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VENTRICULAR FUNCTION

Impact of Papillary Muscles in Ventricular Volume and Ejection Fraction Assessment by Cardiovascular Magnetic Resonance

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ABSTRACT

Cardiovascular magnetic resonance (CMR) is an accurate tool for the determination of right and left ventricular volumes and ejection fractions. However, the current standard short-axis technique is time-consuming and thus, often not practicable for routine daily use, because papillary muscles and trabeculations have to be marked and their volumes subtracted from the total ventricular volume. To reduce calculation time we evaluated the volumetric data that included papillary muscle and trabecular volumes and compared the outcome with the results of the standard technique. Thirty patients (17 healthy, 13 with coronary heart disease) were examined by CMR using TrueFISP (Magnetom, Siemens, Erlangen, Germany). Right and left ventricular volumes and ejection fractions were calculated using the standard short-axis technique and then again without subtracting papillary and trabecular volumes. The two methods were compared by determining the differences in results for ventricular volumes and ejection fractions. Statistically significant differences were found between the two methods for right and left ventricular stroke volumes and end-systolic volumes, and left ventricular end-diastolic volumes (EDV) ($p \le 0.011$). No significant difference was found for right ventricular end-diastolic volumes ($p \ge 0.149$) or left or right ventricular ejection fraction ($p \ge 0.130$). Except in the case of left ventricular EDV, the deviations in the results of method 1 and method 2 did not vary significantly with the presence or absence of heart disease. Measurements were obtained considerably more quickly with the modified method than with the standard short-axis method (25 ± 4 min vs. 13 ± 3 min, p=0.000). Although systematic differences were found when papillary and trabecular volumes were not subtracted, these differences are small and may not be of clinical relevance in healthy

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subjects or patients with coronary heart disease. Not subtracting the volumes of these structures enables faster determination of right and left ventricular volumes and ejection fractions without loss of the accuracy associated with the standard shortaxis technique.

Key Words: Cardiovascular magnetic resonance imaging; Volume and ejection fraction assessment; Standard short-axis method; Modified method.

INTRODUCTION

Cardiovascular magnetic resonance (CMR) is an accurate and reproducible method of evaluating cardiac function and right and left ventricular volumes (Dulce et al., 1993; Mackey et al., 1990; Matsuoka et al., 1993; Mogelvang et al., 1986, 1988; Pattynama et al., 1995; Sakuma et al., 1993, 1996; van Rossum et al., 1988). Gradient-echo sequences with steady-state free precession [the terminology may vary according to the manufacturer (Brown and Semelka, 1999), offer enhanced blood-myocardium contrast and thus allow precise delineation of the ventricular endocardium and epicardium (Francis et al., 2001; Moon et al., 2002). The short axis method is the standard technique for the determination of right and left ventricular volumes. Since the papillary muscles and trabeculations have to be marked and their volumes subtracted from the total ventricular volume in each section measured (Fig. 1A). the technique is very time-consuming and thus, often not practicable for use in everyday clinical practice (Lorenz et al., 1999). In the search for a less timeconsuming technique that can be applied in daily clinical practice, we evaluated the volumetric data that included the volume of the papillary muscles and trabeculations (Fig. 1B) and compared it with the results of the standard short-axis technique.

METHOD

Patients

A total of 30 patients (12 female, 18 male, mean age 55.3±12.8 years) underwent CMR for the evaluation of cardiac function and cardiac volumes. Before CMR, all patients were examined by noninvasive (electrocardiogram, chest x-ray, treadmill exercise test, echocardiography, thallium-myocardial scintigraphy) and/or invasive diagnostic procedures (coronary angiography with levocardiography and electrophysiological examination). No heart disease was found in 17



Figure 1. Short-axis slice through the middle of the right and the left ventricles. Image acquisition was performed with TrueFISP. Delineation of endocardium and epicardium taking into account the papillary muscles and trabeculations (A) and without subtracting these structures, the modified method (B). Upper panel, ventricular end-diastole; lower panel, ventricular end-systole.

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patients. Of the 13 patients in whom heart disease was detected, 11 had coronary heart disease (five with past myocardial infarction) and two had dilated cardiomy-opathy. Ten patients had hypertension, three patients suffered from diabetes mellitus, and another three had a left ventricular ejection fraction of less than 35%. Informed consent was obtained from all patients before CMR. The study was conducted according to the principles of the Declaration of Helsinki.

Image Acquisition

Cardiovascular magnetic resonance was performed with a 1.5 Tesla CMR Sonata (Siemens, Erlangen, Germany) using a front and rear surface coil and prospective electrocardiographic triggering. The gradient-echo sequence TrueFISP, a fast imaging sequence with steady-state free precession, was used for image acquisition. Short-axis, two-chamber and four-chamber cine images were acquired on the basis of scout images. Short-axis scans were obtained during breathholding in end-expiration from the atrioventricular ring to the apex with a 10-mm slice thickness and a 3-mm interslice gap. The number of cardiac phases per image acquisition totaled 80-90% of the R-R interval divided by the temporal resolution (TrueFISP: 48 ms). Seven to 11 slices were necessary to cover the right and left ventricle. The following parameters were used for TrueFISP sequences: repetition time=3.2 ms, echo time=1.6 ms, slice thickness=10 mm, flip angle= 60° , in-plane pixel size= 2.3×1.4 mm, acquisition time=12 heartbeats.

Image Analysis

Images were evaluated with conventional software (Argus, Siemens, Erlangen, Germany) by two indepen-

Table 1. Mean values±standard deviation and range for volumes and ejection fractions as determined by method 1 (SM) and method 2 (MM).

	Standard 1	nethod	Modified method	
Parameter	Mean±1SD	Range	Mean±1SD	Range
A. All patients $(n=30)$				
EDV left (mL)	103.1 ± 35.5	41-195	113.7 ± 39.9	49-232
ESV left (mL)	40.3 ± 30.5	5-149	45.6 ± 34.7	6-170
SV left (mL)	62.8 ± 18.7	32-103	68.0 ± 18.4	37-106
EF left (%)	63.4 ± 15.2	24-87	62.9 ± 14.9	27-87
EDV right (mL)	104.6 ± 37.9	42-203	106.0 ± 38.2	43-204
ESV right (mL)	45.5 ± 27.7	12-154	47.7 ± 27.9	16-156
SV right (mL)	59.0 ± 20.3	21-108	58.2 ± 20.9	21-110
EF right (%)	58.3 ± 11.6	24-73	56.5 ± 11.3	24-72
B. Healthy subjects $(n = 17)$				
EDV left (mL)	102.5 ± 26.2	72-169	110.6 ± 26.4	78-175
ESV left (mL)	30.5 ± 14.2	12-68	33.9 ± 15.3	15-74
SV left (mL)	71.9 ± 15.9	52-103	76.5 ± 16.3	54-106
EF left (%)	70.4 ± 7.6	56-83	69.9 ± 8.3	55-81
EDV right (mL)	114.9 ± 27.5	60-163	116.1 ± 28.0	60-165
ESV right (mL)	45.9 ± 13.1	20-65	48.2 ± 13.5	22-66
SV right (mL)	68.6 ± 16.5	38-108	67.8 ± 17.5	37-110
EF right (%)	60.3 ± 5.4	53-72	58.8 ± 6.2	48-70
C. Patients with heart disease $(n=13)$				
EDV left (mL)	103.8 ± 46.2	41-195	117.7 ± 53.8	49-232
ESV left (mL)	53.0 ± 40.9	5-149	60.8 ± 46.4	6-170
SV left (mL)	51.0 ± 15.6	32-80	57.0 ± 15.2	37-86
EF left (%)	54.4 ± 17.9	24-87	53.7 ± 16.9	27-87
EDV right (mL)	91.2 ± 46.0	42-203	92.8 ± 46.3	43-204
ESV right (mL)	44.9 ± 40.3	12-154	46.9 ± 40.4	16-156
SV right (mL)	46.3 ± 18.1	21-78	45.7 ± 18.5	21 - 78
EF right (%)	55.6 ± 16.6	24-73	53.5 ± 15.6	24-72

Table 1A shows data from all the subjects, Table 1B data from the healthy subjects, and Table 1C data from the subjects with coronary heart disease.







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dent observers (BS, SK) who were each unaware of the other's findings.

Contour tracing was aided by reviewing the multiple phase scans in the cine mode. For both left and right ventricular volume assessment, end-diastole was defined visually as the phase with the largest volume, and endsystole as the phase with the smallest volume. At the base of the heart, slices were considered to be in the left



Figure 2. The figure shows values for left (A) and right ventricular volumes (B) and ejection fractions obtained by method 1 and 2, as well as the estimated values that were obtained by regression analysis. Comparisons of method 2 with method 1 are displayed as scatter plots. Estimated values (estimated MM and SM) are represented by straight lines.



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Table 2. This table shows parameter estimations of absolute and relative (percentage) differences between method 1 and method 2 (regression analysis).

Parameters	Absolute	e difference	Relative	difference	Heart	disease
EDV left [mL]	-2.77	p=0.551	8.4	p=0.000	5.67	p=0.026
ESV left [mL]	-0.40	p=0.523	13.3	p = 0.000	1.63	p=0.069
SV left [mL]	5.2	p = 0.011	-4.4	p=0.243	0.49	p=0.789
EF left [%]	3.11	p=0.192	-5.0	p=0.130	-1.08	p=0.277
EDV right [mL]	0.16	p=0.865	0.88	p=0.149	0.57	p=0.487
ESV right [mL]	2.2	p = 0.000	0.25	p=0.732	-0.34	p=0.620
SV right [mL]	-3.5	p=0.003	3.8	p=0.009	1.07	p=0.090
EF right [%]	1.72	p=0.525	-5.29	p=0.223	-0.85	p=0.446

In addition, the estimated effects of heart disease on the differences between the two methods are given. The table includes estimations and the corresponding p values (α =0.05).

ventricle if the blood was at least half surrounded by ventricular myocardium. For the basal slice the contours were traced up to the junction of the atrium and the ventricle. Blood volume up to the aortic valve was included in the left ventricular volume. Only the blood volume below the level of the pulmonary valve was included for right ventricular volume assessment. The epicardium and endocardium of the left ventricle and the endocardium of the right ventricle were marked with a cursor in each end-diastolic and end-systolic slice and the sum of the marked areas used to calculate the total volume. Ventricular end-diastolic volume (EDV) and end-systolic volume (ESV) were calculated from the sums of the outlined areas using a modification of Simpson's rule. Ventricular stroke volumes (SV) and ejection fractions (EF) were calculated from the formulas SV=EDV-ESV and EF=SV/EDV $\times 100\%$.

For each patient the same defined end-diastolic and end-systolic images and defined ventricular base

and apex images were used for both methods to ensure that differences in measured volumes would only be due to the inclusion or exclusion of the trabeculations or papillary muscles.

For the investigation of intraobserver variability, the same observer repeated the measurements. To assess interobserver variability, each observer measured the left and right ventricular volumes and ejection fractions on all data sets independently and was unaware of the findings of the other.

After standard short-axis technique volumetric assessment ((Lorenz et al., 1999); referred to in the following as method 1), in which the area of the trabeculations and papillary muscles is subtracted (Fig. 1A), the analysis was repeated by the same examiner without subtracting the area of the trabeculations and papillary muscles (Fig. 1B) (referred to as method 2).

The time required for contour drawing with the two methods was measured and compared.

Table 3. Intra- and interobserver variability. The values are expressed as the mean \pm standard deviation and median (in brackets).

	Intra-observer variability (%)	Inter-observer variability (%)
EDV left	$0.1 \pm 1.8 \ (-0.6)$	$0.2 \pm 1.9 (-1.1)$
ESV left	$1.0 \pm 7.6 (-1.2)$	$1.0 \pm 7.6 (-1.2)$
SV left	$-0.2\pm1.2(-1.1)$	0.0 ± 1.1 (0)
EF left	-0.3 ± 2.1 (-0.4)	-0.2 ± 2.1 (0.6)
EDV right	$0.2 \pm 2.2 (-0.8)$	$0.2 \pm 2.2 (-0.6)$
ESV right	$-0.1\pm5.9(-0.6)$	$0.2\pm5.5(-1.1)$
SV right	0.1 ± 1.3 (0)	-0.1 ± 1.5 (0)
EF right	$0.0 \pm 2.4 \ (0.4)$	$-0.3\pm2.3(-0.2)$
Overall variability	0.1 ± 3.8 (0)	0.1 ± 3.7 (0)

There was no significant difference in intra- and interobserver variability between healthy subjects and patients with heart disease ($p \ge 0.2202$).



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Statistical Methods

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The mean, standard deviation, and range of the values obtained for left and right ventricular volumes and ejection fractions with each method were determined. Deviations between the two methods were measured as differences (method 1 minus method 2). Both methods were compared and deviations of ventricular volumes and ejection fractions were calculated using linear regression analysis. The estimations of parameters in the regression models quantified systematic absolute and relative deviations of method 2 when compared to method 1. On the basis of these estimations, plots were produced for left and right ventricular volumes and ejection fractions. Measurements (method 2 vs. method 1) are displayed as scatter plots. The estimations obtained through the regression are displayed as a straight line.

Time needed to perform the measurements is described by mean value \pm standard deviation and compared by students *t*-test for paired samples.

Intra- and interobserver variability was determined from the absolute value of the difference between the two measurements over the mean of the two measurements. Intra-and interobserver variability of the two patient groups were compared using the Wilcoxon matched-pairs, signed, rank test (two-sided). The significance level (α) was set at 0.05 for all tests.

RESULTS

Table 1 gives the values for left and right ventricular volumes and ejection fractions obtained by method 1 (SM) and method 2 (MM) in all patients (Table 1A), subjects without heart disease (Table 1B), and patients with coronary heart disease (Table 1C). The results of the regression analysis are given in Fig. 2 and Table 2. Significant absolute and relative differences between the results of the two methods were found in right ventricular SV (method 2: absolute: 3.5 mL lower, p=0.003, confidence interval: 1.3-5.6 mL, relative: 3.8% higher, p=0.009, confidence interval: 1.0-6.6%). There was also a significant absolute difference in left ventricular SV (5.2 mL higher, p=0.011, confidence interval: 3.3-7.1 mL) and right ventricular ESV (2.2 mL higher, p=0.000, confidence interval: 1.5-2.9 mL). Values obtained by method 2 for left ventricular EDV (8.4% higher, p=0.000, confidence interval: 5.3-11.4%) and ESV (13.3% higher, p=0.000, confidence interval: 11.2-15.4%) were higher than those obtained by the standard short axis method. In patients with coronary heart disease, left ventricular EDV was significantly higher in method 2 than in method 1 (5.2 mL higher, p=0.020, confidence interval 0.89-9.6 mL), but the values for right EDV and left and right ventricular EF were not found to differ significantly. Except in the case of left ventricular EDV, the deviations in the results of method 1 and method 2 did not vary significantly with the presence or absence of heart disease.

The difference in volumes and EF between patients with previous myocardial infarction and those without myocardial infarction was not significant ($p \ge 0.4642$).

The findings for intraobserver variability (overall $0.1 \pm 3.8\%$) and interobserver variability (overall $0.1 \pm 3.7\%$) demonstrate very good agreement between the measurements (Table 3). No significant difference in intra-and interobserver variability was noted between healthy subjects and patients with heart disease (p ≥ 0.2202).

Method 2 (13 ± 3 min) was significantly faster than method 1 (25 ± 4 min), p=0.000.

DISCUSSION

Not subtracting the area of the trabeculations and papillary muscles in the evaluation of ventricular volumes with the gradient-echo sequence TrueFISP leads to significant differences in the results for patients with and without coronary heart disease, compared to those obtained by the standard short axis method. No differences were found for the evaluation of ejection fractions. Despite the differences noted, we believe that the modified method is a useful technique for the rapid calculation of ventricular volumes and ejection fractions. When evaluating the results, one must bear in mind that left and right ventricular ESV and left ventricular EDV may be overestimated by this technique. However, overestimation of EDV and ESV by method 2 was expected because of the increased area per slice resulting from including trabeculations and papillary muscles for volume calculation. Another reason for the differences in measurements between the two methods may be the partial volume effect, which results in blurring of the boundaries and leads to smaller volumes in the presence of trabeculae that are smaller than the slice thickness used. This effect has to be taken into account in any study in which volume measurements are obtained by boundarv tracing.

In the case of left ventricular EDV, the difference between the two methods was significantly higher in healthy subjects than in patients. The reason might be the poorer contrast between trabeculations, papillary muscles, myocardium, and slow-flowing blood in patients with impaired ventricular function. This might





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left ventricular mean value standard deviation

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Baldy, C., Douek, P., Croisille, P., Magnin, I. E., Revel, D., Amiel, M. (1994). Automated myocardial edge detection from breath-hold cine-MR images:

- end-diastolic volume
- SV

LV

- EF
- Mean
- SD

RV right ventricular EDV **ESV** end-systolic volume stroke volume ejection fraction

compromising the accuracy that is associated with the standard short-axis technique. It remains for further studies to determine whether this technique can also be used in patients with marked myocardial hypertrophy or hypertrophic cardiomyopathy. ABBREVIATIONS

relevance in healthy subjects or patients with heart disease. When these structures are not taken into account, right and left ventricular volumes and ejection fractions can be determined more quickly, without

In view of the fact that automatic contour detection still has some technical limitations and is not yet commercially available, our modified approach for right and left ventricular volume assessment would appear to be reasonable. Although systematic differences were found when

papillary and trabecular volumes were not subtracted, these differences are small and may not be of clinical

10% of the automatically detected endocardial borders and 40% of the automatically detected epicardial borders acquisition (Lalande et al., 1999).

As yet there is no data in the literature comparing the delineation of the contours, assuming accurate border detection (Baldy et al., 1994). It should be borne in mind

required manual correction. Lalande et al. found good

correlation between manual and automatic contour detection using a segmented FLASH sequence for image

time taken for manual contour tracing and automatic contour detection (including manual correction). Baldy et al. reported a time of 4 to 8 min for the automatic

that automatic contouring is currently unable to exclude the papillary muscles from the volumes (Baldy et al.,

1994; Lalande et al., 1999; Plein et al., 2001).

result in larger contour drawings, especially during borders, because of the characteristics of the adjacent end-diastole using the standard short axis method and anatomical structures. In the study of Plein et al. (2001), might lead to larger differences in volumes between SM and MM in patients.

Whether trabeculations and papillary muscles should be considered in the calculation of ventricular mass or volume is a matter of controversy that has been discussed in the literature. Sandstede et al. (2000) decided to include the papillary muscles in ventricular volume and trabeculations in ventricular mass, while Lorenz et al. (1999) included both structures in the ventricular mass. Rominger et al. (1999a,b) determined that papillary muscles and trabeculations, including the moderator band, should belong to the ventricular lumen. Dulce et al. (1993) subtracted the papillary muscles for the determination of left ventricular volumes, while Sakuma et al. (1996) and Matsuoka et al. (1993) did not say whether their calculations included these structures or not. We prefer to use the approach introduced by Lorenz et al. (1999), which is method 1 in this study. Method 2 is comparable to the method used by Rominger et al. (1999a), although they used turbo FLASH gradient-echo sequences and investigated only healthy individuals. Compared to the results reported by Rominger et al., the values for left and right ventricular volumes obtained in our study were lower and the EF of the left and right ventricle were higher. These differences may be due to the enhanced blood/myocardium contrast associated with TrueFISP, which was used in our study, and the more exact differentiation of epicardium and endocardium that this provides. Moon et al. compared TrueFISP and FLASH in cardiac volumetric assessment and concluded that endocardial contours were drawn larger and epicardial contours smaller using TrueFISP (Moon et al., 2002). In addition, they found EDV not to be significantly different, while ESV was significantly higher with TrueFISP than with FLASH in 10 healthy subjects and in 10 subjects with heart disease. No significant differences were found in the evaluation of EF.

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Differences in the parameters employed, such as slice thickness and interslice gaps, as well as differences in techniques used in recent reports, make a comparison of published results difficult.

Automatic contour detection for rapid left ventricular volume and ejection fraction assessment would be of great practical value, but has not yet been perfected and is still unreliable in the analysis of gradient-echo images (Plein et al., 2001). There are no data for automatic contour detection in the right ventricle. Manual correction of automatically detected contours often takes as long as drawing the contours manually. The epicardial borders are more difficult to detect than the endocardial



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