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ORIGINAL PAPER

Left and right ventricular parameters corrected with threshold-based quantification method in a normal cohort analyzed by three independent observers with various training-degree

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Abstract
While cardiac magnetic resonance (CMR) is the reference method to evaluate left and right ventricular functions, volumes and masses, there is no widely accepted method for the quantitative analysis of trabeculae and papillary muscles (TPM). The aim of this study was to investigate the effect of TPM quantification on left and right ventricular CMR values in a normal cohort and to investigate interobserver variability of threshold-based (TB) analysis by three independent observers with variant experience in CMR. At our clinic, 60 healthy volunteers (30 males, mean age 25.6 ± 4.7 years) underwent CMR scan performed on a 1.5T Philips Achieva MR machine. On short-axis cine images, endo- and epicardial contours were detected by three independent observers with variable experience in CMR (low- ca. 120, mid- > 800, high-experienced > 5000 original CMR cases). Using Conv and TB methods (Medis 7.6 QMass software Leiden, The Netherland), we measured LV and RV ejection fractions, end-diastolic, end-systolic, stroke volumes and masses. We used TB method for quantifying TPM in ventricles using epicardial contour layers. Interobserver variability was evaluated, and the observer's experience as an impact on variability of each investigated parameters was assessed. Comparing Conv and TB quantification methods' significant difference were detected for all LV and RV parameters in case of all observers (H, M and L $p < 0.0001$). The global intraclass correlation coefficient (G-ICC) representing interobserver agreement for all investigated parameters was lower with Conv method ($\text{G-ICC}_{\text{Conv}}$ vs. G-ICC_{TB} 0.86 vs. 0.92 $p < 0.0001$). The ICC of LV parameters was higher using TB quantification ($\text{LV-ICC}_{\text{Conv}}$ vs. $\text{LV-ICC}_{\text{TB}}$ 0.92 vs. 0.96 $p < 0.0001$), and for the evaluation of RV values, the TB method also had significantly higher interobserver agreement ($\text{RV-ICC}_{\text{Conv}}$ vs. $\text{RV-ICC}_{\text{TB}}$ 0.80 vs. 0.89 $p < 0.0001$). The TB algorithm could be a consistent method to assess LV and RV CMR values, and to measure trabeculae and papillary muscles quantitatively in various level of experience in CMR.

Keywords Cardiac magnetic resonance · Endocardium · Papillary muscles · Trabeculae · Automated thresholding · Cardiac chamber quantification

Introduction

Cardiovascular magnetic resonance (CMR) is the reference method to evaluate left (LV) and right (RV) ventricular volumes and masses [1, 2], although conventional 2D cine methods are known to cause partial volume artefacts due to the thickness of the slices.

Due to the high spatial resolution and excellent myocardial-blood contrast, CMR provide an accurate evaluation of small myocardial structures like myocardial trabeculae and papillary muscles (TPM) [3, 4]. Quantitative analysis of ventricular trabeculation and papillary muscles is controversial. There is neither generally accepted evaluation for TPM quantification, nor data available about the distribution of CMR performing laboratories regarding TPM quantification. It is difficult to compare literature data because of the diverse evaluation of TPM volumes. The majority of prior studies presented data that was either papillary muscle or trabecular mass measurement in isolation [5–8]; few studies

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are available which reported the sum of papillary and trabecular mass [9–12].

According to literature data, quantitative analysis of TPM could alter normal LV values [10, 13]. Although structural and functional evaluation of RV is challenging, CMR is an accurate method to evaluate thin free wall and trabeculation of right ventricle [1]. The right ventricular trabeculation are pronounced, but limited data is available regarding quantitative measurement of these structures in a normal population [9, 14, 15] or in pathological conditions [6, 16]. Large population based studies provide normal RV values excluding small intracavitary structures from RV mass [17–19].

Cardiovascular magnetic resonance is a rapidly maturing imaging modality. Indications of CMR examinations have continuously expanded, and an increasing number of centers perform CMR scans. Based on UK data, in half of the CMR performing laboratories are working less experienced physicians and a significant proportion of these centers do not have formal training programs for their trainees or supervised by a mentor with Level 3 CMR certification [14]. For trainees with moderate experience, the attributes of the clinically used quantification software are highly important to gain the most optimal interobserver and intraobserver agreement.

In this study we used a threshold-based (TB), semi-automatic cardiac MR quantification software (7.6 QMass Medis, Leiden, The Netherland) for the measurement of TPM. The software could delineate the myocardium from blood pool based on their different signal intensities in the absence of endocardial contour [20]. The algorithm has improved accuracy evaluating left ventricular volumetric parameters compared to flow measurement as a reference [20]. TB quantification also reported less time consuming than conventional (Conv) method regarding LV evaluation [20].

The aim of this study was to investigate the effect of TPM quantification on left and right ventricular parameters in a normal cohort and explore how varying experience in utilizing CMR influences reproducibility.

Methods

Patients' characteristics

A total of 30 male and 30 female Caucasian healthy individuals (age 25.6 ± 4.7 years) underwent cardiovascular magnetic resonance imaging. Volunteers' personal and family history were obtained using a uniform patient questionnaire focusing on cardiovascular diseases and risk factors. All subjects were free of complaints and had no known cardiovascular diseases. All volunteers underwent on a detailed medical check-up included physical examination, 12-lead resting electrocardiography and echocardiography examination. The study protocol was approved by the national ethics committee and informed consent was obtained from all individual participants included in the study.

Image acquisition

CMR examinations were conducted on a 1.5 T MRI scanner (Achieva, Philips Medical Systems) with a 5-channel cardiac coil. Retrospectively-gated, balanced steady-state free precession (bSSFP) cine images were acquired in conventional 2-chamber, 3-chamber and 4-chamber views. Short-axis cine images with full coverage of the left and right ventricle and left and right ventricular outflow tract (LVOT, RVOT) movies were also obtained. Slice thickness was 8 mm without interslice gap, field of view was 350 mm on average adapted to body size.

Image analysis

On cine short axis images end-diastolic and end-systolic cardiac phases were identified (Fig. 1). The most basal section was required to show ≥ 50% visible myocardial circumference in order to be included. For the correct visualization of LV and RV contours, additional LVOT and RVOT cine images were performed.

During conventional contouring epi- and endocardial layers were manually traced. Endocardial layer was detected along the compact myocardium resulting that TPM being included in the ventricular cavity (Fig. 1). We measured the following CMR parameters in left and right ventricles: ejection fraction (EF), end-diastolic (EDV), end-systolic (ESV), stroke volumes (SV), cardiac output (CO) and myocardial mass in end-diastolic (EDM) and end-systolic (ESM) phases. Parameters corrected for body surface area were calculated.

For TB quantification, we used the same end-systolic and end-diastolic phases. A thresholding algorithm (MassK 7.6, Medis, Leiden, The Netherlands) was used to discriminate between chamber blood and myocardium based on their alter signal intensity. The algorithm calculates blood percentage value for each pixels with the previously described equation [7]. For the evaluation of TPM, we used the application default 50% thresholding value for both left and right ventricles without manual correction and TPM, TPMi (TPM/BSA), TPM% (TPM/EDM × 100) were calculated (Fig. 1).

Three independent observers evaluated CMR images both with conventional (Conv) and threshold-based (TB) methods. The most experienced reader has 15 years of experience with more than 5000 original CMR cases and Level3 certification proved by the European Association of Cardiovascular Imaging. The mid-experienced reader had more than 800 individual original CMR cases during

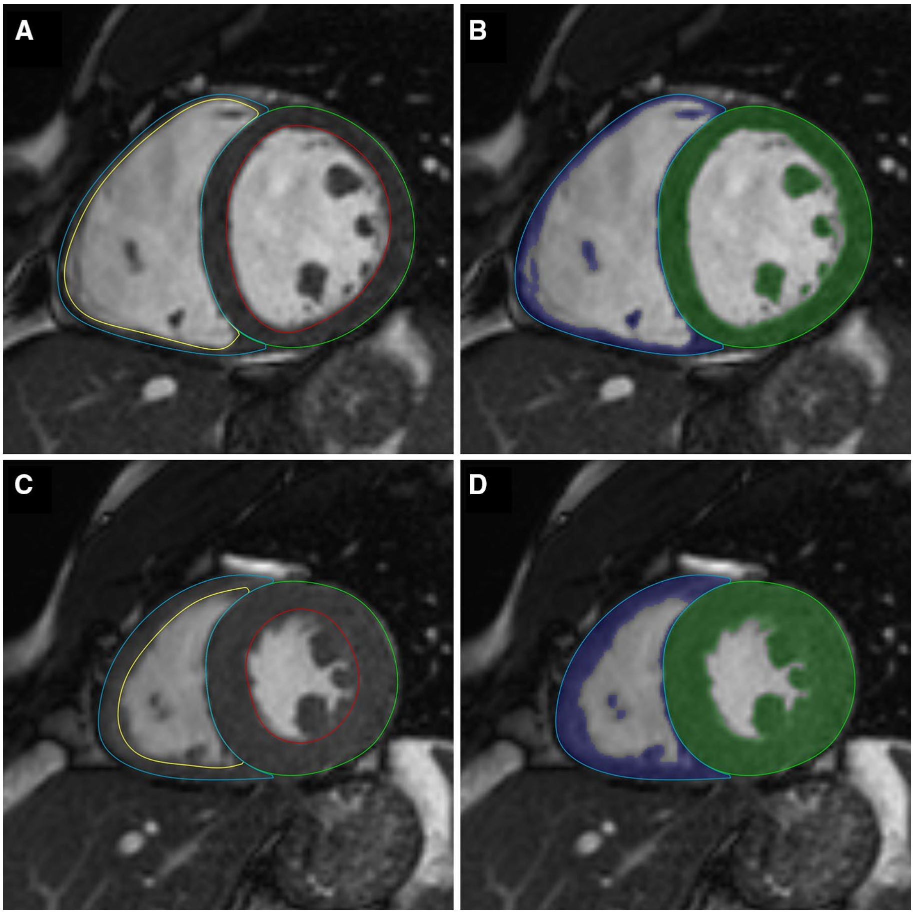

Fig. 1 During conventional contouring (**a, c**) epi- and endocardial layers were manually traced and trabeculae and papillary muscles (TPM) included in the ventricular cavity. For threshold-based quantification we used the same end-systolic and end-diastolic phases and TPM were measured as part of the ventricular mass (**b, d**)

the last 5 years and low-experienced reader independently analyzed ca. 120 CMR cases.

Statistical analysis

Statistical analyses were performed using MedCalc 13.2.2 (MedCalc Software, Ostend, Belgium). The Kolmogorov–Smirnov test was used to assess the normal distribution of the data. Continuous variables were reported as mean ± SD. p values of less than 0.05 were considered significant. The comparison of conventional and threshold-based methods was performed with repeated measures one-way ANOVA with a within-subjects design and Tukey–Kramer post hoc multi-comparison test. Equality of left and right ventricular stroke volumes was tested with paired samples t-tests. The effect of gender on the outcome of the evaluation methods was investigated with a multi-level repeated measured ANOVA. The interobserver agreement of the three MRI evaluation methods was examined with the intraclass correlation coefficients (ICC score). ICC was interpreted as follows: less than 0.4, poor; 0.4 to 0.75, fair to good; and greater than 0.75, excellent.

Results

Comparison of conventional and threshold-based methods

The various CMR parameters were compared against each other to detect differences between conventional and threshold-based methods and systematic differences were found. All of the investigated LV and RV parameters were significantly different: volumetric values were lower and masses were higher with the TB method in case of all observers (H, M, L observers $p < 0.001$). LV mass differed substantially by method with absolute difference of 34.4–43.8% and relative difference of 30.4–40.9% ($p < 0.001$). RV mass differed by method with absolute difference of 83.0–121.6% and relative difference of 86.4–114.3% ($p < 0.001$). Mean differences between Conv and TB CMR values are shown in Table 1. Left and right ventricular stroke volumes over all three observers were different using the conventional method [(1) High vs. Mid LVSVi: 51.7 ± 6.5 vs. 54.9 ± 5.9 $p < 0.001$ (2) High vs. Low-experienced LVSVi: 51.7 ± 6.5 vs.

Table 1 During comparison Conv and TB methods, all LV and RV parameters were significantly different: with TB method volumetric values were lower and masses were higher (independent-sample t-test *p < 0.001) in case of all three observers. The [Conv–TB] values show mean differences and standard deviation values between Conv and TB parameters

	High-experienced			Mid-experienced			Low-experienced		
	Conv Mean ± SD	TB Mean ± SD	Conv–TB Mean ± SD	Conv Mean ± SD	TB Mean ± SD	[Conv–TB]	Conv Mean ± SD	TB Mean ± SD	Conv–TB Mean ± SD
LVEF (%)	56.0 ± 4.8	66.8 ± 4.8*	− 10.8 ± 3.5	58.9 ± 4.7	68.1 ± 4.7*	− 9.2 ± 4.4	59.6 ± 5.0	68.3 ± 4.9*	− 8.7 ± 1.9
LVEDVi (ml/m^2)	92.6 ± 11.0	73.3 ± 8.3*	19.3 ± 4.4	93.5 ± 10.6	75.0 ± 8.8*	18.5 ± 3.3	94.9 ± 10.8	73.8 ± 7.8*	21.1 ± 4.8
LVESVi (ml/m^2)	41.0 ± 7.5	24.4 ± 5.0*	16.6 ± 4.2	38.6 ± 7.3	24.1 ± 5.4*	14.5 ± 3.0	38.5 ± 7.5	23.6 ± 5.1*	14.9 ± 3.3
LVSVi (ml/m^2)	51.7 ± 6.5	48.8 ± 5.9*	2.9 ± 3.6	54.9 ± 5.9	50.9 ± 5.5*	4.0 ± 2.8	56.4 ± 6.2	50.3 ± 5.3*	6.1 ± 2.9
LVEDMi (g/m^2)	46.1 ± 8.7	66.1 ± 11.7*	− 20.0 ± 4.6	55.1 ± 12.7	74.3 ± 14.5*	− 19.2 ± 3.3	50.6 ± 9.4	72.8 ± 13.5*	− 22.2 ± 6.0
RVEF (%)	54.0 ± 5.2	59.3 ± 5.6*	− 5.3 ± 2.5	57.7 ± 4.1	63.2 ± 4.8*	− 5.5 ± 2.8	56.7 ± 4.7	64.2 ± 5.1*	− 7.5 ± 2.8
RVEDVi (ml/m^2)	92.6 ± 10.0	76.5 ± 9.9*	16.1 ± 3.2	93.5 ± 11.2	78.9 ± 11.9*	14.6 ± 3.3	93.7 ± 13.1	77.1 ± 11.2*	16.6 ± 3.9
RVESVi (ml/m^2)	42.7 ± 7.5	31.2 ± 6.3*	11.5 ± 5.7	39.7 ± 6.7	29.0 ± 5.6*	10.7 ± 2.5	40.8 ± 8.4	27.7 ± 6.1*	13.1 ± 3.3
RVSVi (ml/m^2)	50.0 ± 6.0	45.3 ± 6.6*	4.7 ± 3.1	53.8 ± 6.6	49.9 ± 8.5*	3.9 ± 3.7	52.9 ± 7.0	49.4 ± 7.7*	3.5 ± 3.0
RVEDMi (g/m^2)	18.8 ± 4.4	35.6 ± 5.3*	− 16.8 ± 3.1	17.7 ± 6.5	33.0 ± 5.7*	− 15.3 ± 3.5	14.7 ± 3.9	32.5 ± 5.8*	− 17.8 ± 3.8

56.4 ± 6.2 p < 0.001; same significance for RV parameters (1) RVSVi: 50.0 ± 6.0 vs. 53.8 ± 6.6 p < 0.01 (2) 50.0 ± 6.0 vs. 52.9 ± 7.0 p < 0.01]. Equality of left ventricular stroke volumes was excellent with the TB method, and no significant differences were found between observers (High vs. Mid vs. Low-experienced LVSVi: 48.8 ± 5.9 vs. 50.9 ± 5.5 vs. 50.3 ± 5.3). We found that the lowest deviation between the two measurement in case of the distinct parameters were not consequently associated to one observer.

Trabeculation and papillary muscles in left and right ventricles

The average LV-TPM in end-diastolic phase was around one-third of the left ventricular mass in all observers (LV-TPM% of observers: H 30.3 ± 3.9%, M 30.0 ± 4.04%, L 26.5 ± 4.0%) while TPM in the right ventricle was measured as approximately half of the right ventricular mass (RV-TPM% of observers: H 54.6 ± 6.6%, M 48.3 ± 5.8%, L 47.0 ± 9.4%). The LV-TPM in end-diastolic and end-systolic phases was not different in observers regardless of the level of experience.

In both the left and right ventricles, the expert reader measured the highest TPMi compared to other observers (LV-EDTPMi H vs. M and L-experienced 22.5 ± 4.9 vs. 19.9 ± 4.7 and L 19.4 ± 3.4 RV-EDTPMi H vs. M-experienced 18.2 ± 4.1 vs. 15.8 ± 2.9 p < 0.001).

Gender differences

The volumetric and masses parameters of male subjects were significantly higher than that of the concomitant female parameter, across all methods and observers (p < 0.001). Differences between male and female identical CMR parameters were determined to be independent from different methods and observers (e.g., H-experienced male vs. female $\text{LVMi}_{\text{Conv}}$ 57.9 ± 7.3 vs. 43.3 ± 4.2 LVMi_{TB} 52.7 ± 6.1 vs. 39.5 ± 5.1 p < 0.001).

Interobserver reliability of different MRI methods

Comparing the two methods, interobserver variability of LV parameters was lower using TB analysis and for the evaluation of RV values TB method had superiority against Conv analysis (Table 2). Global intraclass correlation (G-ICC) value represents interobserver agreement of all investigated LV and RV parameters. $\text{G-ICC}_{\text{Conv}}$ and G-ICC_{TB} were excellent, G-ICC of TB quantification was higher than G-ICC of Conv method (Table 2).

Regarding distinct CMR parameters, interobserver agreement was excellent for volumetric parameters with both methods (ICC of $\text{LV-EDVi}_{\text{Conv}}$ 0.978 and $\text{LV-EDVi}_{\text{TB}}$ 0.969, $\text{RV-EDVi}_{\text{Conv}}$ 0.947 and $\text{RV-EDVi}_{\text{TB}}$ 0.960). When

Table 2 The ICC scores representative of conventional and threshold-based methods calculated for LV, RV and all CMR parameters for all observers

	Conventional		Threshold-based		p
	Mean ± SD		Mean ± SD		
Left ventricular CMR parameters	0.92	0.04	0.96	0.03	p < 0.0001
Right ventricular CMR parameters	0.80	0.02	0.89	0.08	p < 0.0001
Global ventricular CMR parameters	0.86	0.03	0.92	0.02	p < 0.0001

Table 3 The ICC scores representative of conventional and threshold-based methods calculated for each parameter separately for high-experienced observer

	Conventional method			Threshold-based method		
	ICC	95% confidence interval		ICC	95% confidence interval	
LVEF	0.882	0.653	0.947	0.915	0.863	0.948
LVEDVi	0.978	0.962	0.987	0.969	0.950	0.981
LVESVi	0.959	0.914	0.978	0.956	0.932	0.973
LVSVi	0.897	0.674	0.955	0.927	0.874	0.957
LVCOi	0.975	0.909	0.990	0.985	0.973	0.991
LVEDMi	0.868	0.604	0.942	0.936	0.738	0.975
RVEF	0.819	0.625	0.905	0.761	0.479	0.878
RVEDVi	0.947	0.919	0.967	0.960	0.935	0.975
RVESVi	0.910	0.849	0.947	0.897	0.779	0.946
RVSVi	0.880	0.757	0.936	0.883	0.742	0.940
RVCOi	0.966	0.930	0.981	0.952	0.893	0.976
RVEDMi	0.748	0.537	0.858	0.920	0.801	0.961

measuring LV and RV masses, TB quantification seems to be more reliable (ICC of LV-EDMi$_{\text{Conv}}$ 0.868 and LV-EDMi$_{\text{TB}}$ 0.936, RV-EDMi$_{\text{Conv}}$ 0.748 and RV-EDMi$_{\text{TB}}$ 0.920). It should be mentioned, however, that based on the data in Table 3 the ICC scores of the methods showed variability within the different parameters: the above observed trend is not reflected for the case of RVESVi, RVCOi, and RVEF and the ICC scores of RVEF have large confidence intervals.

Discussion

Left and right ventricular parameters can change depending on a different contouring process resulting in diverse normal CMR values.

In this study, we compared two different LV and RV measurements focusing on interobserver variability of readers with different experience. We determined the global ICC score for all measured CMR parameters and the TB method showed significantly higher interobserver agreement. TB-method surpassed the first method significantly with G-ICC scores of over 0.9. The threshold-based method has improved accuracy comparing aortic flow measurement as a reference [20]; accordingly, our data proved excellent equality of left and right ventricular stroke volumes with TB analysis compared to the conventional method.

Left ventricular mass is a widely accepted morphological parameter to assess and predict clinical and cardiovascular outcomes, respectively [15, 21]. Our data regarding the sum of papillary muscle and trabecular mass in the left ventricle was consistent with large population based literature data in all observers [10].

Although right ventricular morphology and function have a diagnostic and prognostic value in cardiovascular [22–25] and pulmonary diseases [18, 24, 26], TPM and TPM corrected RV parameters are not-well understood. Trabeculation in RV significantly affects quantifications of volumes and masses; indeed, in our study ca. half of the right ventricular mass was measured as TPM which is not a negligible fraction. As we previously mentioned, right ventricular trabeculation is physiologically more pronounced than the left ventricular, and the evaluation of the right ventricular contours are more challenging. Delineating the highly trabeculated endocardial surface from the ventricular cavity is more complicated in the RV than along the smooth LV surface. Manually contouring the epicardial surface of the thin RV wall is also more difficult than is the case with the thick LV wall. With the TB method after epicardial contouring, the software defines the endocardial surface based on the different signal intensity of myocytes and blood. These anatomical and technical differences could explain the large differences regarding RV mass measurement.

Threshold-based semi-automatic quantification systems are a user-friendly, accurate and consistent method for evaluating left and right ventricular CMR parameters. As it was apparent based on the above, the experience of the evaluator did not have any considerable effect on either LV or RV CMR parameters while using the TB quantification method.

Limitations of the study: the limited patient number and the lack of scan-rescan reproducibility. The high differences of ICC values between the conventional and TB methods partially may come from the altering ranges of the measured parameters.

The precise and standard measurement of left and right ventricular CMR parameters is crucial and plays a major role during patient follow-up. This study highlights the necessity of a consistent method for evaluation of papillary muscle and trabecula mass in ventricles to uniform normal CMR values, and to avoid misinterpretation of various methods and inaccurate clinical decision-making. The superior reproducibility of TPM corrected LV and RV parameters regardless of the readers' experience favors this TB algorithm for clinical use.

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Compliance with ethical standards

Conflict of interest The authors declares that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the National Research Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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