51 ± 13 years, range 21–84 years). Their baseline characteristics are provided in Table 1.

LV volume, function and mass

We observed strong correlations for LV-$EDV_{include}$ and LV-$EDV_{exclude}$ ($r = 0.998$, $p < 0.0001$) and for LV-$ESV_{include}$ and LV-$ESV_{exclude}$ ($r = 0.997$, $p < 0.0001$), respectively.

Absolute values as well as normalized values for end-diastolic and end-systolic volumes were significantly higher for the simplified delineation method (Table 2).

The differences showed a significant volume dependency with greater differences for larger volumes ($p < 0.0001$) (Fig. 2a, b). Regarding LV-EF, values were significantly lower when assessed with the "exclude" approach (Table 2; Fig. 2c), while correlation between both methods was strong ($r = 0.99$, $p < 0.0001$).

The measurements of LV-M also correlate strongly between the different methods. Absolute and normalized values for LV-M were significantly lower, when assessed with the simplified method in end systole as well as in end diastole (Table 2). Corresponding to LV volumes, the differences showed a significant mass dependency with greater differences for higher values ($p < 0.0001$) (Fig. 3a, b).

Values for LV-M were significantly higher when assessed in end systole in the "exclude" approach (127.6 ± 32.3 g vs 122.9 ± 32.0 g, $p < 0.05$) as well as in the "include" approach (119.6 ± 30.7 g vs 111.5 ± 29.1 g, $p = 0.0005$) (Fig. 3c, d).

Regression analysis revealed a significant decrease with age in LV volumes and LV-SV for both delineation methods in men and women, while LV-$EF_{include}$ and LV-$EF_{exclude}$ significantly increased with age (Figs. 4, 5a–h).

In men, values for end-diastolic LV-$M_{exclude}$, end-diastolic LV-$M_{include}$ and end-systolic LV-$M_{include}$ showed

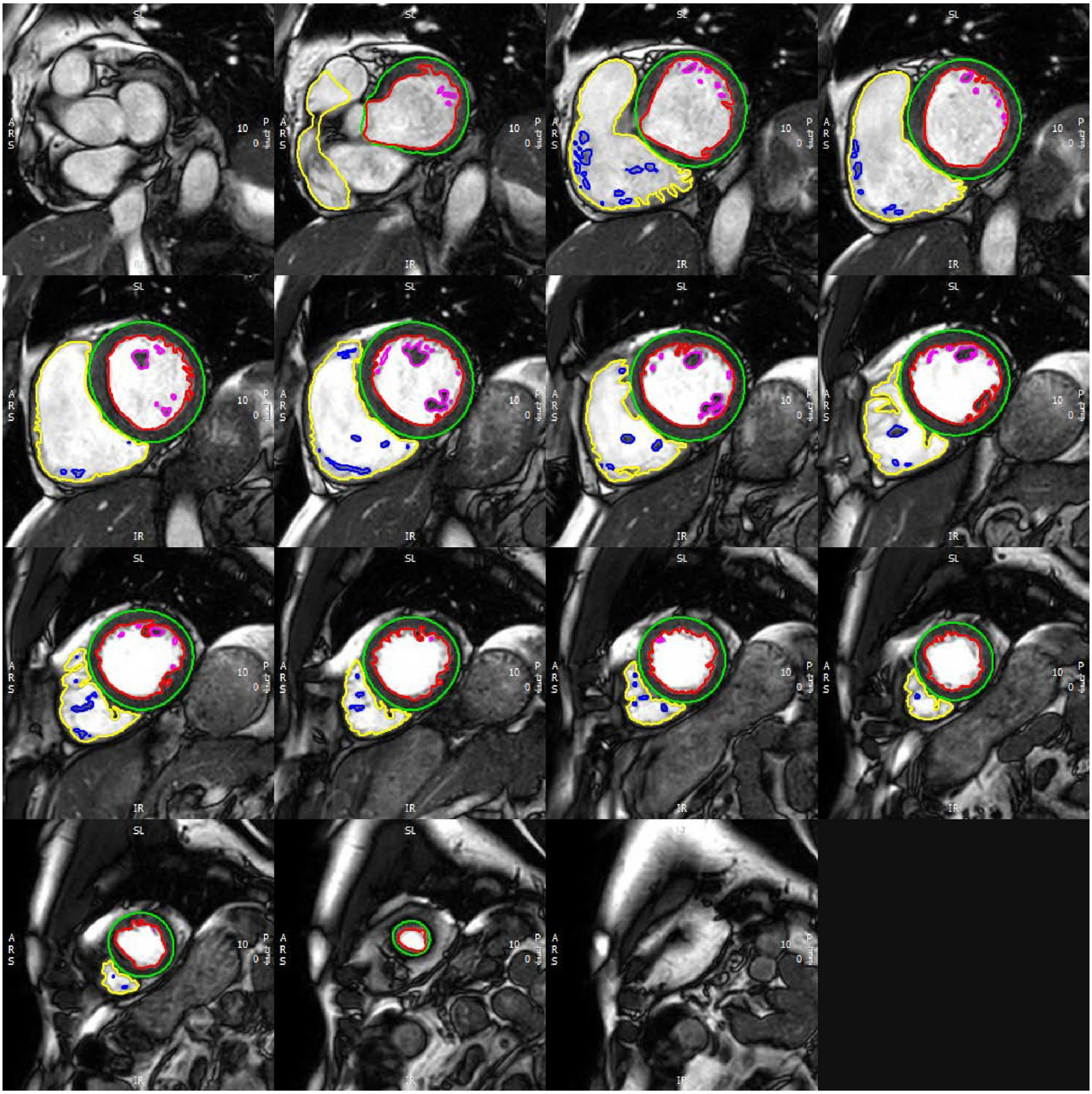


Fig. 1 Representative examples for the assessment of cardiac volumes and LV-M: endocardial contours were delineated in end diastole and end systole with either inclusion (**a, b**) or exclusion of the papillary muscles and trabeculae (**c, d**) from myocardial mass. LV-M was assessed in end systole and end diastole. *LV-M* left ventricular mass

a significant age-related decrease, while end-systolic LV-$M_{exclude}$ did not display a significant correlation (Fig. 6a–d). In women, regression analysis did not reveal any significant correlation for LV-M with age irrespective of the underlying delineation method (Fig. 7a–d).

Absolute values as well as normalized values to BSA or height for LV volumes, LV-M and LV-SV were significantly higher in men compared with women, independent of the underlying measurement technique. For LV-EF there was no significant difference between men and women. Absolute values and normalized values for men and women regarding LV volumes, function and mass obtained by the different methods are shown in supplement Tables 1 and 2.

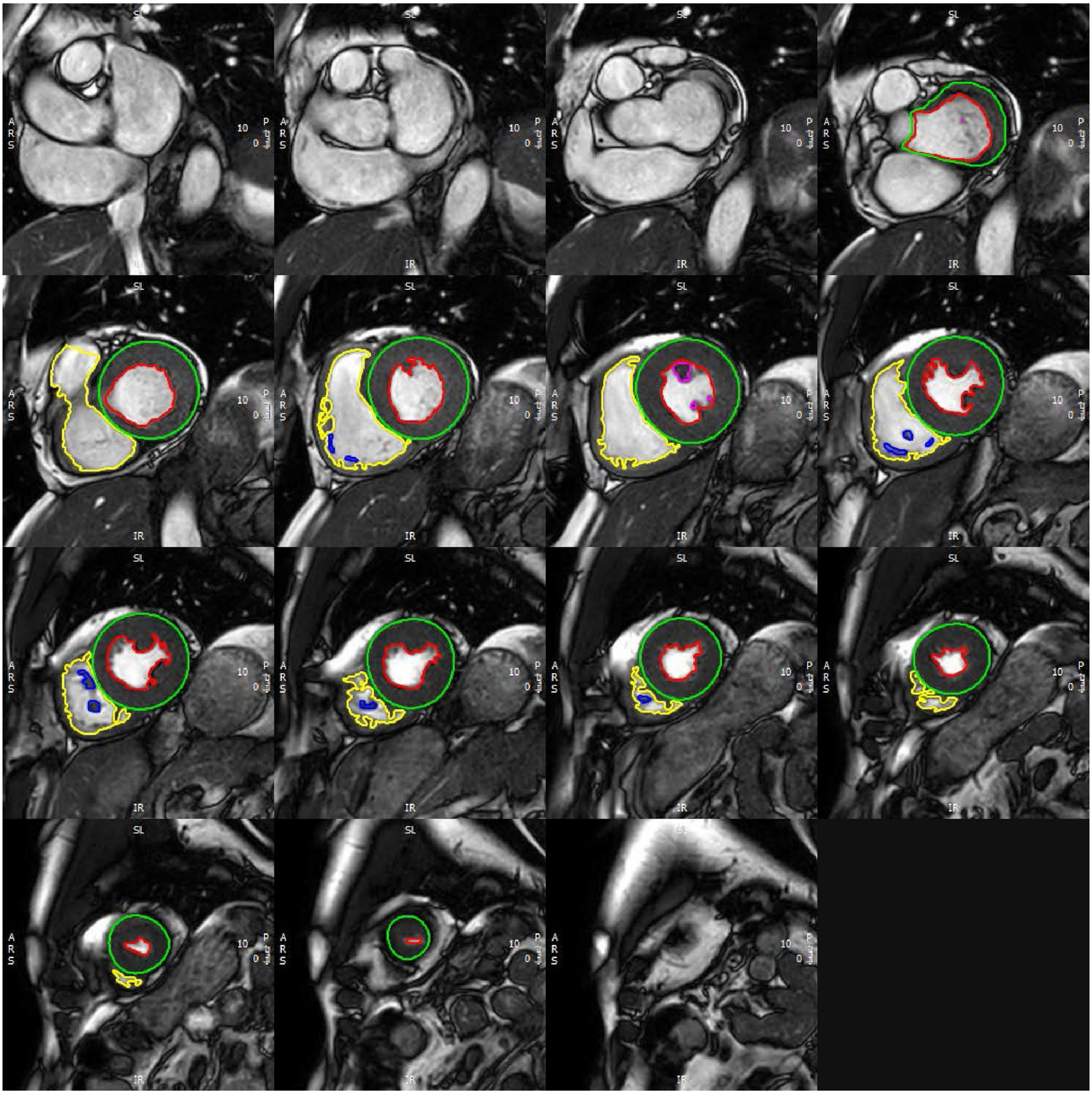


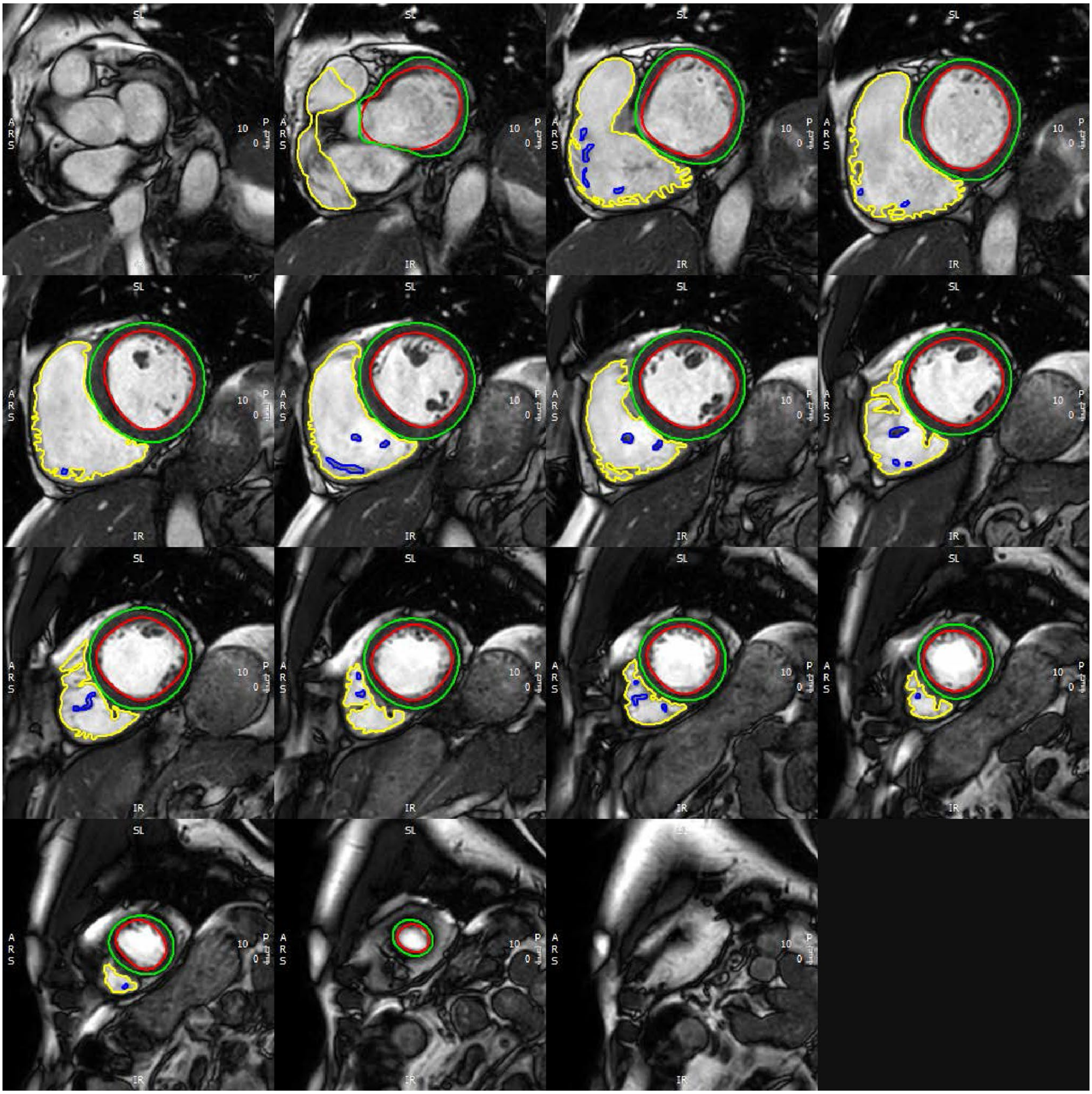
Fig. 1 (continued)

RV volumes and function

Similar results were observed for the RV measurements. Absolute values for RV-EDV, RV-ESV and RV-SV were significantly higher in men compared to women. Normalized values of RV-EDV, RV-ESV and RV-SV to BSA or height remained significantly larger in men compared to women. Corresponding to the LV, RV-EDV, RV-ESV and RV-SV (absolute values and normalized values) showed a negative correlation with age. RV-EF was higher in women compared to men and showed a positive correlation with age in women, while correlation in men was not significant with age (Figs. 8, 9a–d). Absolute values and normalized values for men and women regarding RV volumes and function are given in supplemental Table 3.

Indexing of LV parameters

For evaluation of indexing of LV parameters, we compared subjects with a body mass index (BMI) > 25 and those



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with BMI < 25 in men and women. We observed that for LV-EDV, absolute values and values normalized to height tend to be higher in subjects with greater BMI, while values were lower in those subjects when normalized to BSA.

Absolute values and values normalized to height were significantly greater in subjects with BMI > 25, irrespective of the underlying delineation approach.

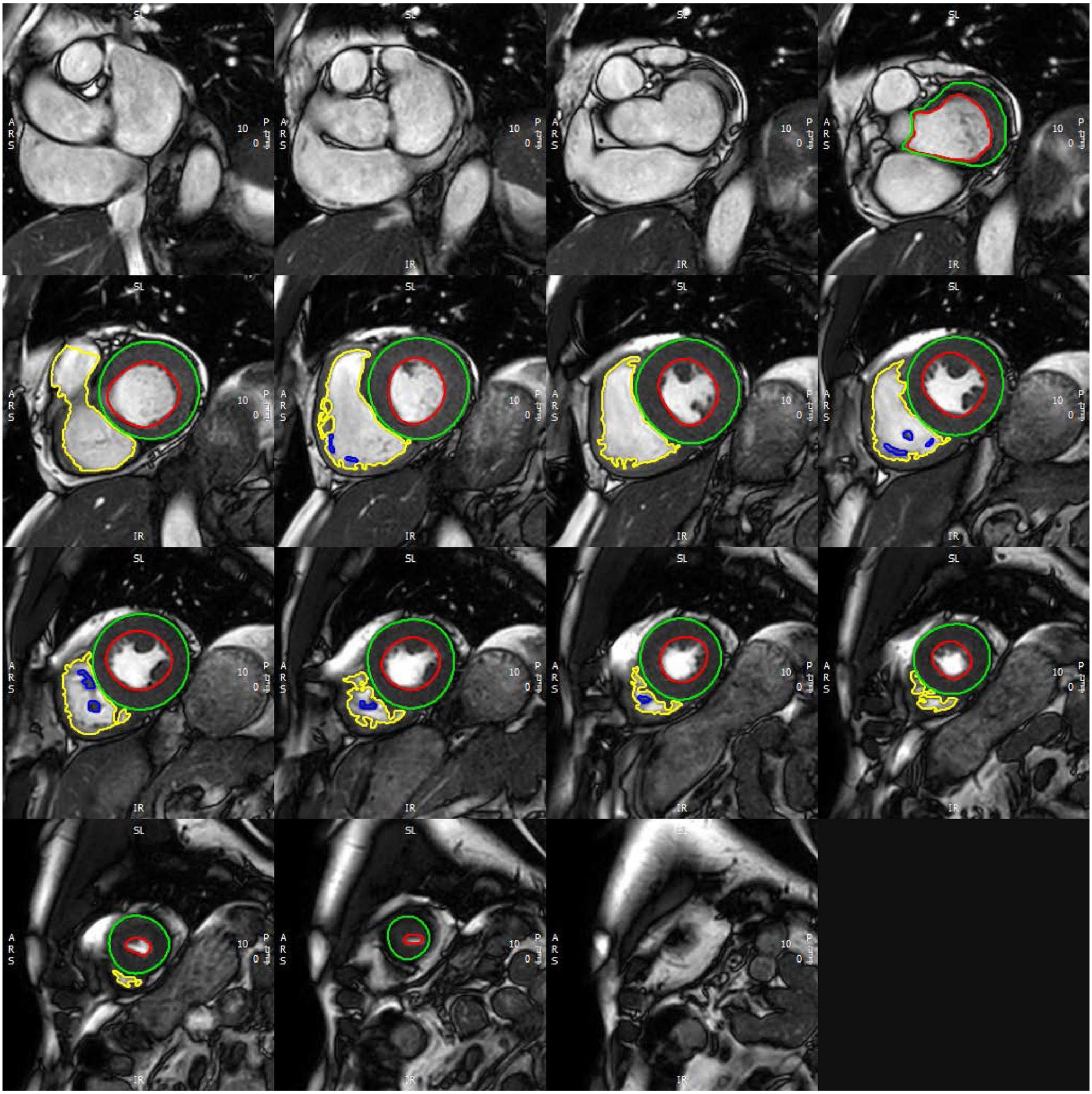

Fig. 1 (continued)

When normalizing to BSA, differences for LV-M between both BMI groups were no longer apparent (Tables 3, 4).

Reproducibility

Overall, the inter- and intraobserver agreements for the determination of LV-EDV, LV-ESV, LV-EF LV-SV and LV-M were high, while there was no significant difference between both methods. Correlation coefficients are given in Table 5.

Discussion

Our data support the suggestions that (1) it is of major importance to report the method applied for quantification of LV function and mass, as values are significantly different

Table 1 Population characteristics

	Total ($n = 362$)	Men ($n = 190$)	Women ($n = 172$)	p value
Age (years)	50.5 ± 13.0	51.4 ± 12.7	49.6 ± 13.3	NS
Height (cm)	173 ± 9	179 ± 7	167 ± 7	< 0.0001
Weight (kg)	74.3 ± 13.5	81.6 ± 11.8	66.1 ± 10.2	< 0.0001
Body mass index (kg/m^2)	24.6 ± 3.3	25.3 ± 3	23.8 ± 3.5	< 0.0001
BSA (m^2)	1.9 ± 0.2	2.0 ± 0.2	1.7 ± 0.1	< 0.0001
Heart rate (bpm)	68 ± 11	67 ± 10	69 ± 11	NS
Systolic BP (mmHg)	126 ± 13	129 ± 12	122 ± 14	< 0.0001
Diastolic BP (mmHg)	78 ± 10	80 ± 10	76 ± 10	0.002

Values are presented as means ± SD

BSA body surface area, *BP* blood pressure

Table 2 Left ventricular parameters of all subjects ($n = 362$) assessed with inclusion of papillary muscles and trabeculae as part of myocardial tissue (include) and with a simplified approach (exclude)

Approach	Include			Exclude			p value
	Mean ± SD	5th	95th	Mean ± SD	5th	95th	
LV-EDV (mlML)	149.7 ± 32.5	104.9	209.0	160.5 ± 35.0	112.3	226.4	< 0.0001
LV-ESV (ml)	48.7 ± 14.5	28.2	76.8	56.4 ± 16.7	32.9	89.2	< 0.0001
LV-SV (ml)	101.0 ± 22.0	70.4	142.7	104.2 ± 22.9	73.0	148.0	NS
LV-EF (%)	67.7 ± 5.4	58.3	76.0	65.1 ± 5.6	55.7	73.8	< 0.0001
ED LV-M (g)	122.9 ± 32.0	80.9	179.4	111.5 ± 29.1	73.5	163.9	< 0.0001
ES LV-M (g)	127.6 ± 32.3	84.5	185.5	119.6 ± 30.7	78.9	175.2	0.0009
Normalized to BSA							
LV-EDV/BSA (ml/m^2)	79.4 ± 13.1	59.4	102.6	85.1 ± 13.9	64.1	109.7	< 0.0001
LV-ESV/BSA (ml/m^2)	25.8 ± 6.7	16.0	38.0	29.9 ± 7.7	18.2	43.8	< 0.0001
LV-SV/BSA (ml/m^2)	53.5 ± 8.9	40.2	69.1	55.2 ± 9.1	41.5	71.0	0.01
ED LV-M/BSA (g/m^2)	64.8 ± 12.4	48.1	86.0	58.8 ± 11.3	43.4	78.2	< 0.0001
ES LV-M/BSA (g/m^2)	67.3 ± 12.4	50.2	90.0	63.1 ± 11.8	46.5	83.7	< 0.0001
Normalized to height							
LV-EDV/height (ml/m)	85.9 ± 15.7	63.2	113.9	92.1 ± 16.9	68.2	122.1	< 0.0001
LV-ESV/height (ml/m)	27.9 ± 7.6	17.0	42.1	32.3 ± 8.7	19.9	48.8	< 0.0001
LV-SV/height (ml/m)	57.9 ± 10.7	43.0	78.0	59.8 ± 11.1	44.3	80.5	0.03
ED LV-M/height (g/m)	70.4 ± 15.9	48.5	98.2	63.8 ± 14.4	44.5	89.7	< 0.0001
ES LV-M/height (g/m)	73.1 ± 15.9	51.7	102.1	68.5 ± 15.2	47.8	96.7	0.0001

Data are presented as means ± SD (5th and 95th percentiles)

P value is for *t* test between both methods

NS non-significant

when papillary muscles and trabeculae were included in LV-M, (2) the phase in which LV-M is assessed has to be standardized and (3) values for LV-M may better be indexed to height and not BSA to avoid bias in overweight and obese subjects.

CMR is currently the gold standard to measure LV and RV volumes and function with high accuracy and reproducibility [4]. Despite SCMR recommendations [11] and a general agreement that trabeculae and papillary muscles should be accounted as myocardial mass [10], clinical practice varies. The most important reason for using a simplified approach is probably tradition carried over from times when any other approach appeared too difficult. Still, not all analysis tools allow for a semi-automatic or automatic

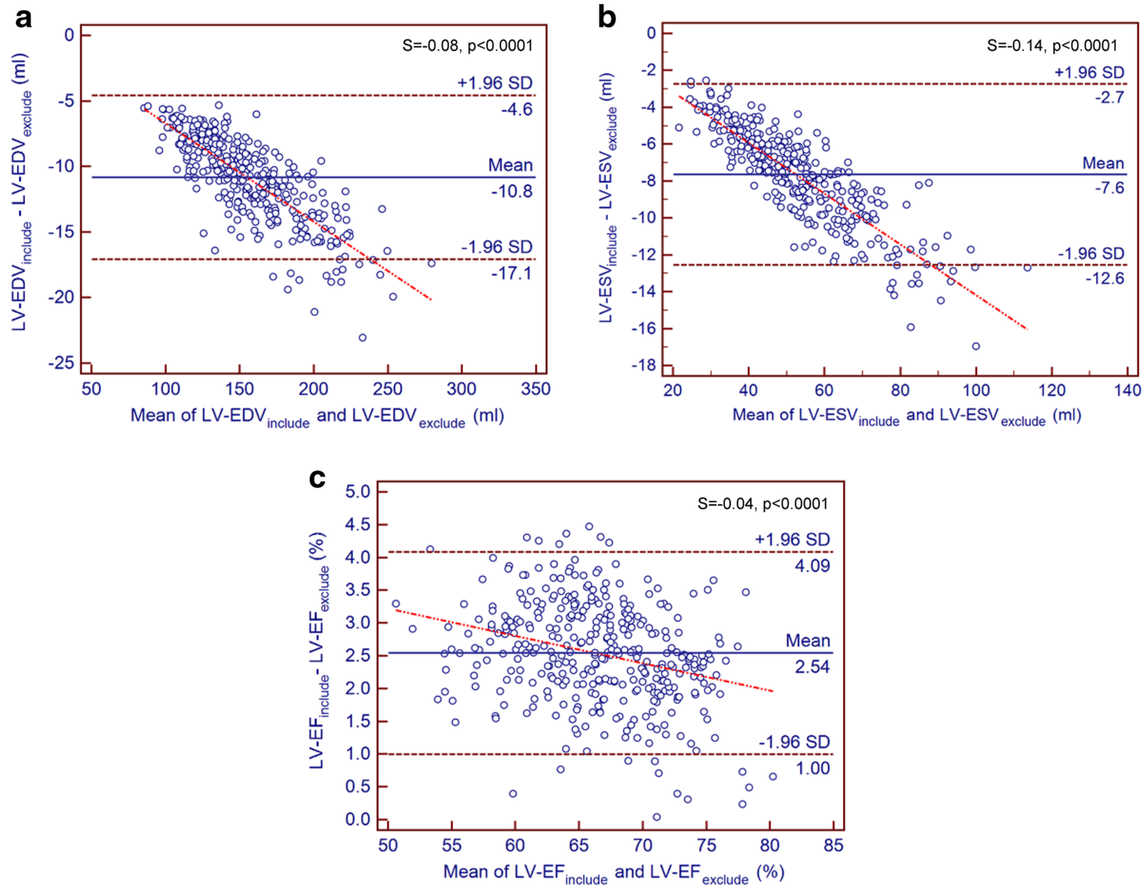

Fig. 2 Bland–Altman plots of LV-$EDV_{include}$ and LV-$EDV_{exclude}$ (**a**), LV-$ESV_{include}$ and LV-$ESV_{exclude}$ (**b**) and LV-$EF_{include}$ and LV-$EF_{exclude}$ (**c**), values for LV-$EDV_{include}$ and LV-$ESV_{include}$ were significantly lower compared to the simplified technique, while values for LV-$EF_{include}$ were higher compared to the simplified approach. *LV-EDV* left ventricular end-diastolic volume, *LV-EDV* left ventricular end-systolic volume, *LV-EF* left ventricular ejection fraction, *S* slope

detection of trabecular borders, which makes inclusion of papillary muscles and trabeculae more laborious for readers. Another reason may be that published literature serves as an incorrect role model, as papillary muscles and trabecular tissue are often excluded from LV-M. Finally, some argue that the reproducibility may be better with a simpler shape of the contours.

Impact of contouring on LV volumes and mass

Values for LV-EDV and LV-ESV were significantly higher in the "Exclude" approach, increasingly so with larger volumes. For LV-EF, we observed the contrary: excluding this tissue from the LV-M led to an underestimation of LV-EF, more so for lower values. As expected, LV-M values were significantly higher when papillary muscles and trabeculae were included and hence underestimated with the simplified approach. This finding was irrespective of the phase (end systole or end diastole) in which LV mass was assessed and—corresponding to LV-volumes—greater differences were found for higher values.

Irrespective of the underlying method, we observed higher values for LV-M, LV volumes and LV-SV in male vs female participants. We also found that LV volumes and LV-SV decrease significantly with age, while LV-EF increases with age in both sexes.

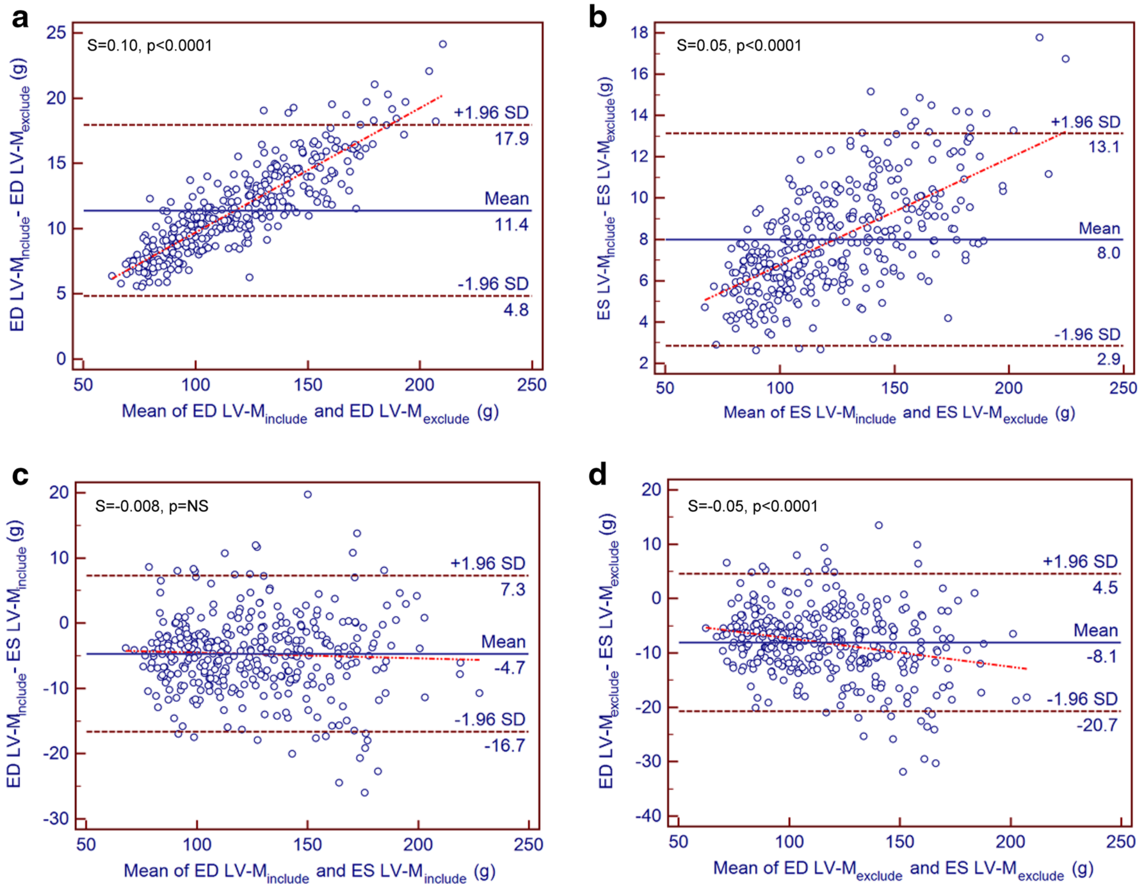

Fig. 3 Bland–Altman plots of ED LV-$M_{include}$ and ED LV-$M_{exclude}$ (**a**), ES LV-$M_{include}$ and ES LV-$M_{exclude}$ (**b**), ED LV-$M_{include}$ and ES LV-$M_{include}$ (**c**) and ED LV-$M_{exclude}$and ES LV-$M_{exclude}$ (s) (**d**). Values for ED LV-$M_{exclude}$ and ES LV-$M_{exclude}$ were significantly lower compared to ED LV-$M_{include}$ and ES LV-$M_{include}$, respectively. Values for ED LV-M differ significantly from values for ES LV-M in both techniques. *ED* end diastolic, *ES* end systolic, *LV-M* left ventricular mass, *S* slope

Our results are in line with findings of other groups, which analyzed the impact of trabeculae and papillary muscles in hypertrophy. Kozor et al. analyzed both delineation methods in patients with Fabry disease and controls and observed significant differences between the two measurement methods for cardiac volumes, LV-M and LV-EF in both groups. Interestingly, the differences were significantly greater in the Fabry group, leading to the conclusion that it is of great importance to account papillary muscles and trabeculae to LV-M particularly in hypertrophic ventricles [15]. In a study of Janik et al. variable exclusion of papillary muscles and trabeculae tissue led to significant differences in LV-EF and LV-M in patients with LV hypertrophy. The authors speculated that ignoring papillary muscles and trabeculae may have great impact for instance when LV-EF or LV-M was used to find physiological changes or to predict prognosis [14].

Moreover, several ex vivo studies showed good agreement between LV-M assessed in CMR when papillary muscles and trabeculae were included and actual LV-M [3, 12, 13], further emphasizing that inclusion of all myocardial tissue should be regarded as the favorable approach to assess myocardial mass and volumes.

In our study, RV volumes were exclusively derived from short axis stacks and not from transversal slices. However, according to published literature, both ways to assess RV function provide reliable and reproducible measures for follow-up of RV volumes and global function. Transverse

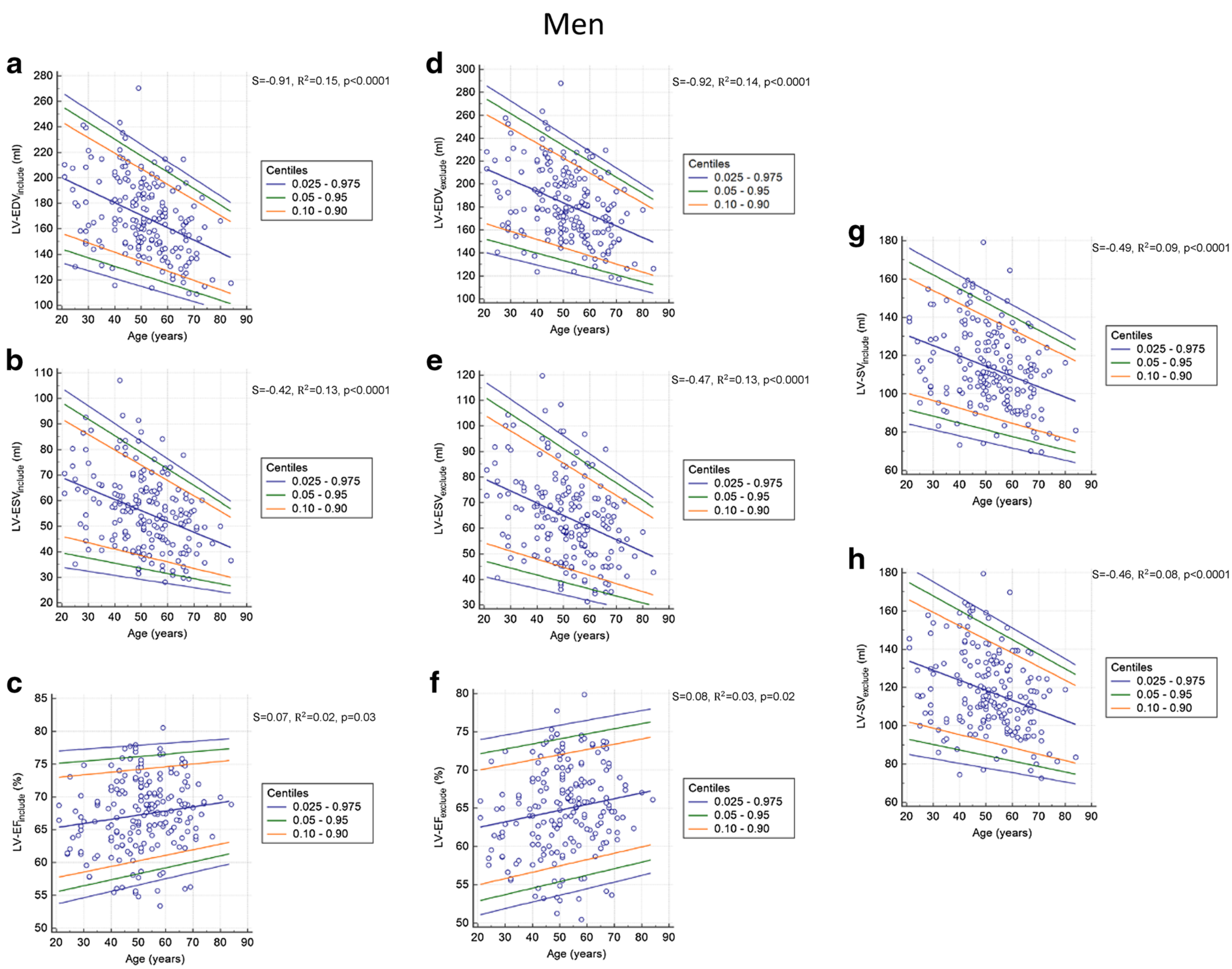

Fig. 4 Age-related regression analyses for LV-EDV, LV-ESV, LV-EF and LV-SV in men. Values were assessed with inclusion of papillary muscles and trabeculae with the myocardium as well as with exclusion of papillary tissue. The scatter diagram includes the regression line with the respective 97.5, 95 and 90 percentiles. *LV-EDV* left ventricular end-diastolic volume, *LV-EDV* left ventricular end-systolic volume, *LV-EF* left ventricular ejection fraction, *LV-SV* left ventricular stroke volume, *S* slope, R^2 coefficient of determination

SSFPs may, therefore, not necessarily be required for RV volumetric analysis [23].

For quantification of the RV volume, we excluded trabeculae and papillary muscles from RV volume, which is contrary to current practice in most centers. It seems obvious, however, that corresponding to the LV, all myocardial tissue should be regarded as part of the myocardium and, therefore, be excluded from RV volume.

The fact that we found a significant difference between LV-SV and RV-SV only when LV volume was assessed with the “Exclude” approach suggests that it leads to an overestimation of LV volumes and underestimation of LV-EF and LV mass.

For clinical routine, this may be a relevant problem, potentially leading to misdiagnosis in patients with hypertrophy or different treatment strategies, for instance for therapy induction in patients with heart failure or the need of an implantable cardiac defibrillator in patients with ischemic or non-ischemic cardiomyopathy.

Therefore, in our opinion, LV volumes, function and mass should be routinely measured with careful inclusion of papillary muscles and trabecular tissue to myocardial mass, consistent with the actual anatomy.

Systolic vs diastolic measurement of LV mass

LV-M does not change during the cardiac cycle and, therefore, measurements ideally should be identical in end systole and end diastole. We, however, observed systematically higher values for LV-M in end systole when compared to end

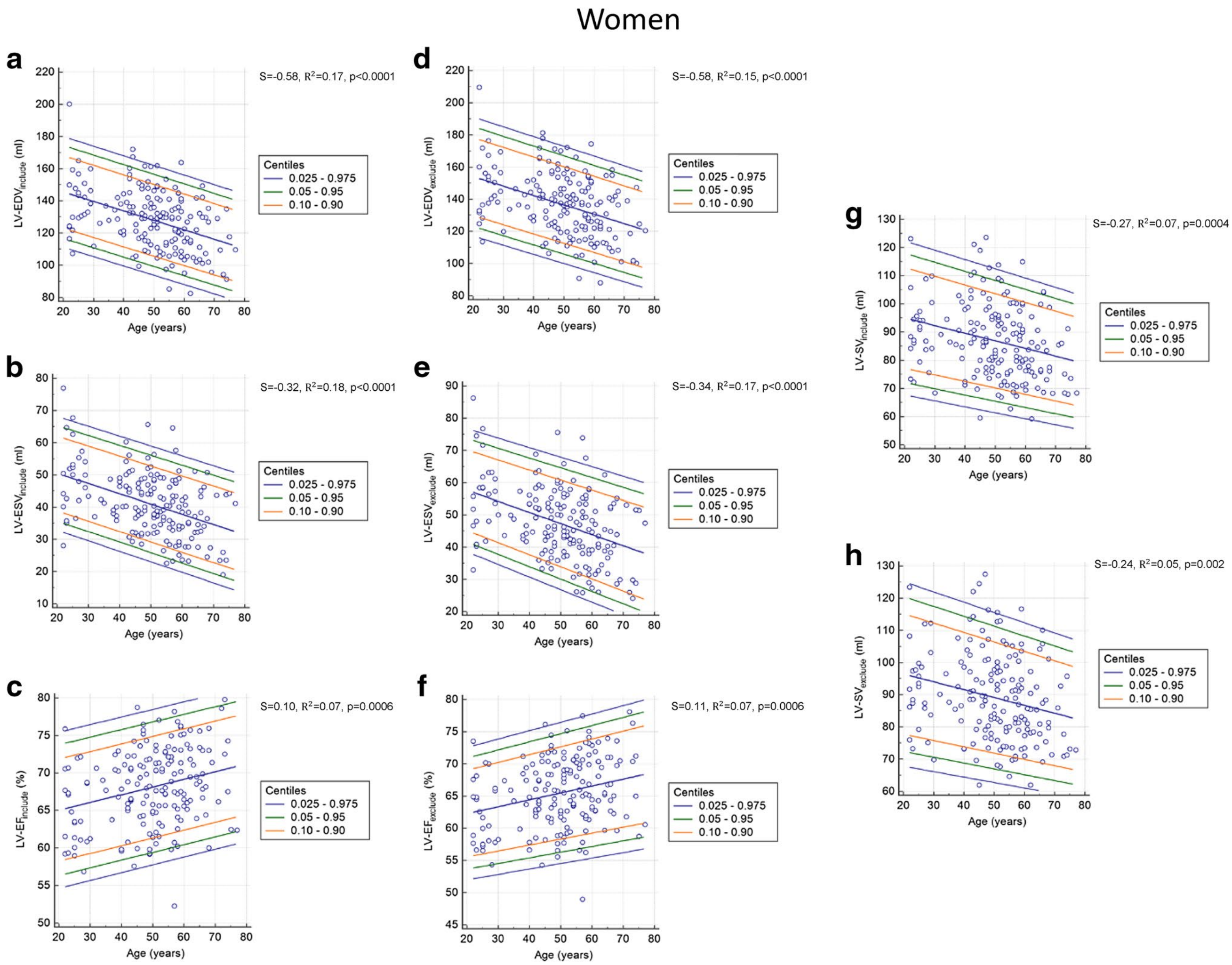

Fig. 5 Age-related regression analyses for LV-EDV, LV-ESV, LV-EF and LV-SV in women. Values were assessed with inclusion of papillary muscles and trabeculae with the myocardium as well as with exclusion of papillary tissue. The scatter diagram includes the regression line with the respective 97.5, 95 and 90 percentiles. *LV-EDV* left ventricular end-diastolic volume, *LV-EDV* left ventricular end-systolic volume, *LV-EF* left ventricular ejection fraction, *LV-SV* left ventricular stroke volume, *S* slope, R^2 coefficient of determination

diastole for both delineation methods. One simple explanation for these findings is that trabecular tissue is more compacted at end systole and thus less likely leads to partial-volume errors, caused by the mix of small trabeculae and blood. The systematic difference between end-systolic and end-diastolic results indicates that end-diastolic results likely systematically underestimate LV-M and overestimate LV volume. Considering that data about ex vivo validation of LV-M is exclusively available in end systole [12], end-systolic measurements appear to be more accurate. Another practical advantage of systolic measurements is that the number of slices is typically smaller during systole and the length of the subendocardial contour to be drawn is shorter. Our findings emphasize the importance of standardizing the phase in which LV-M is quantified and propose to use the end-systolic phase for contours.

Impact of indexing

Values for LV and RV parameters are commonly indexed to BSA. However, former studies showed that obesity (through an increase of fat-free mass) is associated with an increased

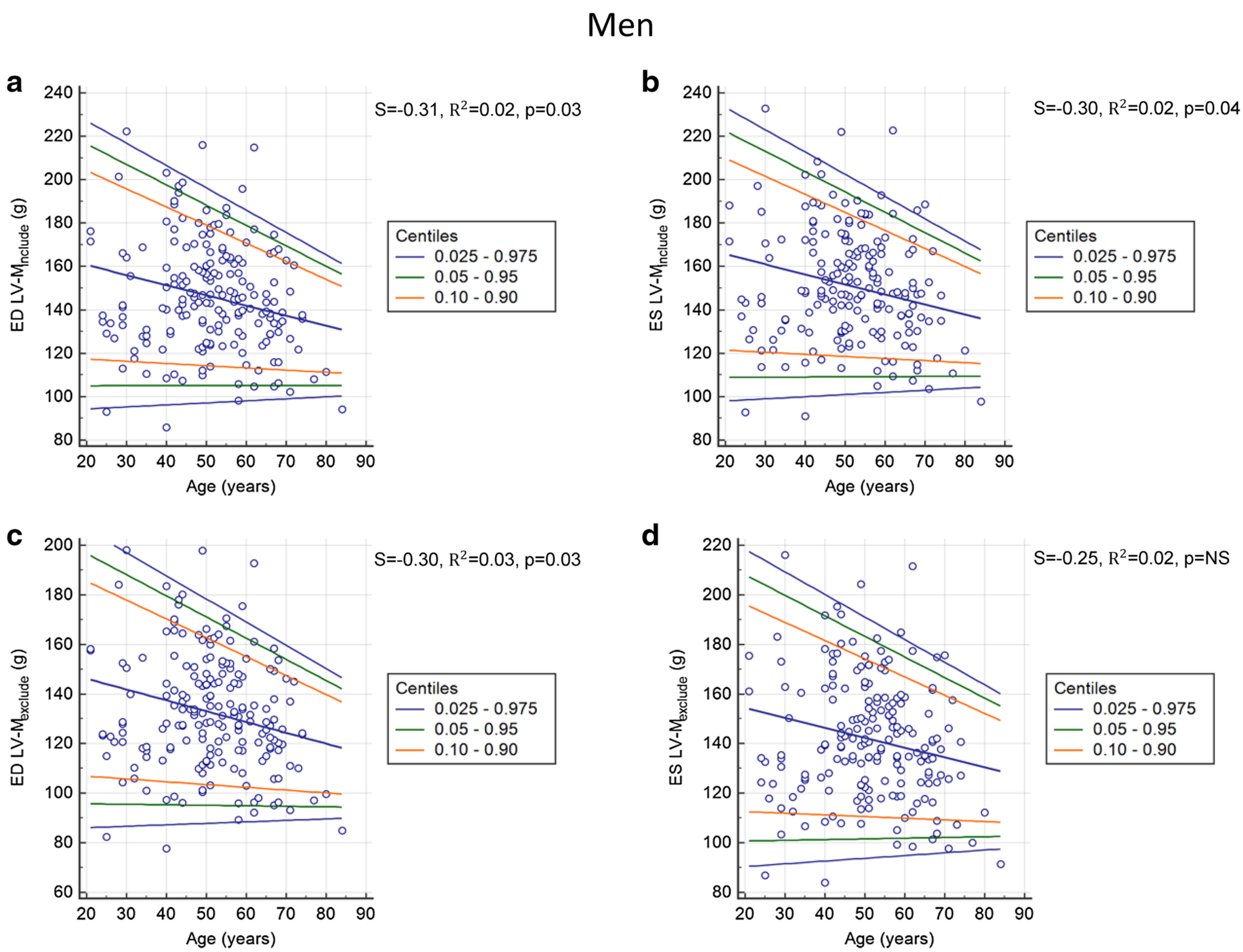

Fig. 6 Age-related regression analyses for LV-M measured in end diastole (ED) and end systole (ES) assessed with inclusion and with exclusion of papillary muscles and trabeculae as part of LV-M in men. The scatter diagram includes the regression line with the respective 97.5, 95 and 90 percentiles. *LV-M* left ventricular mass, *S* slope, R^2 coefficient of determination

LV-M. This hypertrophic response to obesity was mainly attributable to an increase in lean body mass [24]. Therefore, one would have to expect an increased LV-M in terms of obesity and absence of other cardiovascular risk factors. However, it has been shown that in obese subjects, indexation to BSA—contrary to indexation to height—failed to identify LV hypertrophy [18]. Furthermore, indexing LV parameters to height has been shown to be highly suitable for follow-up studies in obesity interventions [19–21].

We observed that absolute values for LV-M and indexed values to height were significantly higher in overweight subjects (defined as BMI > 25) compared to subjects with a BMI within normal range (< 25). Interestingly, these differences were no longer persistent when normalizing values for LV-M to BSA. In concordance with above-mentioned studies, the values for LV-M may, therefore, be considered as "pseudo-normalized" in terms of obesity or overweight. Regarding LV-EDV, absolute values and values indexed to height tend to be higher in overweight subjects, while values indexed to BSA were lower and hence may be underestimated in terms of overweight. Although the clinical impact of these findings has still to be evaluated in outcome studies, the present data provide evidence that overweight- or obesity-induced hypertrophy may be missed when indexing to BSA and, therefore, at least both—BSA-based and height-based indices—should be reported.

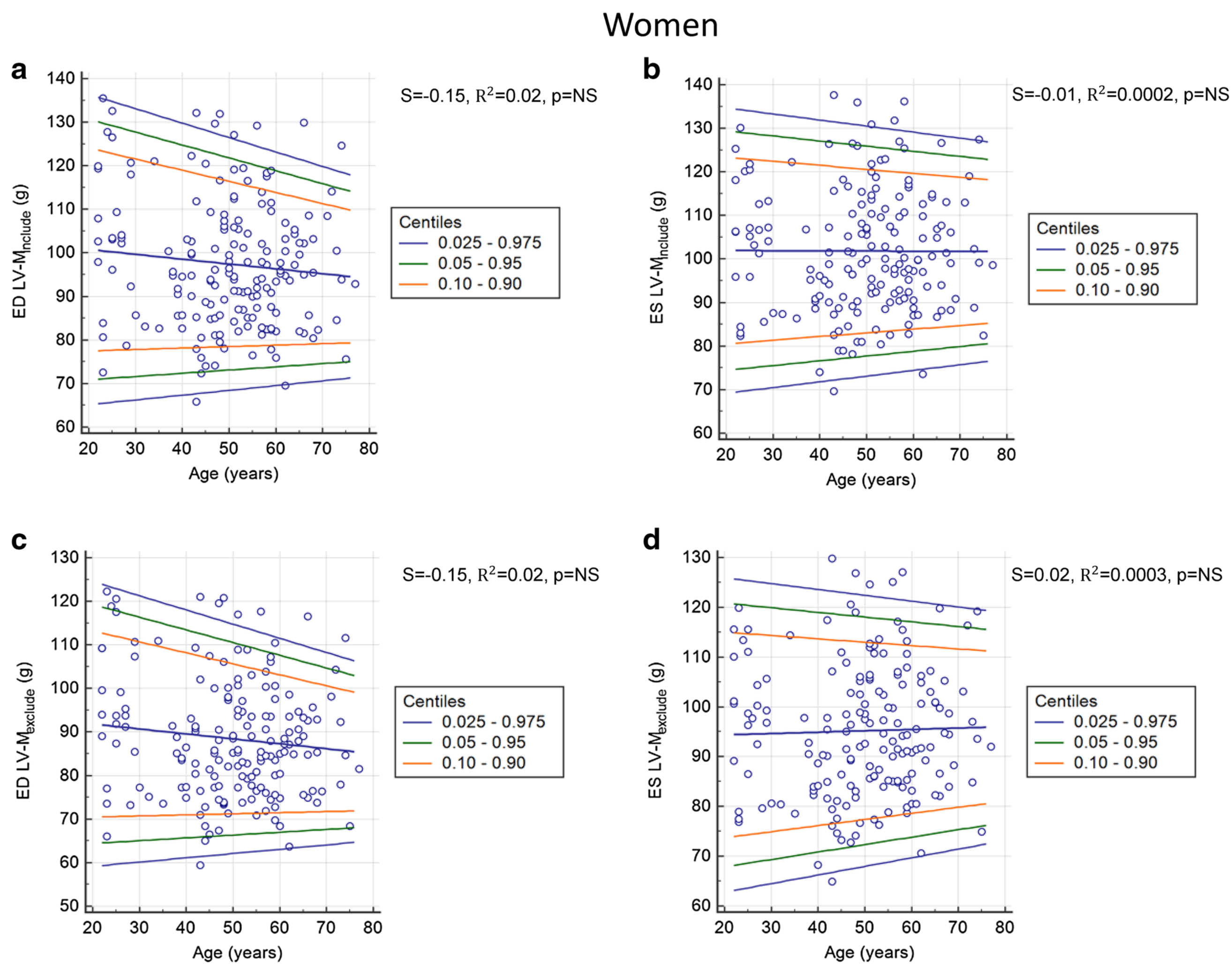

Fig. 7 Age-related regression analyses for LV-M measured in end diastole (ED) and end systole (ES) assessed with inclusion and with exclusion of papillary muscles and trabeculae as part of LV-M in women. The scatter diagram includes the regression line with the respective 97.5, 95 and 90 percentiles. *LV-M* left ventricular mass, *S* slope, R^2 coefficient of determination

Limitations

All values were derived from a Caucasian population and may, therefore, not be representative for other ethnicities. The age-related observations should be interpreted keeping in mind that these are cross-sectional data.

We do not have follow-up data of our population. Information about the impact of delineation approaches and indexing on prognosis and outcome is lacking. Our study did, therefore, not allow drawing conclusions about the clinical value or impact of the different volumetric approaches. This has to be addressed in further studies.

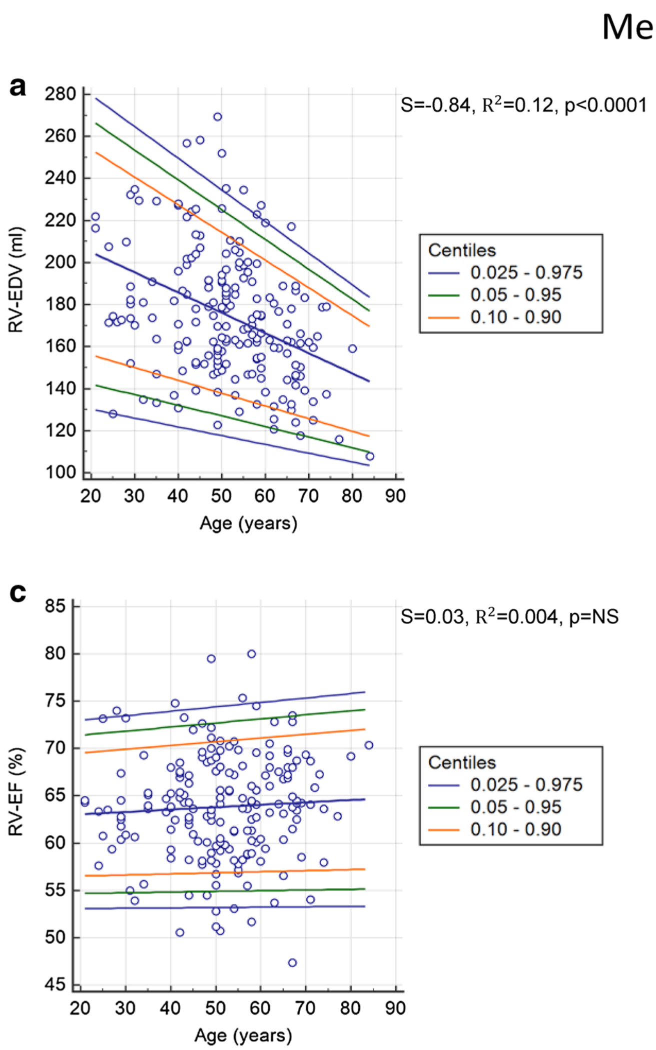

Fig. 8 Age-related regression analyses for RV volumes, RV-EF and RV-SV in men. The scatter diagram includes the regression line with the respective 97.5, 95 and 90 confidence percentiles. *RV-EF* right ventricular ejection fraction, *RV-SV* right ventricular stroke volume, *S* slope, R^2 coefficient of determination

Conclusion

Our data indicate that trabecular tissue and papillary muscles have significant impact on quantification of LV volume and mass. Inclusion of all myocardial tissue in LV-M—as the more accurate approach—appears advantageous, while results for LV-M may better be indexed to height instead to BSA, to avoid bias through pseudo-normalization in overweight subjects.

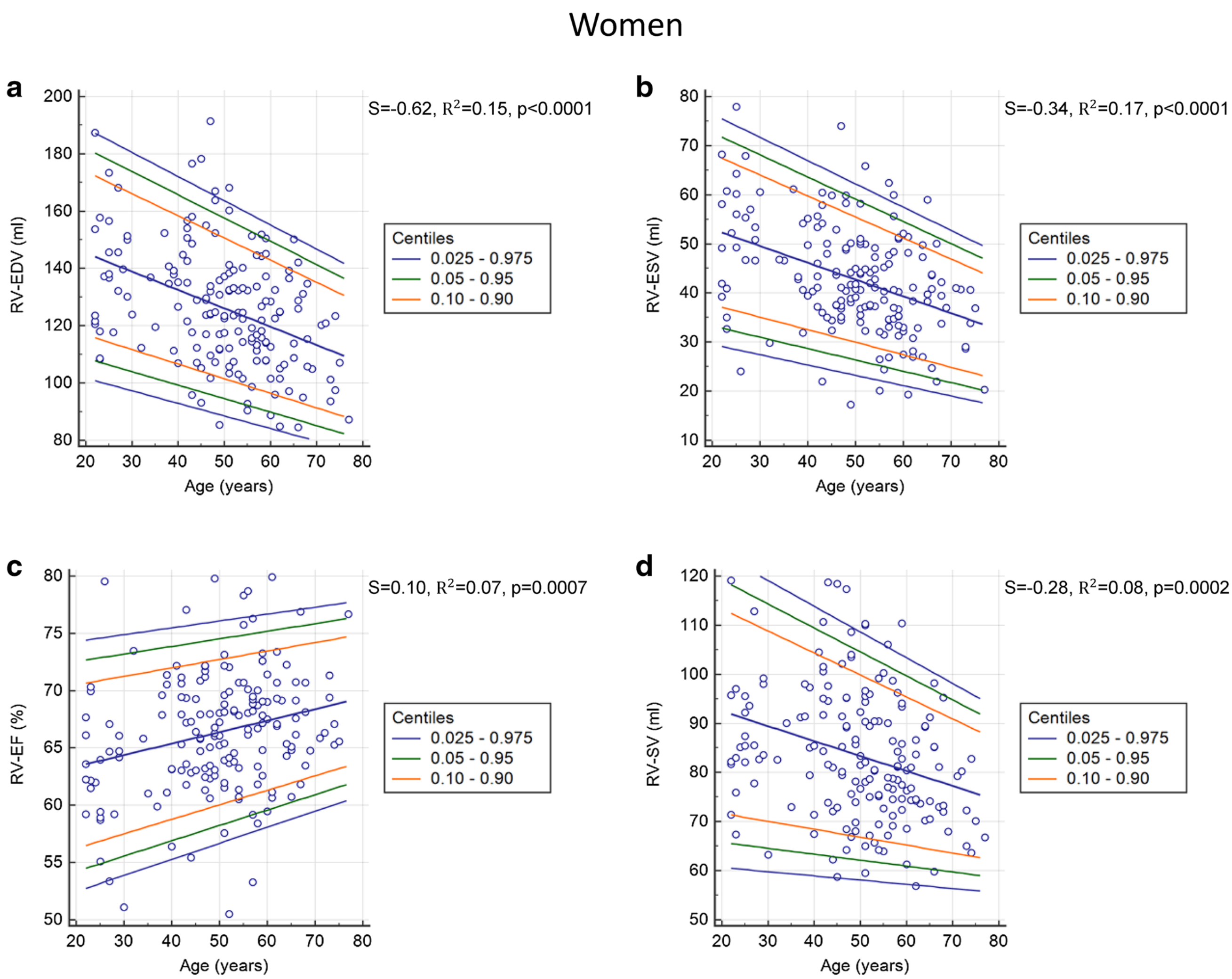

Fig. 9 Age-related regression analyses for RV volumes, RV-EF and RV-SV in women. The scatter diagram includes the regression line with the respective 97.5, 95 and 90 confidence percentiles. *RV-EF* right ventricular ejection fraction, *RV-SV* right ventricular stroke volume, *S* slope, R^2 coefficient of determination

Table 3 Comparison of absolute left ventricular parameters and indexed left ventricular parameters in male subjects with BMI < 25 and BMI > 25, *P* value is for *t* test between both BMI groups

	No Indexing			Indexing to BSA			Indexing to height		
	BMI < 25	BMI > 25	*p* value	BMI < 25	BMI > 25		BMI < 25	BMI > 25	*p* value
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	*p* value	Mean ± SD	Mean ± SD	
$LV\text{-}EDV_{include}$	166.5 ± 29.6	172.5 ± 29.0	0.15	86.0 ± 13.8	82.2 ± 12.5	0.04	92.9 ± 15.1	95.7 ± 14.5	0.2
$LV\text{-}ESV_{include}$	55.1 ± 14.5	56.4 ± 14.8	0.5	28.4 ± 7.0	26.9 ± 6.8	0.1	30.7 ± 7.7	31.3 ± 7.9	0.6
$LV\text{-}SV_{include}$	111.5 ± 20.4	116.1 ± 20.5	0.1	57.6 ± 9.7	55.4 ± 8.9	0.08	62.2 ± 10.6	64.4 ± 10.3	0.1
ED $LV\text{-}M_{include}$	140.0 ± 24.4	154.0 ± 23.5	< 0.0001	72.2 ± 11.2	73.4 ± 9.7	0.4	78.2 ± 12.7	85.5 ± 11.8	< 0.0001
ES $LV\text{-}M_{include}$	145.3 ± 25.0	158.9 ± 23.7	< 0.0001	75.0 ± 11.3	75.8 ± 10.1	0.6	81.1 ± 12.9	88.3 ± 12.2	< 0.0001
$LV\text{-}EDV_{exclude}$	178.8 ± 31.2	186.2 ± 30.9	0.1	92.3 ± 14.5	88.8 ± 13.2	0.07	99.8 ± 15.9	103.3 ± 15.4	0.1
$LV\text{-}ESV_{exclude}$	63.8 ± 16.6	65.2 ± 16.9	0.6	32.9 ± 8.1	31.1 ± 7.8	0.1	35.6 ± 8.8	36.2 ± 9.0	0.6
$LV\text{-}SV_{exclude}$	115.0 ± 20.5	120.9 ± 20.9	0.04	56.4 ± 9.6	57.6 ± 9.0	0.2	64.2 ± 10.6	67.1 ± 10.5	0.05
ED $LV\text{-}M_{exclude}$	127.1 ± 22.5	139.6 ± 21.3	< 0.0001	65.6 ± 10.3	66.6 ± 8.9	0.5	71.0 ± 11.7	77.5 ± 10.8	< 0.0001
ES $LV\text{-}M_{exclude}$	136.1 ± 23.6	149.6 ± 22.8	< 0.0001	70.2 ± 10.7	71.4 ± 9.8	0.4	76.0 ± 12.3	83.1 ± 10.8	< 0.0001

Table 4 Comparison of absolute left ventricular parameters and indexed left ventricular parameters in female subjects with BMI < 25 and BMI > 25

	No indexing			Indexing to BSA			Indexing to height		
	BMI < 25	BMI > 25	*p* value	BMI < 25	BMI > 25		BMI < 25	BMI > 25	*p* value
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	*p* value	Mean ± SD	Mean ± SD	
$LV\text{-}EDV_{include}$	127.1 ± 18.6	129.2 ± 18.6	0.5	74.6 ± 9.9	70.3 ± 8.6	0.004	76.0 ± 10.1	78.2 ± 10.2	0.2
$LV\text{-}ESV_{include}$	41.1 ± 9.7	41.2 ± 9.7	0.9	24.2 ± 5.6	22.5 ± 5.2	0.05	24.6 ± 5.6	24.9 ± 5.8	0.7
$LV\text{-}SV_{include}$	86.0 ± 13.1	88.0 ± 13.5	0.4	50.5 ± 6.9	47.8 ± 6.0	0.01	51.4 ± 7.2	53.2 ± 7.4	0.1
ED $LV\text{-}M_{include}$	96.1 ± 14.7	101.7 ± 14.6	0.02	56.3 ± 7.4	55.3 ± 6.9	0.4	57.4 ± 8.1	61.58.0	0.002
ES $LV\text{-}M_{include}$	100.1 ± 14.0	106.9 ± 13.8	0.004	58.7 ± 7.1	58.2 ± 6.5	0.6	59.9 ± 7.9	64.6 ± 7.5	0.0002
$LV\text{-}EDV_{exclude}$	135.5 ± 19.6	138.5 ± 19.7	0.4	79.6 ± 10.4	75.3 ± 9.1	0.007	81.0 ± 10.6	83.7 ± 10.8	0.1
$LV\text{-}ESV_{exclude}$	47.4 ± 11.0	47.9 ± 11.1	0.8	27.9 ± 6.3	26.1 ± 5.9	0.07	28.4 ± 6.4	29.0 ± 6.6	0.6
$LV\text{-}SV_{exclude}$	88.1 ± 13.4	90.6 ± 13.9	0.3	51.7 ± 7.0	49.2 ± 6.1	0.02	52.6 ± 7.3	54.8 ± 7.6	0.08
ED $LV\text{-}M_{exclude}$	87.2 ± 13.4	92.0 ± 13.5	0.03	51.2 ± 6.8	50.1 ± 6.4	0.3	52.1 ± 7.5	55.7 ± 7.5	0.005
ES $LV\text{-}M_{exclude}$	93.5 ± 13.2	100.0 ± 13.2	0.004	54.9 ± 6.7	54.4 ± 6.2	0.7	55.9 ± 7.4	60.5 ± 7.2	0.0002

p value is for *t* test between both BMI groups

Table 5 Intra- and interobserver reproducibility of LV volumes, LV-EF and LV-M

	Intraobserver variability	Interobserver variability		Intraobserver variability	Interobserver variability
$LV\text{-}EDV_{include}$	0.98	0.96	$LV\text{-}EDV_{exclude}$	0.98	0.96
$LV\text{-}ESV_{include}$	0.96	0.93	$LV\text{-}ESV_{exclude}$	0.96	0.94
$LV\text{-}SV_{include}$	0.96	0.94	$LV\text{-}SV_{exclude}$	0.96	0.94
$LV\text{-}EF_{include}$	0.90	0.89	$LV\text{-}EF_{exclude}$	0.90	0.89
ED $LV\text{-}M_{include}$	0.99	0.98	ED $LV\text{-}M_{exclude}$	0.99	0.96
ES $LV\text{-}M_{include}$	0.97	0.94	ES $LV\text{-}M_{exclude}$	0.95	0.91

Reproducibility was assessed applying correlation coefficient (p for all < 0.05)

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Authors' contributions JR—drafting of the manuscript, acquisition and analysis of data, interpretation of data. KS—drafting of the manuscript, analysis and interpretation of data. FA—acquisition of data, analysis and interpretation of data. MO—acquisition of data, revising the manuscript critically for important intellectual content. KH—acquisition of data, revising the manuscript critically for important intellectual content. ES—acquisition of data, revising the manuscript critically for important intellectual content. TF—analysis of data, revising the manuscript critically for important intellectual content. MM—acquisition of data, revising the manuscript critically for important intellectual content. EG—analysis and interpretation of data, revising the manuscript critically for important intellectual content. HK—drafting of the manuscript, final approval of the manuscript submitted. MF—drafting of the manuscript, conception and design, analysis and interpretation of data.

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Compliance with ethical standards

Conflict of interest Matthias G. Friedrich is advisor, board member and shareholder of Circle Cardiovascular Imaging Inc., Calgary.

Ethics approval The study was approved by the local ethics committee (Ethikkommission Medizinische Fakultät Heidelberg (S038-2007)).

Consent for publication Not applicable.

Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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