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VENTRICULAR FUNCTION

Evaluation of Left Ventricular Volumes and Ejection Fraction Using Fast Steady-State Cine MR Imaging: Comparison with Left Ventricular Angiography

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ABSTRACT

Previous studies demonstrated that magnetic resonance (MR) imaging consistently underestimated angiographic measurements of left ventricular (LV) volumes. The purpose of this study was to determine whether MR imaging with steady-state free precession acquisition (SSFP) can provide improved accuracy and reproducibility in measuring cardiac function in comparison with fast spoiled gradient echo cine MR imaging (SPGR). Twenty patients with cardiovascular diseases who underwent breath-hold cine MR imaging within one week of LV angiography were studied. Two sets of breath-hold cine MR images were obtained, one with SSFP and another with SPGR. The LV volumes determined by two breath-hold cine MR sequences were compared with the results by LV angiography. SPGR cine MR imaging consistently underestimated angiographic LV volumes. The mean difference of LV end-diastolic volume was -22.5 ± 14.8 ml ($p < 0.001$) for short-axis planes and -27.7 ± 21.5 ml ($p < 0.001$) for long-axis planes. In contrast, LV volumes measured by the SSFP imaging showed a good agreement with the results by angiography. The mean difference of LV end-diastolic volume was -2.5 ± 14.3 ml ($p =$ N.S.) for short-axis planes and -10.9 ± 15.1 ml ($p < 0.01$) for long-axis planes. Standard error of the estimation in measuring LV end-diastolic volume with the SSFP imaging was 3.9% for short-axis images and 4.9% for long-axis images. These values were 7.2% and 8.7% with the SPGR imaging. In conclusion, the SSFP acquisition can provide accurate and noninvasive assessments of LV volumes and ejection fraction within a reduced imaging time.

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Key Words: Left ventricular function; Magnetic resonance imaging; Steady-state free precession; Left ventricular angiography.

INTRODUCTION

Accurate and reproducible assessment of left ventricular (LV) volumes and ejection fraction is essential for assessing the prognosis of patients with heart diseases and for evaluating therapeutic responses (Chuang et al., 2000; Volpi et al., 1993; Wong et al., 1993;). Cine magnetic resonance (MR) imaging has been shown to be useful for assessing cardiac function (Buser et al., 1989; Lorenz et al., 1999; Pattynama et al., 1993; Sandstede et al., 2000; Sechtem et al., 1987; Semelka et al., 1990a; Semelka et al., 1990b; Strohm et al., 2001). When images for the entire heart are obtained, direct and precise measurement of cardiac volumes can be achieved by simply adding luminal and myocardial areas determined on each section. It is independent of geometric assumptions, noninvasive, and free of exposure to ionizing radiation.

Fast cine MR sequences using fast gradient echo acquisition (SPGR) significantly improved time efficiency of cine MR imaging and permitted breath-hold acquisition (Atkinson and Edelman, 1991; Sakuma et al., 1993; Sakuma et al., 1996). However, one major disadvantage of SPGR sequences is decreased blood pool signal because of multiple radio-frequency excitations with short repetition time, which may result in poor definition of endocardial borders (Stillman et al., 1997).

A new cine MR sequence with steady-state free precession (SSFP) can provide shorter imaging time and improved image quality in comparison with the SPGR sequences (Barkhausen et al., 2001; Bloomer et al., 2001; Moon et al., 2002; Plein et al., 2001; Thiele et al., 2001;). The image contrast with SSFP sequence is largely dependent on T2 and T1 properties (Haacke et al., 1990; Sekihara, 1987), and is less sensitive to in-flow enhancement effects of the blood. This permits more accurate delineation of the endocardial borders, particularly in areas affected by slow flow, such as around the papillary muscles. As the results show, SSFP cine MR imaging is recognized the an most accurate "gold standard" method in measuring LV volumes.

It is known that different modalities for LV function assessment, such as echocardiography, radionuclide ventriculography, angiography, and cardiovascular MR imaging, have different measurement properties and as a consequence have different reference ranges. For example, several studies demonstrated that LV volumes assessed by SSFP cine MR imaging were significantly greater than those by SPGR cine MR imaging (Moon et al., 2002; Plein et al., 2001; Thiele et al., 2001). With the continued evolution of cardiovascular MR imaging and the introduction of a new technique such as SSFP cine MR imaging, it will be important to ensure comparability between new and old techniques. If they are not comparable, it may be necessary to derive new reference ranges for each technique and to be aware of the differences when comparing images obtained with different modalities, even if the new technique is recognized as a gold standard and is much more accurate than old techniques (Moon et al., 2002).

LV angiography is one of several old modalities for assessing LV function. LV angiography is invasive and depends on irradiation and the geometric assumption. On the other hand, LV angiography has been used for assessing LV volume and function in many clinical patients for many years. The accumulation of LV angiographic data cannot be ignored. Several investigators reported the comparison of LV volume quantification between cine MR imaging and LV angiography (Buckwalter et al., 1986; Cranny et al., 1990; Higgins et al., 1988; Hundley et al., 1996; Lethimonnier et al., 1999; Mogelvang et al., 1992). Previous studies demonstrated significant underestimation of LV volumes by MR imaging in comparison with catheter LV angiography (Buckwalter et al., 1986; Cranny et al., 1990; Higgins et al., 1988). However, there is no report about the comparability between LV angiography and SSFP cine MR imaging in assessing LV function.

The purpose of this study was to determine whether the SSFP cine MR imaging can provide improved accuracy and reproducibility in measuring global cardiac function in comparison with the SPGR cine MR imaging. In addition, we evaluate the comparability of LV volume measurements between LV angiography and cine MR imaging, including a new SSFP cine MR acquisition technique.

METHODS

Twenty patients with cardiovascular diseases (15 men and five women, aged 36–85 years with mean age of 61.4 ± 13.5 years) were studied. Informed consent was obtained from each patient prior to MR

study and catheterization. These subjects included seven patients with old myocardial infarction, eight with angina pectoris, four with aortic aneurysm (three thoracic, one abdominal), and one with mitral regurgitation. Seven patients with myocardial infarction had single vessel disease. While regional wall motion abnormality was observed in patients with myocardial infarction, LV function was generally preserved in all patients, with LV ejection fraction ranging from 51.0% to 74.5%. The heart rates ranged from 60 to 86 beats per minute (the average rates of 72.2 ± 12.1 beats per minute). All patients underwent LV angiography within one week of the MR study. There were no changes in the patients' clinical status during this period.

MR images were acquired with a 1.5-T cardiac MR imager (Signa CV/i, GE Medical Systems, Milwaukee, WI) equipped with gradients that had a maximum slew rate of 150 T/m/sec and a gradient strength of 40 mT/m. Cardiac multicoil array was used for radio-frequency reception. Two sets of breath-hold cine MR images were obtained, one with the fast cine MR sequence using SPGR acquisition and another with the fast cine MR sequence using SSFP acquisition. Cine MR images were acquired on short-axis imaging planes of the LV from apex to base without intersection gaps, as well as on long-axis planes of the LV. The SPGR cine MR images were acquired with an echo time of 2.3 msec, a repetition time of 6.7 msec, a flip angle of 20°, views per segment of 8, a bandwidth of ± 32 kHz, a field of view of 28 cm, a section thickness of 10 mm, and acquisition matrices of 256 × 128. The SSFP cine MR images were acquired with an echo time of 1.8 msec, a repetition time of 3.7 msec, a flip angle of 45°, views per segment of 12, a bandwidth of ± 128 kHz, a field of view of 28 cm, a section thickness of 10 mm, and acquisition matrices of 256 × 128. The imaging time for each location was 8 cardiac cycles by SSFP cine MR imaging and 12 cardiac cycles by SPGR cine MR imaging. Reconstruction time was similar for both methods. Twenty cine frames were reconstructed per slice location.

LV volumes and ejection fractions were analyzed independently by two observers (Y.I. and K.K.) with manual tracing of the endocardial borders on cine MR images using a commercially available software (MASS-Plus, Medis, Leiden, The Netherlands). To standardize the window and level settings for visual edge detection, the level was set to 25% and the width to 100% of the difference in the signal intensities between the blood pool and myocardium for cine MR images. For short-axis cine MR studies, the area within the endocardial border was determined on end-diastolic and end-systolic images at every level of LV. The LV end-systolic volume (LVESV) and LV end-diastolic volume (LVEDV) were obtained by integrating these areas and multiplying by the section thickness. For long-axis cine MR imaging, the LVESV and LVEDV were calculated with an area-length algorithm. Stroke volume was calculated as the difference between LVEDV and LVESV. LV ejection fraction was calculated as stroke volume divided by LVEDV. These measurements were done without knowing the results obtained by LV angiography. Contrast-to-noise ratio was calculated by

contrast-to-noise ratio = (SI of LV blood − SI of myocardium)/Noise;

where SI is the signal intensity. Regions of interest (ROI) were placed in the LV chamber and in the LV myocardium. Signal intensities of the myocardial on short axis images were measured at four different locations in the septum, anterior wall, lateral wall, and inferior wall, and the results were averaged. Myocardial signal intensities on long-axis images were measured at five locations in the anterior wall, inferior wall, and apex. Large ROI for blood pool was placed within the LV chamber. Noise was measured as the standard deviation of the signal intensity within ROI placed in an artifact-free area outside the subject. The sets of ROIs were placed in similar positions on both steady state and fast-gradient echo cine MR images.

In all patients, LV angiography was performed in standard biplane 30° right anterior oblique projection and 60° left anterior oblique projection with a cineangiographic system (ADVANTX LCN, GE Medical Systems, Milwaukee, WI). A five-French pig-tail catheter was introduced into the LV via the right femoral artery. A dose of 35 ml of iopamidol (Iopamiron 370, Schering Ins., Berlin, Germany) was injected into the LV at a rate of 7 ml/sec at suspended shallow inspiration, using an injector (Mark V PLUS, Medrad Inc, Indiana, PA). The LV volumes were analyzed by two observers without knowledge of the results obtained by cine MR imaging. The LV volumes and ejection fractions were analyzed by a commercially available software (ADVANTAGE CRS Version 5.5, GE Medical Systems, Milwaukee, WI) using an area-length method (Dodge et al., 1966). End-diastolic and end-systolic projections were obtained by selecting images with the largest and smallest contours, respectively.

Data are presented as mean ± standard deviation. Linear regression analysis was performed to determine the strength of correlation between the LV volumes obtained by cine MR imaging and those obtained by LV angiography. A Bland-Altman plot was used to assess systematic trends in the differences of LVEDV

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between breath-hold cine MR imaging and LV angiography. A paired Student *t*-test was used to determine the statistical significance of the difference in the LV volumes and contrast-to-noise ratios. A p value <0.05 was considered statistically significant. Inter-observer variabilities were computed as the root of the mean squared differences divided by the average of all observations. Standard error of the estimation (SEE) was also calculated as the absolute value of the difference between the two measurements over the mean of the two measurements.

RESULTS

The SSFP cine MR imaging demonstrated sharp interfaces between the blood pool and the myocardium (Fig. 1). In contrast, the SPGR cine MR sequence generated images with less distinct blood-myocardial interface (Fig. 2). The mean contrast-to-noise ratio of SSFP cine MR images was significantly higher than that of SPGR cine MR images ($p < 0.001$, Table 1). The improvement of contrast-to-noise ratio with the SSFP cine MR imaging was most marked on long-axis images acquired at end-systole by an average of 249%.

Table 2 summarizes the LV volumes and ejection fractions measured by cine MR imaging and LV angiography, and Fig. 3 shows the mean difference between LVEDV measurements by cine MR imaging and LV angiography. The mean difference between LVEDV measurements by the SPGR cine MR imaging

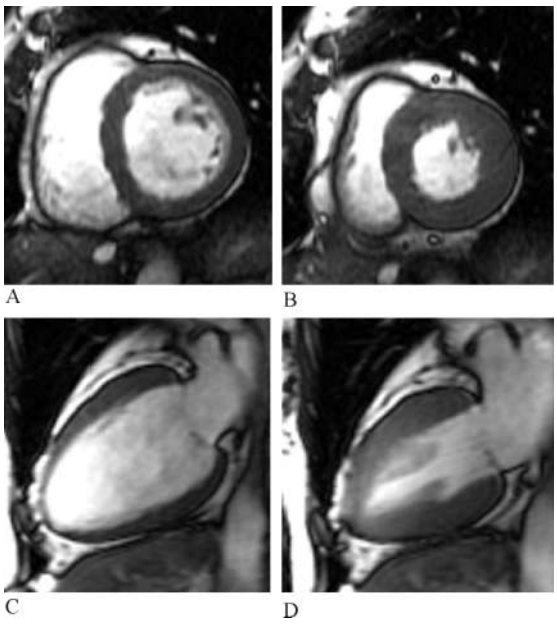

Figure 1. Breath-hold cine MR images of the left ventricle acquired with SSFP sequence in a patient with angina pectoris. A, Short-axis image at end-diastole; B, short-axis image at end-systole; C, long-axis image at end-diastole; D, long-axis image at end-systole. Excellent contrast is observed between the blood pool and the myocardium throughout the cardiac cycle.

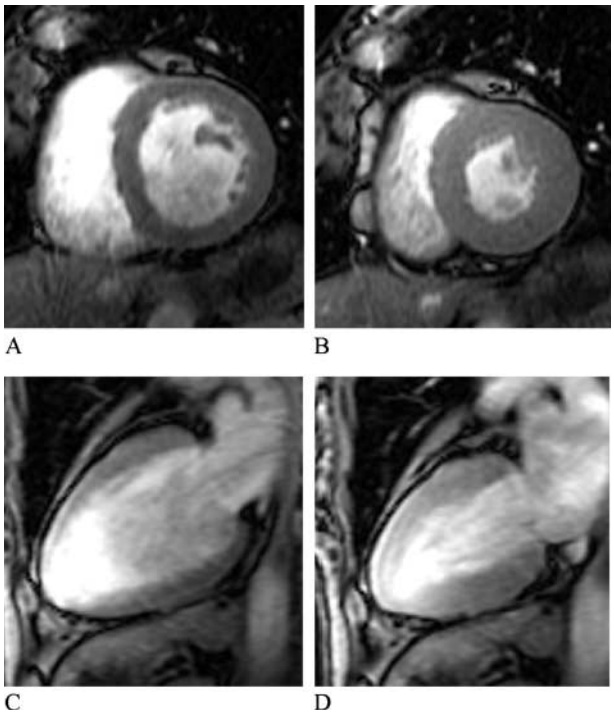

Figure 2. Breath-hold cine MR images of the left ventricle acquired with SPGR sequence in a patient with angina pectoris (the same patient in Fig. 1). A, Short-axis image at end-diastole; B, short-axis image at end-systole; C, long-axis image at end-diastole; D, long-axis image at end-systole.

Table 1. Contrast to noise ratio of breath-hold cine magnetic resonance imaging (mean ± standard deviation).

		End-systole	End-diastole
Short axis	SSFP	87.9 ± 23.0[a]	81.7 ± 19.1[a]
	SPGR	55.5 ± 12.3	45.8 ± 13.5
Long axis	SSFP	68.9 ± 22.9[a]	52 ± 18.5[a]
	SPGR	24.5 ± 11.5	14.9 ± 10.9

Abbreviations: SSFP = steady-state free precession, SPGR = fast spoiled gradient echo acquisition.
[a] $p < 0.001$.

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Table 2. Left ventricular volumes and ejection fractions measured by breath-hold cine magnetic resonance imaging and angiography (mean ± standard deviation).

		LVEDV (ml)	LVESV (ml)	LVEF (%)
Short axis	SSFP	150.7 ± 31.9[b]	59.5 ± 20.4[a]	60.8 ± 9.6
	SPGR	130.7 ± 24.9[a,b]	50.2 ± 16.5[a]	61.7 ± 9.9
Long axis	SSFP	142.2 ± 36.4[b]	55.6 ± 20.3[a]	61.8 ± 8.3
	SPGR	125.4 ± 32.4[b]	49.8 ± 20.0[a]	61.4 ± 8.3
Angiography		153.2 ± 34.6[b]	58.1 ± 19.6[a]	62.6 ± 7.7

Abbreviations: LVEDV = left ventricular end-diastolic volume, LVESV = left ventricular end-systolic volume, LVEF = left ventricular ejection fraction, SSFP = steady state free precession, SPGR = fast spoiled gradient echo acquisition.
[a] $p < 0.01$.
[b] $p < 0.001$.

and LV angiography was −22.5 ± 14.8 ml ($p < 0.001$) for short-axis planes and −27.7 ± 21.5 ml ($p < 0.001$) for long-axis planes. Agreement of the measurements between the SSFP cine MR imaging and LV angiography was substantially better, with the average difference of LVEDVs of −2.5 ± 14.3 ml (p = N.S.) for short axis planes and −10.9 ± 15.1 ml ($p < 0.01$) for long axis planes. Significant difference in LVEDV was also found between the SSFP and the SPGR imaging ($p < 0.01$).

Table 3 demonstrates correlation coefficients between the LV volumes measured by breath-hold cine MR imaging and LV angiography. The r-values between the LV volumes measured by the SSFP cine MR imaging and LV angiography ranged from 0.911 to 0.954, while the r-values between LV volumes measured by the SPGR cine MR imaging and LV angiography ranged from 0.797 to 0.927. Table 4 summarizes the inter-observer variabilities and SEE in measuring the LV volumes and ejection fractions. The SEE in measuring LVEDV with the SSFP cine MR imaging was 3.9% for short-axis images and 4.9% for long-axis images. These values were 7.2% and 8.7% with the SPGR cine MR imaging.

DISCUSSION

In the current study, the SSFP cine MR imaging demonstrated significantly increased blood to myocardial contrast in comparison with the SPGR cine MR imaging. The results of LV volume analysis showed an excellent agreement between the results by the SSFP cine MR imaging and LV angiography, while the LV volumes measured with the SPGR cine MR imaging were systemically underestimated. The inter-observer variability and SEE for measuring LV volumes was smaller with SSFP cine MR imaging than with SPGR cine MR imaging.

Comparison of Cine MR Imaging Sequences

On SSFP cine MR images, the signal intensity of tissues with long T2, such as blood, is strongly enhanced without use of the contrast medium (Oppelt et al., 1986; Zur et al., 1990). The SSFP cine MR imaging, the blood signal intensity is less dependent on in-flow enhancement effects (Oppelt et al., 1986; Zur et al., 1990). Decreased blood signal due to saturation of blood spins has been a major limitation with the SPGR cine MR imaging, particularly in patients with decreased cardiac function. Stillman, Wilke, and Jerosch-Herold (1997) demonstrated the usefulness of an intravascular contrast agent for improving blood-to-myocardial contrast on fast cine MR images. In their study, administration of an intravascular contrast medium improved the contrast-to-noise ratio of cine MR images by an average of 128% ($p < 0.05$) on long-axis planes and 34% ($p = 0.17$) on short-axis planes. In the current study, the SSFP sequence demonstrated significantly increased contrast-to-noise ratios without use of MR contrast medium, by an average of 249% on long-axis cine MR images ($p < 0.001$) and 78% on short-axis cine MR images ($p < 0.001$) when compared with the SPGR cine MR imaging.

Because of the improved blood pool signal, images with the SSFP cine MR sequence permit better definition of the endocardial border when compared images with the SPGR cine MR sequence (Moon et al., 2002; Plein et al., 2001; Thiele et al., 2001). Measurements of LV volumes revealed significant differences between the two cine MR methods. The differences in LV volumes were mainly due to

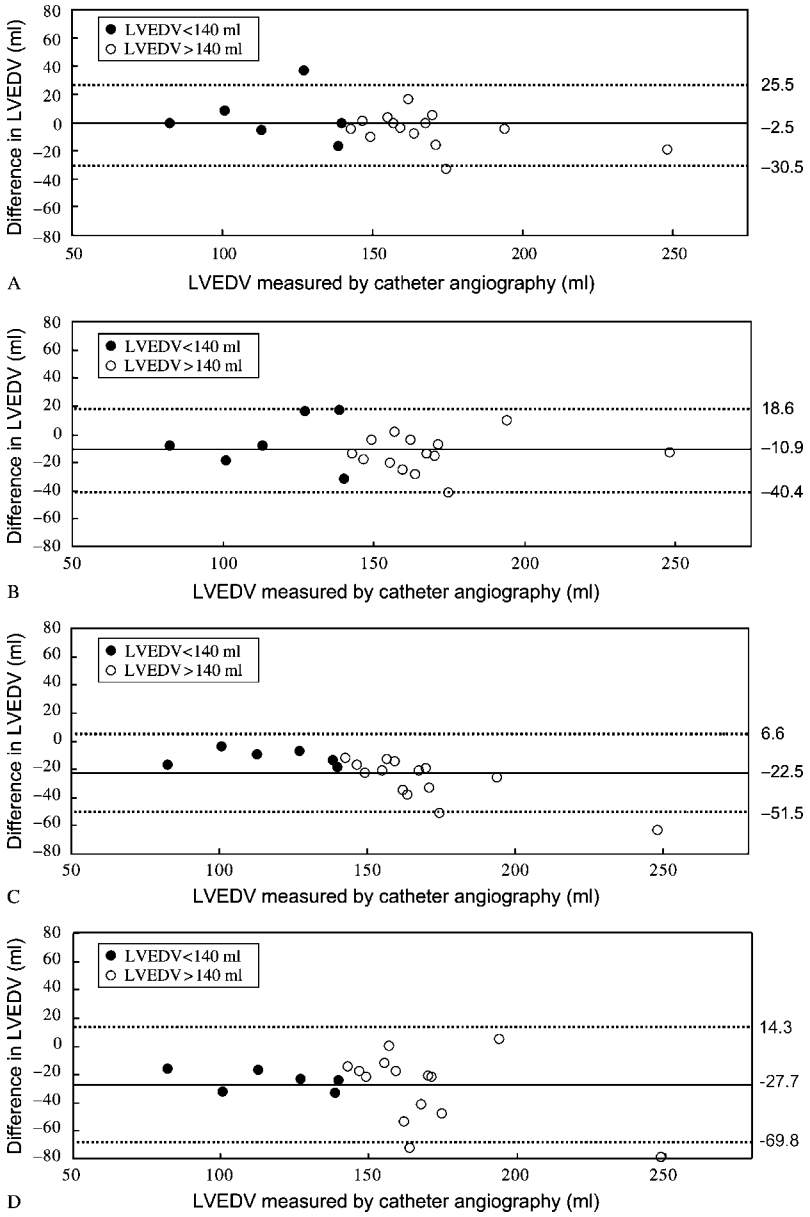

Figure 3. Bland-Altman plots for the left ventricular end-diastolic volumes between catheter angiography and cine MR methods, including short-axis (A) and long-axis (B) SSFP cine MR imaging, and short-axis (C) and long-axis (D) SPGR cine MR imaging. The vertical axis in each graph represents LVEDV by catheter angiography. The central horizontal line indicates the mean difference, and upper and lower lines represent 95% confidence intervals. LVEDV = left ventricular end-diastolic volume. MRI = magnetic resonance imaging.

a difference in positioning of the endocardial boundary, which was consistently placed outward on the SSFP cine MR images compared with the SPGR cine MR images. Contour positioning at the apparent endocardial boundary resulted in higher EDV and ESV measurements for SSFP acquisition. On SPGR cine MR images, slow flow near the endocardial border generates decreased signal and may not be well separated from myocardium. This can result in an underestimation of LV volume measurements (Plein et al., 2001; Thiele et al., 2001). The inter-observer variabilities for measuring the LV volumes with the SSFP cine MR sequence were smaller than those obtained with the SPGR cine MR sequence. The improved border

Table 3. Correlation between left ventricular volumes measured by breath-hold cine magnetic resonance imaging and angiography.

		LVEDV (ml)	LVESV (ml)
Short axis	SSFP	r = 0.911, slope = 0.839	r = 0.954, slope = 0.990
	SPGR	r = 0.927, slope = 0.667	r = 0.903, slope = 0.762
Long axis	SSFP	r = 0.911, slope = 0.958	r = 0.949, slope = 0.982
	SPGR	r = 0.797, slope = 0.746	r = 0.866, slope = 0.883

Abbreviations: LVEDV = left ventricular end-diastolic volume, LVESV = left ventricular end-systolic volume, SSFP = steady-state free precession, SPGR = fast spoiled gradient echo acquisition.

delineation in SSFP and generally better blood-to-myocardial contrast might explain the improved interobserver variability, as it makes contour detection less observer-dependent. In clinical practice, the reproducibility of a measurement is at least as important as its absolute accuracy (Plein et al., 2001). The lower inter-observer variabilities with SSFP cine MR imaging are important for clinical use.

LV Volumes Measured by Cine MR Imaging and Catheter LV Angiography

In the current study, the SPGR cine MR imaging consistently underestimated angiographic LV volumes, whereas LV volumes measured by the SSFP cine MR imaging showed a good agreement with the results by catheter LV angiography. With the SPGR cine MR sequences, the blood pool near the endocardium may not be optimally visualized due to saturation of spins from the multiple radio-frequency excitations, resulting in poor endocardial border definition and decreased LV volume measurements. This can be a problem, particularly in patients with impaired LV function or wall motion abnormalities.

The underestimation of LV volumes with MR imaging compared to LV angiography has been reported by many investigators. Buckwalter et al. (1986) determined LV volumes by using a gated spin-echo MR sequence and catheter angiography. MR imaging

Table 4. Inter-observer reproducibilities for left ventricular volume and ejection fraction.

	Short axis		Long axis	
	SSFP	SPGR	SSFP	SPGR
LVEDV				
Variability (%)	6.7	11.1	8.3	12.4
Mean ± SD (ml)	74.5 ± 5	8.5 ± 7.3	2.6 ± 8.1	1.8 ± 12.5
SEE	3.9	7.2	4.9	8.7
r^2	0.98	0.92	0.95	0.87
LVESV				
Variability (%)	4	9.7	7.1	8.1
Mean ± SD (ml)	2.4 ± 3.3	5.5 ± 8.2	1.9 ± 7	2.1 ± 8
SEE	6.5	15.4	8.3	12.3
r^2	0.98	0.78	0.9	0.85
LVEF				
Variability (%)	2	5.8	5.3	4.4
Mean ± SD (%)	−0.4 ± 2	−1.7 ± 5.7	−1 ± 5.3	−0.6 ± 4.4
SEE	2.9	7.8	6.6	5.8
r^2	0.97	0.72	0.69	0.77

Abbreviations: LVEDV = LV end-diastolic volume, LVESV = LV end-systolic volume, LVEF = LV ejection fraction, SD = standard deviations, SEE = standard error of the estimation, SSFP = steady-state free precession, SPGR = fast spoiled gradient echo acquisition.

underestimated angiographic measurements of LVEDV and LVESV by 28% and 26%, respectively. In a study reported by Cranny et al. (1990), LVEDV evaluated by long axis MR imaging (161 ± 85 ml) and short-axis MR imaging (151 ± 81 ml) was systematically less than those by LV angiography (182 ± 85 ml). Higgins et al. (1988) also documented that LV volumes measured by cine MR imaging were smaller than those from angiographic measurements.

On the Bland-Altman plots in this study, the average difference of LVEDVs between the SSFP cine MR imaging and LV angiography was only −2.5 ±14.3 ml for short-axis planes and −10.9 ± 15.1 ml for long-axis planes. Considering volume of the contrast medium injected during LV angiography (7 ml/sec), LV volumes determined by short-axis and long-axis SSFP cine MR images showed a fairly good agreement with the results by LV angiography in the current patients with relatively normal LV function.

Comparison of Imaging Planes

Breath-hold cine MR images were acquired on short-axis imaging planes as well as on long axis imaging planes. When cine MR images were acquired on multiple short-axis imaging planes encompassing the entire LV, direct and precise measurement of LV volumes and mass could have been achieved by simply adding luminal and myocardial areas determined on each section. This short-axis approach is ideal for accurate assessments of LV volumes and mass, since it does not relay on geometric assumptions or calculations based on partial sampling of the LV. LV volume measurement using cine MR images on long-axis planes requires shorter time for both image acquisition and analysis. However, LV volume quantification using the long-axis approach depends on the geometric assumption and may not be accurate in patients with LV deformity or regional wall motion abnormality.

In this study, long-axis cine MR images were obtained in addition to short-axis cine MR images, in order to make a direct comparison between cine MR imaging and catheter LV angiography for calculating the LV volumes using an area-length method. Both short-axis and long-axis SSFP cine MR images showed an excellent agreement with LV angiography in quantifying the LV volumes. Most patients enrolled in this study demonstrated relatively normal LV function, with an averaged LVEF of 61–63%. The results with the short-axis approach and the long-axis approach might be different if patients with severe LV dysfunction and LV deformity were evaluated.

Study Limitations

Catheter LV angiography and cine MR studies were performed within a one-week interval. We tried to minimize the possibility of a change in LV function during this time by excluding patients with acute myocardial infarction or change in cardiac medication.

Although catheter LV angiography has several limitations, it has been used for many years and is still frequently performed in clinical patients. The major point of this study is that the SSFP cine MR imaging can substitute for invasive catheter angiography for determining the LV volumes and ejection fractions.

In the current study, the results of LV volume analysis showed an excellent agreement between the results by the SSFP cine MR imaging and LV angiography in subjects with generally normal LV function. It is also important to know the comparability of LV volume measurements between cine MR imaging and LV angiography in patients with impaired LV function. The volume analysis using LV angiography depends on the geometric assumption and may demonstrate a limited accuracy in patients with significant regional LV dysfunction. The agreement between LV angiography and SSFP cine MR imaging in those patients with decreased LV function may not be as good as that in subjects with preserved LV wall motion.

CONCLUSIONS

The SSFP cine MR imaging shows a significantly improved blood-to-myocardial contrast and improved endocardial border definition within a reduced imaging time in comparison with the SPGR cine MR imaging. Although the SPGR cine MR imaging consistently underestimated angiographic LV volumes, the SSFP cine MR imaging showed good agreement with catheter LV angiography in measuring the LV volumes and ejection fractions. These results indicat that SSFP cine MR imaging can substitute for invasive LV angiography in quantification of LV function.

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