



STRUCTURE AND FUNCTION

**Qualitative Assessment of Regional Left Ventricular Function
Can Predict MRI or Radionuclide Ejection Fraction: An Objective
Alternative to Eyeball Estimates****Lilia M. Sierra-Galan, W. Patricia Ingkanisorn, Kenneth L. Rhoads,
Kwabena O. Agyeman, and Andrew E. Arai***Laboratory of Cardiac Energetics, National Heart, Lung and Blood Institute,
National Institutes of Health, Bethesda, Maryland, USA**ABSTRACT**

Purpose. Assessment of left ventricular function is important in patients with heart disease. We hypothesized that regional wall motion assessed qualitatively by cine magnetic resonance imaging (MRI) can predict the left ventricular ejection fraction (EF). *Methods.* The correlations between MRI EF and the American Society of Echocardiography (ASE) score index and a modified ASE score index were established in 117 subjects. The model was tested in the next 86 patients. Interobserver variability was studied in 30 patients. Radionuclide EF was compared in 81 patients. Cine MRI studies were performed on a 1.5 T scanner. *Results.* From the initial 117 patients, there was a linear correlation between the ASE score index and MRI ($r = 0.85$), but the relationship improved by including a category of hyperkinetic wall motion ($r = 0.90$). Using these correlations to predict MRI EF in the next 86 patients, there was a good agreement ($r = 0.93$ for the ASE score index and $r = 0.97$ for the modified ASE score index). Correlations between radionuclide EF and the EF predicted by the modified ASE score index or the MRI EF by planimetry were similar ($r = 0.91$ vs. $r = 0.90$, respectively). Four observers tested the model and achieved comparable results ($r = 0.88$ to 0.95). *Conclusions.* There is a close relationship between ejection fraction and the ASE score index or modified ASE score index. This correlation can provide an objective prediction of ejection fraction based solely on a qualitative reading of regional wall thickening.

Key Words: Magnetic resonance imaging; Regional wall motion abnormalities; Left ventricular function; Ejection fraction; Ischemic heart disease; Hyperkinetic; Myocardial contraction.

*Correspondence: Andrew E. Arai, M.D., Laboratory of Cardiac Energetics, National Heart, Lung, and Blood Institute, National Institutes of Health, Bldg 10, B1D61, MSC 1061, 10 Center Drive, Bethesda, MD 20892; Fax: 301 402 2389; E-mail: arai@nih.gov.

INTRODUCTION

The ejection fraction (EF) has prognostic value in a wide range of cardiac diagnoses (The Multicenter Postinfarction Research Group, 1983; Bigger et al., 1984; Bonow et al., 1985; Chaitman et al., 1980; Gersh et al., 1985; Gradman et al., 1989; Lee et al., 1993; Passamani et al., 1985). Magnetic resonance imaging (MRI) is accepted as a gold standard measure of left ventricular volumes and EF. However, qualitative decisions regarding how many slices to analyze near the base of the ventricle must be made even with automatic analysis methods. This decision can introduce 15% errors in estimating left ventricular volumes (Marcus et al., 1999) since the basal slice of the ventricle contributes disproportionately to the volume of the ventricle.

Thus far, echocardiography and MRI have primarily used a qualitative wall motion score for most clinical purposes including stress testing. While echocardiographic image quality has precluded accurate measurements of wall thickening in most clinical settings, measurements are more feasible with cardiac MRI studies (van Ruge et al., 1994). Even if wall thickening is quantified, clinicians still need to assess regional function qualitatively.

The purpose of this study was to investigate the relationship between EF and regional wall thickening assessed by cine MRI. We hypothesized that the 16-segment model of the American Society of Echocardiography (ASE) (Schiller et al., 1989), as summarized by the ASE score index, should correlate with global measures of contractile function such as left ventricular EF. We also measured wall thickening to provide a quantitative comparison for each of the qualitative wall motion scores.

METHODS

Study Population

This study retrospectively analyzed the relationship between global and regional left ventricular systolic function. The initial cohort used to establish the relationship between measured left ventricular EF and regional wall motion was composed of 117 patients, aged 47 ± 17 years (range 12–78), with 68% males and 32% females, and the following diagnoses in order of prevalence: ischemic heart disease, chemotherapy, aortic disease, congenital heart disease, cardiac masses, pericardial disease, pulmonary

hypertension, heart transplant, valvular heart disease, hypertrophic cardiomyopathy, normal volunteer, right ventricular (RV) dysplasia, dilated cardiomyopathy, hypertension, and cardiac sarcoidosis.

A second cohort was used to test the relationships in a completely independent group of patients. The second cohort was composed of 86 patients, aged 52 years \pm 16 (range 10–86), with 59% males and 41% females, and the following diagnoses: ischemic heart disease, hypertrophic cardiomyopathy, aortic disease, normal volunteer, pericardial disease, dilated cardiomyopathy, valvular heart disease, chemotherapy, and cardiac tumors.

Cardiac MRI Examination

Patients were scanned in a 1.5 T scanner (General Electric CV/i, Waukesha, WI) using a 4-element cardiac phased array coil. Left ventricular systolic function and mass were evaluated in continuous short-axis slices using either electrocardiogram (ECG)-gated cine MRI in steady state free precession (SSFP) (Barkhausen et al., 2001) or an ECG-gated fast gradient echo cine sequence (FGRE). Both sequences imaged the entire cardiac cycle (Feinstein et al., 1997). For the SSFP cine method, the scan parameters selected included a slice thickness of 8 mm, in-plane resolution of 1.5×1.9 mm/pixel, and temporal resolution of 41 ms (12 views per segment, TR = 3.4 ms, TE 0.8 to 1.0 ms). For the FGRE cine acquisitions, typical parameters included a slice thickness of 8 mm, in-plane resolution of 1.4×1.7 mm/pixel, and temporal resolution of 56 ms (6 views per segment, TR = 9.3 ms, TE 3.5 ms). Imaging was performed during short breath holds.

Regional Wall Motion Assessment

The cardiologist reading the studies was blinded to the diagnosis and the EF. The regional wall motion was entered into a database following the guidelines of the American Society of Echocardiology (ASE). Based on the initial correlations, a cardiologist reviewed the studies in a second reading with the express purpose of subdividing normal segments into hyperkinetic or normal segments. Each of the 16 segments was assigned a score (normal = 1 to aneurysm = 5). The ASE score index was the sum of the regional wall motion scores divided by the number of segments analyzed. To calculate the modified ASE score index, a hyperkinetic segment was given a score of 0.

Quantitative and Qualitative Left Ventricular Function

453

Data Analysis

A cardiologist used computer-assisted planimetry to delineate the epicardial and endocardial borders on short-axis images of the left ventricle. Quantitative MRI EF was calculated from end-diastolic and end-systolic volumes. Left Ventricular wall thickening in mm was calculated from end-diastolic and end-systolic LV wall thickness measured using a centerline chordal thickness calculated from epicardial and endocardial contours. Measurements of LV wall thickness were performed in all 16 segments of myocardium. Quantitative measurements for each qualitative grade of regional wall motion were averaged to provide ranges corresponding to these abnormalities.

Validations in an Independent Cohort and Against Radionuclide Ventriculography

Since the initial correlations were derived from two separate readings of the same studies, independent validations of the methods were performed in three ways. First, the methods developed in the initial cohort were prospectively applied to a completely *independent cohort* of 86 patients. Next, the relationship between ASE score index and the modified ASE score index was assessed in a subgroup analysis of the 81 subjects from either cohort that had a radionuclide ventriculogram. No significant clinical event occurred between the cardiac MRI scan and the radionuclide ventriculogram. Finally, the sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of predicting left ventricular ejection fraction (LVEF) above or below thresholds of 55%, 45%, and 35% were calculated against both quantitative MRI and radionuclide EF.

Interobserver Variability and Image Quality Assessments

Four cardiologists interpreted 30 MRI scans to test interobserver variability of qualitative regional wall motion reading. Readings of regional wall motion were committed to paper prior to any discussion of the study. Next, the endocardial and epicardial traces were reviewed. A consensus reading of regional wall motion was recorded as the average of the four readers with consensus used to resolve split decisions.

Each observer rated overall image quality independently on a scale of excellent, good, fair, poor, and nondiagnostic. The grading was based on the clinician's

confidence in interpreting regional wall thickening. The difference between predicted LVEF and measured LVEF was determined for a subgroup of MRI scans performed with FGRE ($n = 69$) and SSFP ($n = 49$). We also determined the range of normal ejection fraction by FGRE and SSFP in subjects with qualitatively normal regional wall motion.

Statistical Analysis

Results are expressed as mean \pm standard deviation (SD). A simple linear regression was used to compare continuous variables. The method of Bland and Altman (1986) was used to describe differences between two observations or measurements. The Spearman Rank Order correlation was used to compare regional wall motion on a segment-by-segment basis.

RESULTS

Development of the Model Relating Wall Motion to Ejection Fraction

The initial cohort of 117 subjects demonstrates a linear correlation between the ASE score index and the MRI left ventricular EF (Fig. 1a). Since it is impossible for a patient to have a more normal ASE score index than that associated with all normal segments, any normal-to-hyperdynamic EF is associated with an ASE score of 1 unless there was also a regional wall motion abnormality. This appears graphically as a clustering of points with ASE score equal to 1. The clustering of points appears particularly prominent on the figures because there are approximately five times as many studies with a wall motion score index of 1 than any other bin of wall motion scores. As shown in Table 1, the ranges of ejection fractions associated with normal wall motion by either FGRE or SSFP methods agree well with values in the literature (Bellenger et al., 2000; Beranek et al., 1976; Butler et al., 1998; Federman et al., 1978; Hains et al., 1987; Hood et al., 1968; Kennedy et al., 1966; Kuikka and Ahonen, 1977; Longobardi et al., 1998; Lorenz et al., 1999; Moon et al., 2002; Moraski et al., 1975; Nakhjavan et al., 1975; Pfisterer et al., 1980; Pietras et al., 1985; Plein et al., 2001; van Rugge et al., 1993; Steele et al., 1976; Wachspress et al., 1988; Wackers et al., 1979; Waiter et al., 1999; Wynne et al., 1978).

The modified ASE score index correlates with the MRI EF as shown in Fig. 1b. This correlation was used in all subsequent test groups to provide an estimate of the left

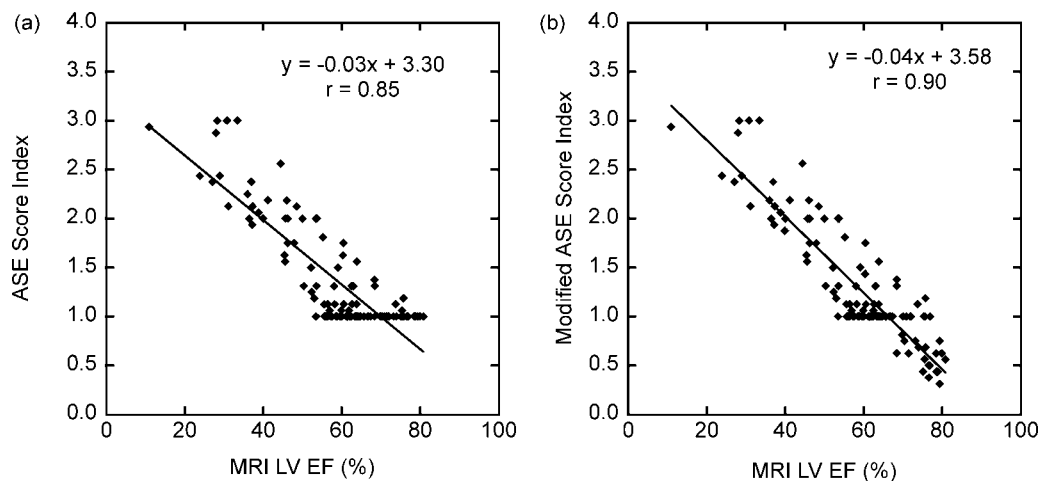


Figure 1. Correlation between MRI ejection fraction and the ASE score index and the modified ASE score index in the initial cohort of 117 patients used to develop the model.

ventricular EF based solely on qualitative regional wall motion. Since the formula for either correlation is similar (Fig. 1a or 1b), we used the same formula for either the ASE score index or the modified ASE score index.

Test of the Model in an Independent Cohort

The second cohort of 86 patients was used to validate the methods developed in the initial 117 subjects. Figure 2a shows the correlation between the predicted left ventricular EF calculated using the ASE score index and the EF measured by planimetry of cine MRI ($y = 0.69x + 14.6$, $r = 0.93$, $p < 0.001$). The Bland-Altman analysis (Fig. 2c) shows slight bias between the predicted and measured EF. There is a systematic error related to the range of ejection fractions encountered in people with normal wall motion. This effect is evident in both displays as a clustering of points related to a normal ASE score index. The predicted EF is higher than the measured EF for all subjects with measured EF $< 45\%$ (Fig. 2a and 2c). The lack of a hyperkinetic score for regional wall motion would be expected to result in a shift toward underestimation of high ejection fractions. This effect is seen by the large number of points below the line of identity for ejection fractions above 60% (Fig. 2a) and on the corresponding Bland-Altman plot (Fig. 2c).

Use of the modified ASE score index improves the relationship between predicted EF and MRI EF by planimetry ($y = 0.88x + 7.05$, $r = 0.97$, $p < 0.001$, Fig. 2b). This effect is qualitatively evident in

the patients with normal to high ejection fractions. While it would be difficult to tell the difference between two correlations with an r value of 0.93 and 0.97 since much of the correlation is weighted by low ejection fractions from patients with few or no hyperkinetic segments, the differences become more obvious by studying the predicted ejection fractions in patients with normal or higher EF. In patients with a normal or supranormal MRI EF, the MRI EF averaged $70\% \pm 7\%$ while the ASE score index predicted $63\% \pm 2\%$ ($p < 0.001$) and the modified ASE score index predicted $69\% \pm 7\%$ ($p = 0.03$). Thus, the addition of the hyperkinetic segment reduces the error in estimating normal to high ejection fractions.

Comparisons with Radionuclide Ejection Fraction

A total of 81 subjects had a radionuclide ventriculogram available for comparison with MRI. Fifty-three percent of the studies were performed within 1 day of each other, 79% within 1 week, but 11% were separated in time by more than 1 month. In the studies more than a month apart, the difference between MRI and radionuclide EF averaged $0\% \pm 7\%$. Thirty radionuclide ventriculograms were from the initial cohort and 51 were from the second cohort.

There is a close correlation between the MRI EF measured by planimetry and the radionuclide EF (Fig. 3a, $y = 0.99x - 1.8$, $r = 0.90$, $p < 0.001$) despite the wide range of patients included in this study. The Bland Altman analysis (Fig. 3b) shows increased scatter



Table 1. Comparison of normal LV EF determinations with published values.

Method	LVEF (%) + /- SD	Reference	Comments
MRI (GRE)	64 + /- 7	Current paper	N = 20 normal RWM
MRI (GRE)	70 + /- 7	Bellenger et al. (2000)	N = 20
MRI (GRE)	70 + /- 4	Butler et al. (1998)	N = 20 volunteers
MRI (GRE)	67 + /- 5	Lorenz et al. (1999)	N = 75
MRI (GRE)	66 + /- 3	Moon et al. (2002)	N = 10
MRI (GRE)	64 + /- 16	Plein et al. (2001)	N = 16 (10 volunteers; 6 normal RWM)
MRI (GRE)	65 + /- 3	Van Ruge et al. (1993)	N = 23 normal volunteers
MRI (GRE)	69 + /- 6	Waiter et al. (1999)	N = 10
MRI (SSFP)	64 + /- 6	Current paper	N = 45 normal RWM
MRI (SSFP)	60 + /- 17	Plein et al. (2001)	N = 16 (10 volunteers; 6 normal RWM)
MRI (SSFP)	64 + /- 4	Moon et al. (2002)	N = 10
X-ray LV angiography	73 + /- 7	Beranek et al. (1976)	N = 50 normal RWM
X-ray LV angiography	67 + /- 7	Hood et al. (1968)	N = 6
X-ray LV angiography	67 + /- 8	Kennedy et al. (1966)	N = 16
X-ray LV angiography	75 + /- 9	Nakhjavan et al. (1975)	N = 8
X-ray LV angiography	55 + /- 4	Moraski et al. (1975)	N = 15 normal RWM
X-ray LV angiography	68 + /- 7	Pietras et al. (1985)	N = 17
X-ray LV angiography	72 + /- 8	Wynne et al. (1978)	N = 17
Gated radionuclide	66 + /- 8	Wackers et al. (1979)	N = 34 normal RWM
Gated radionuclide	66 + /- 6	Longobardi et al. (1998)	N = 12 volunteers
Gated radionuclide	61 + /- 5	Pfisterer et al. (1980)	N = 20 volunteers
Gated radionuclide	63 + /- 6 semiautomatic	Hains et al. (1987)	N = 24 volunteers
	60 + /- 6 manual		
Gated radionuclide	62 + /- 9	Federman et al. (1978)	N = 14 normal X-ray LVEF
First pass radionuclide	62 + /- 8	Kuikka and Ahonen (1977)	N = 16
First pass radionuclide	65 + /- 8	Wackers et al. (1979)	N = 34 normal RWM
First pass radionuclide	66 + /- 1 (SEM)	Steele et al. (1976)	N = 14 volunteers
Ultrafast CT	70 + /- 7	Wachspress et al. (1988)	N = 10

Abbreviations: LV = left ventricular, EF = ejection fraction, SD = standard deviation, SEM = standard error of mean, RWM = regional wall motion, GRE = gradient recalled echo, SSFP = steady-state free precession.

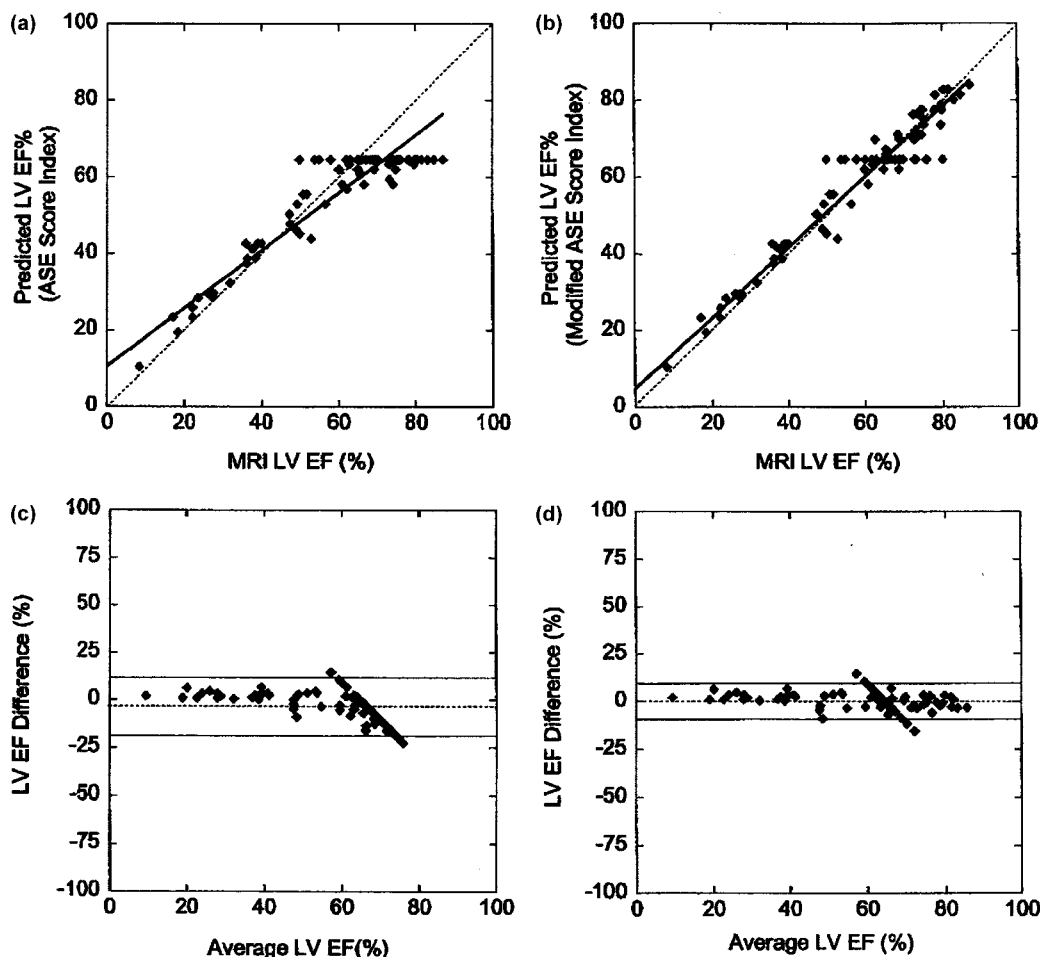


Figure 2. Correlation and Bland-Altman analysis comparing the measured MRI ejection fraction with the ejection fraction predicted by the ASE score index and the modified ASE score index in the test cohort of 86 patients. For the correlations, the solid line represents the linear regression and the dashed line is the line of identity. For the Bland-Altman analysis, the solid lines indicate two standard deviations from the mean (dashed line).

at higher ejection fractions but no other significant bias. The standard deviation of the difference in measured ejection fractions is 10%.

The ASE score index can predict the radionuclide EF (Fig. 4a, $y = 0.56x + 21.6$, $r = 0.87$, $p < 0.001$) almost as well as it can predict the MRI EF (Fig. 2a). However, the lack of a hyperkinetic segment leads to similar underestimations at normal-to-high ejection fractions. The artificial maximal predicted EF is also evident on both the correlation (Fig. 4a) and the Bland-Altman analysis (Fig. 4c).

The predicted EF based on the modified ASE score index correlates with the radionuclide EF (Fig. 4b, $y = 0.73x + 16.31$, $r = 0.91$, $p < 0.001$), as well as the MRI EF by planimetry correlates with the radionuclide ventriculogram (Fig. 3a). Perhaps as a result of referral patterns for

radionuclide ventriculography in National Institutes of Health (NIH) research protocols, only eight subjects had a modified wall motion score index of 1 and thus the cluster of points corresponding to normal wall motion is much less obvious than in prior figures. Table 2 summarizes the ability of the predicted LVEF to dichotomize the quantitative MRI EF or radionuclide EF above or below thresholds between normal, mild, moderate, and severe LV dysfunction (LVEF 55%, 45%, and 35%, respectively).

Wall Thickening vs. ASE Score Index and Modified ASE Score Index

The average wall thickening plus or minus 1 standard deviation is shown in Fig. 5a for the ASE

Quantitative and Qualitative Left Ventricular Function

457

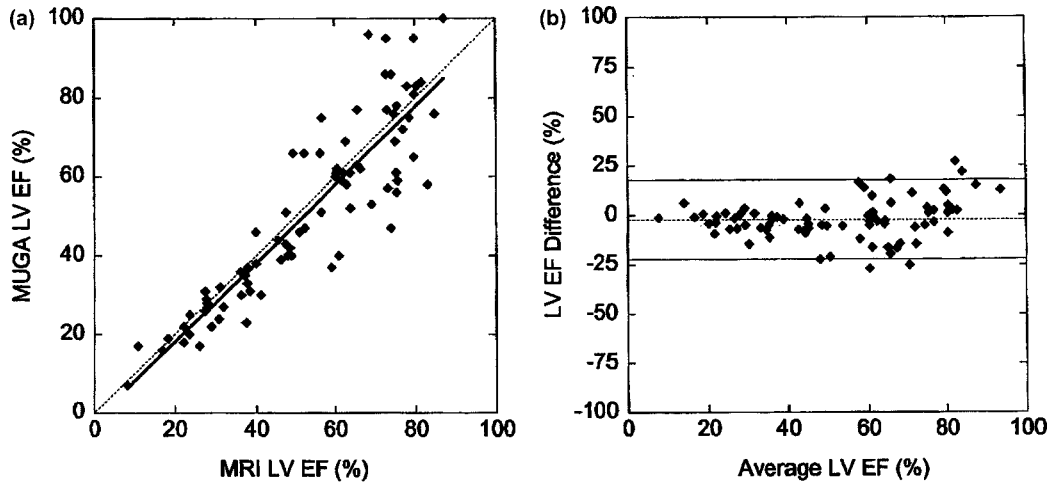


Figure 3. Correlation and Bland-Altman analysis comparing the measured MRI ejection fraction with the radionuclide ejection fraction. Lines and symbols as in Fig. 2.

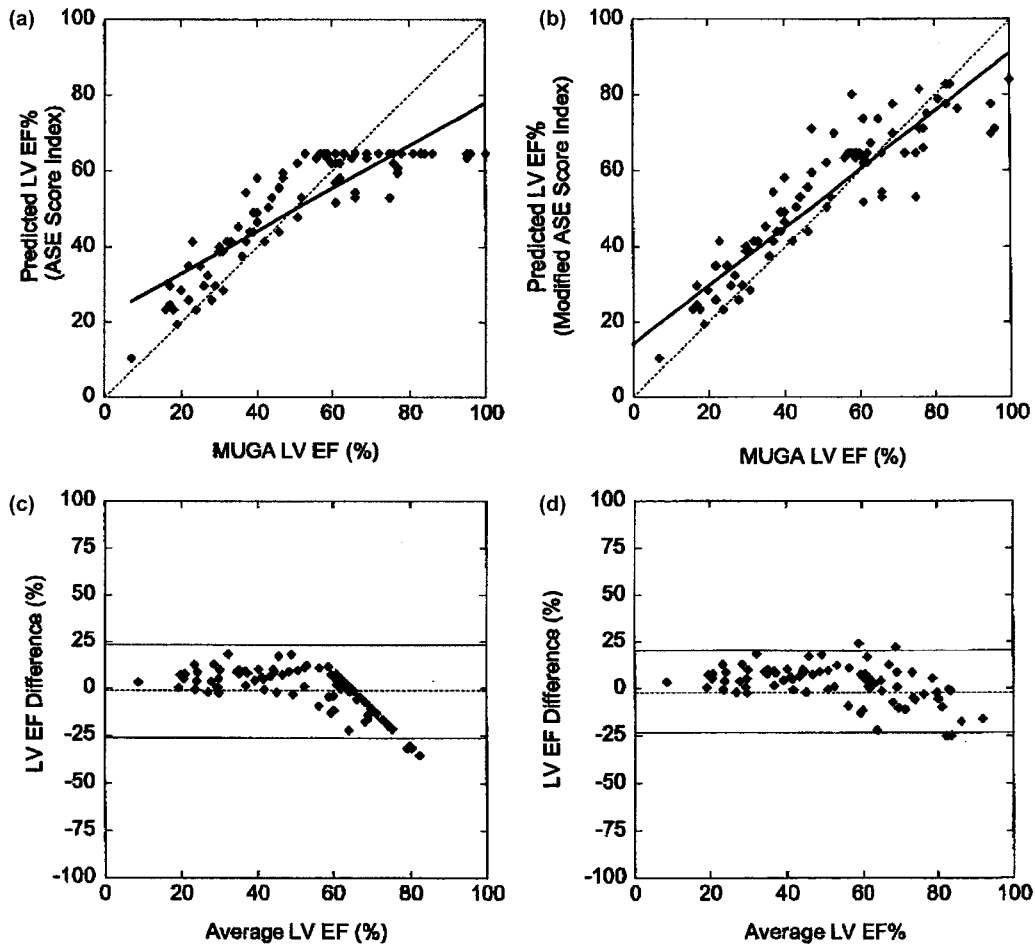


Figure 4. Correlation and Bland-Altman analysis comparing radionuclide ejection fraction with the ejection fraction predicted by the ASE score index and the modified ASE score index. Lines and symbols as in Fig. 2.

Table 2. Sensitivity, specificity, and positive and negative predictive value of the predicted LVEF as a predictor of thresholds for mild, moderate, and severe LV dysfunction.

LV EF (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Initial cohort (n = 117)					
Qualitative predicted MRI vs. measured MRI LVEF					
< 55	88	94	85	95	92
< 45	73	98	89	93	93
< 35	86	98	75	99	97
Independent cohort (n = 86)					
Qualitative predicted MRI vs. measured MRI LVEF					
< 55	96	92	84	98	93
< 45	95	100	100	98	99
< 35	100	100	100	100	100
Radionuclide group (n = 81)					
Qualitative predicted MRI vs. measured MRI LVEF					
< 55	90	95	95	90	93
< 45	93	98	96	96	96
< 35	100	98	94	100	99
Radionuclide group (n = 81)					
Qualitative predicted MRI vs. radionuclide LVEF					
< 55	90	85	86	89	88
< 45	96	85	77	98	89
< 35	100	89	68	100	91

score and in Fig. 5b for the modified ASE score. Due to the presence of some markedly hyperkinetic segments, the standard deviation of normal segments is 2.8mm using the ASE score but decreases to 2.4mm with the modified ASE score. Since there were only 153 hyperkinetic segments, the 1177 normal segments disproportionately influence the average wall thickening on either chart.

The correlation between absolute wall thickening and the MRI EF ($y = -0.19x - 2.27$, $r = 0.78$, $p < 0.001$) improves by binning the wall thickening measurements into hyperkinetic (>7 mm), normal (7 to 3 mm), hypokinetic (3 to 1 mm), akinetic (1 to -1 mm), and dyskinetic (<-1 mm) ($y = -0.04x + 3.2$, $r = 0.86$, $p < 0.001$). There was a linear correlation between the qualitative ASE score and the quantitative wall

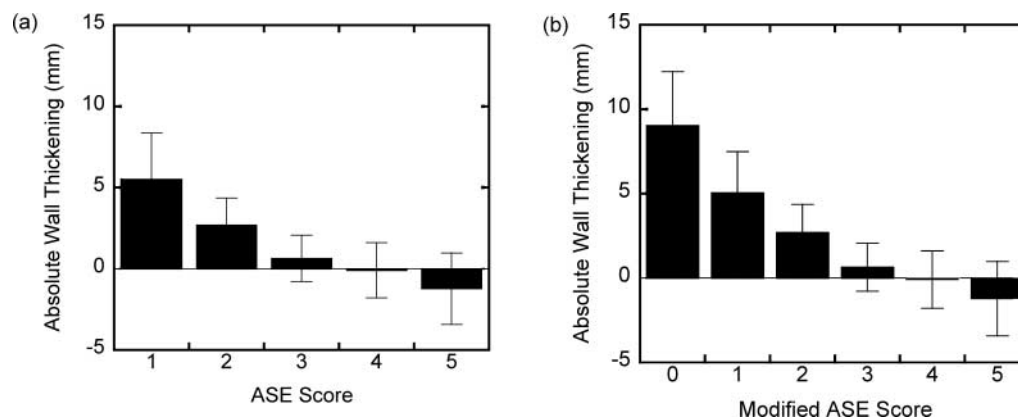


Figure 5. Quantitative wall thickening corresponding to wall motion scores. The left panel does not include a hyperkinetic score (0).

Quantitative and Qualitative Left Ventricular Function
Table 3. Correlation between each observer ASE score and the consensus ASE score.

Observer	Correlation ASE vs. MRI EF	Bland-Altman ASE vs. consensus 1 SD	Bland-Altman ASE vs. consensus 2 SD	Correlation modified ASE vs. consensus	Bland-Altman modified ASE 1 SD	Bland-Altman modified ASE 2SD
1	R = 0.97	+/- 0.19	+/- 0.38	R = 0.99	+/- 0.12	+/- 0.24
2	R = 0.95	+/- 0.23	+/- 0.47	R = 0.97	+/- 0.19	+/- 0.37
3	R = 0.98	+/- 0.17	+/- 0.33	R = 0.99	+/- 0.11	+/- 0.23
4	R = 0.95	+/- 0.19	+/- 0.37	R = 0.97	+/- 0.17	+/- 0.33

Error bars representing 1 and 2 standard deviations for the estimates based on Bland-Altman analysis are provided.

thickening score using these ranges ($y = 0.93x + 0.21$, $r = 0.88$, $p < 0.001$).

Interobserver Variability

The correlation between the consensus reading of ASE score and the individual observer interpretation ranged from an r value of 0.97 to 0.99 (Table 3). For all observers, the standard deviation of the difference from the consensus reading was less than 0.19 units. Even when analyzed on a segment-by-segment basis, the observers agreed well with the consensus reading. The Spearman Rank correlation coefficient was 0.87, 0.87, 0.92, and 0.88 for the four observers when comparing their individual regional wall motion score with the consensus score. Approximately 80% of segments were in complete agreement with the consensus and 1% or fewer segments differed by more than one grade. Note that some of the differences between readers and the consensus result from

errors due to registration of segments, but we did not adjust for this factor.

For the four observers and the consensus, the correlation between quantitative EF and the predicted EF ranged from 0.88 to 0.95 index (Table 4) using the ASE score index or the modified ASE score. The one- and two-standard deviation error bars for the predicted ejection fractions were the same or smaller than the errors associated with comparing radionuclide ventriculography and MRI ejection fractions.

Image Quality

The majority of studies were rated good (56.7%). Only 2.5% of studies were judged excellent, 3.3% were rated poor, and no studies were nondiagnostic. Out of 3248 possible segments, no segments were excluded from regional wall motion analysis. The average absolute difference between the predicted and measured LVEF

Table 4. Correlation coefficients between the MRI ejection fraction and the left ventricular ejection fractions predicted by the individual observer's ASE score index or the modified ASE score index.

Observer	Correlation ASE vs. MRI EF	Bland-Altman ASE 1SD	Bland-Altman ASE 2SD	Correlation modified ASE vs. MRI EF	Bland-Altman modified ASE 1 SD	Bland-Altman modified ASE 2SD
1	R = 0.93	+/- 10	+/- 19	R = 0.95	+/- 8	+/- 16
2	R = 0.89	+/- 11	+/- 21	R = 0.91	+/- 9	+/- 19
3	R = 0.89	+/- 10	+/- 21	R = 0.92	+/- 9	+/- 18
4	R = 0.88	+/- 11	+/- 23	R = 0.89	+/- 10	+/- 20
Consensus	R = 0.92	+/- 10	+/- 20	R = 0.94	+/- 8	+/- 17
Radionuclide EF	R = 0.87	+/- 12	+/- 25	R = 0.91	+/- 10	+/- 20

Error bars for the estimates based on Bland-Altman analysis are provided for 1 and 2 standard deviations (SD). For comparison, the same statistics for the radionuclide ejection fraction in place of MRI ejection fraction are also included.



was $5.4 + / - 3.9$ for FGRE and minimally better for SSFP $4.7 + / - 3.3$.

DISCUSSION

Based on the philosophy that global left ventricular function should equal the sum of regional function, we studied the relationship between the 16-segment ASE score index and EF. While there is a good correlation between the ASE score index and EF, the relationship improves when considering hyperkinetic segments. Thus, the modified ASE score index generally does a better job of predicting EF but this benefit is largely restricted to normal and hyperdynamic ventricles. The strength of these relationships are demonstrated by the fact that the developed model could predict MRI EF in a completely independent cohort of 86 patients. In addition, the model could predict EF measured by radionuclide ventriculography.

An important question regarding this approach relates to the difficulty in reading regional contractile function. It is generally agreed that assessing regional wall motion is the most challenging aspect in interpreting echocardiograms (Oh et al., 1999). Indeed, with MRI studies using fast gradient echo techniques, we found the long-axis views of the heart difficult to interpret near the apex, but short-axis views were quite good. The introduction of fast cine imaging in steady-state free precession has substantially improved the depiction of regional wall motion on cardiac MRI studies (Barkhausen et al., 2001). It should be noted that no segments were excluded from regional wall motion assessment in this study of 203 patients. This was possible because the image quality of cardiac MRI studies is reasonably consistent from patient to patient. Furthermore, the wide range of patients studied includes individuals with ejection fractions ranging from 8–87%. It should be noted that approximately 5–10% of patients may have exclusions to MRI, and this retrospective study did not have a method to track eligibility for the MRI study.

The current study includes an analysis of the interobserver variability of MRI assessment of regional wall motion. Although all readers had completed standard cardiology fellowships, two of the cardiologists had less than 6 months experience in cardiac MRI and one had one year of training. Despite this, excellent interobserver agreement was achieved both on a regional basis and on a global basis in terms of the ASE score index.

Some of the best evidence that MRI is an accurate method for assessing regional wall motion comes from the dobutamine stress MRI literature. Dobutamine stress MRI appears at least equivalent to stress echocardiography for detecting significant coronary artery stenosis. (Hundley et al., 1999; Nagel et al., 1999; Pennell et al., 1992; Rerkpattanapipat et al., 2001; van Ruyge et al., 1994) In addition, dobutamine MRI can predict viable myocardium in intermediate dose dobutamine stress (Baer et al., 1998; 2000; Sandstede et al., 1999). Recent attempts to use real-time cine MRI methods appear promising for assessment of regional function (Yang et al., 1998) but may quantitatively underestimate wall thickening due to suboptimal temporal or spatial resolution (Plein et al., 2001). We have preferred the higher resolution and image quality afforded by averaging several heartbeats during short breath holds. Thus, in patients able to tolerate a gated cardiac MRI study, the assessment of regional wall motion appears at least as good as echocardiographic methods.

The relationship between a qualitative assessment of regional wall motion and global function has been studied by echocardiography. In a 9-segment model of regional wall motion (Berning et al., 1992; McGowan et al., 2001) and a 5-segment model (Erbel et al., 1985), there were comparable correlations between global and regional function. We have not seen a study using the standard 16-segment model of the ASE.

The incorporation of a hyperkinetic segment needs to be considered depending on the purpose of the test (Kjoller et al., 1999). The relationship between EF and the ASE score index or the modified score index clearly indicates that the current standard of using a single category of normal function does not adequately describe regional contractile function. In fact, most echocardiographers incorporate the hyperkinetic segment when interpreting dobutamine stress tests. At the same time, if the purpose of the ASE score index is to detect ischemic heart disease, it has been noted that a hyperkinetic segment can cancel out a regional wall motion abnormality in the modified ASE score index (Feigenbaum, 1994a, b). In fact, this is one mechanism by which patients with myocardial infarctions maintain normal global function.

The relative value of regional wall motion assessment is also dependent on the clinical setting. For example, rest regional wall motion and EF is insensitive to significant coronary stenosis. In the other extreme of characterizing viable myocardium, rest regional wall motion has diagnostic limitations as well (Klein et al., 2002). In some settings such as acute coronary syndromes, rest regional wall motion is

Quantitative and Qualitative Left Ventricular Function

461

particularly powerful since it can detect stunned myocardium with no evidence of infarction (Kwong et al., 2003).

Based on this study and prior experience (Kwong et al., 2003), we find that thresholds of > 7 mm, $7-3$ mm, $3-1$ mm, 1 to -1 mm, and < -1 mm are reasonable quantitative correlates to the qualitative categories of hyperkinetic, normal, hypokinetic, akinetic, and dyskinetic. The category of aneurysm is reserved for the specific distorted anatomy characteristic of a thin wall with a systolic and diastolic bulge from the normal endocardial contour. Based on Fig. 5b, there is a nonlinear relationship between the amount of wall thickening and the qualitative wall motion score. Since the correlation between ASE score and EF is linear (Fig. 1a and 1b), there must be a nonlinear relationship between wall thickening and EF.

For subjects with a normal modified ASE score index, the measured MRI EF ranged from 53% to 80% ($64\% \pm 7\%$). Analyzed from the perspective of expecting 90% of subjects to fit within the 95% confidence limits in a two-tailed model, 60 of 67 patients (90%) were within our previously determined normal range from 55% to 75%. Thus, the prominent cluster of points corresponding to the normal wall motion score index in most of the figures represents the large number of points at this discrete value.

CONCLUSIONS

Despite improvements in the quantification of EF by MRI, it is still the responsibility of the interpreting physician to verify the final report. In our experience, qualitative predicted assessment of regional wall motion provides a practical and objective method for estimating EF. In the data presented in this study, the model predicts the MRI EF as well as a radionuclide scan can predict the MRI findings. Interobserver variability appears promising. Compared with having two observers quantify LVEF at 15 minutes per observer, the use of a qualitative LVEF based on the ASE score index could save 12 minutes of analysis per study since wall motion can be read qualitatively in ~ 3 minutes. Since completing this study, we have used the method in quality assurance to objectively decide whether regions of interest reasonably summarize LVEF. For practical implementation, a site should use a cohort of patients that covers the entire range of ejection fractions encountered when establishing their local standards.

REFERENCES

- Baer, F. M., Theissen, P., Schneider, C. A., Voth, E., Sechtem, U., Schicha, H., et al. (1998). Dobutamine magnetic resonance imaging predicts contractile recovery of chronically dysfunctional myocardium after successful revascularization. *J. Am. Coll. Cardiol.* 31(5):1040-1048.
- Baer, F. M., Theissen, P., Crnac, J., Schmidt, M., Deutsch, H. J., Sechtem, U., et al. (2000). Head to head comparison of dobutamine-transoesophageal echocardiography and dobutamine-magnetic resonance imaging for the prediction of left ventricular functional recovery in patients with chronic coronary artery disease. *Eur. Heart J.* 21(12):981-991.
- Barkhausen, J., Ruehm, S. G., Goyen, M., Buck, T., Laub, G., Debatin, J. F. (2001). MR evaluation of ventricular function: true fast imaging with steady-state precession versus fast low-angle shot cine MR imaging: feasibility study. *Radiology* 219(1):264-269.
- Bellenger, N. G., Davies, L. C., Francis, J. M., Coats, A. J., Pennell, D. J. (2000). Reduction in sample size for studies of remodeling in heart failure by the use of cardiovascular magnetic resonance. *J. Cardiovasc. Magn. Reson.* 2(4):271-278.
- Beranek, I., Moore, R., Kim, S., Formanek, A., Amplatz, K. (1976). Comparison of ejection fraction calculated by nine different volume calculation methods. *Radiology* 120(3):553-556.
- Berning, J., Rokkedal, N. J., Launbjerg, J., Fogh, J., Mickley, H., Andersen, P. E. (1992). Rapid estimation of left ventricular ejection fraction in acute myocardial infarction by echocardiographic wall motion analysis. *Cardiology* 80(3-4):257-266.
- Bigger, J. T. Jr., Fleiss, J. L., Kleiger, R., Miller, J. P., Rolnitzky, L. M. (1984). The relationships among ventricular arrhythmias, left ventricular dysfunction, and mortality in the 2 years after myocardial infarction. *Circulation* 69(2):250-258.
- Bland, J. M., Altman, D. G. (1986). Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1(8476):307-310.
- Bonow, R. O., Picone, A. L., McIntosh, C. L., Jones, M., Rosing, D. R., Maron, B. J., et al. (1985). Survival and functional results after valve replacement for aortic regurgitation from 1976 to 1983: impact of preoperative left ventricular function. *Circulation* 72(6):1244-1256.
- Butler, S. P., McKay, E., Paszkowski, A. L., Quinn, R. J., Shnier, R. C., Donovan, J. T. (1998). Reproducibility study of left ventricular measurements with breath-hold cine MRI using a semiautomated volumetric image analysis program. *J. Magn. Reson. Imaging* 8(2):467-472.
- Chaitman, B. R., Rogers, W. J., Davis, K., Tyras, D. H., Berger, R., Bourassa, M. G., et al. (1980). Operative risk factors in patients with left main coronary-artery disease. *N. Engl. J. Med.* 303(17):953-957.

- Erbel, R., Schweizer, P., Meyer, J., Krebs, W., Yalkinoglu, O., Effert, S. (1985). Sensitivity of cross-sectional echocardiography in detection of impaired global and regional left ventricular function: prospective study. *Int. J. Cardiol.* 7(4):375–389.
- Federman, J., Brown, M. L., Tancredi, R. G., Smith, H. C., Wilson, D. B., Becker, G. P. (1978). Multiple-gated acquisition cardiac blood-pool isotope imaging. Evaluation of left ventricular function correlated with contrast angiography. *Mayo. Clin. Proc.* 53(10):625–633.
- Feigenbaum, H. (1994a). Echocardiographic Evaluation of Cardiac Chambers. In: Lea & Febiger, ed. *Echocardiography*. Indianapolis, Indiana, pp. 134–180.
- Feigenbaum, H. (1994b). Coronary Artery Disease. In: Lea & Febiger, ed. *Echocardiography*. Indianapolis, Indiana, pp. 447–510.
- Feinstein, J. A., Epstein, F. H., Arai, A. E., Foo, T. K., Hartley, M. R., Balaban, R. S., et al. (1997). Using cardiac phase to order reconstruction (CAPTOR): a method to improve diastolic images. *J. Magn. Reson. Imaging* 7(5):794–798.
- Gersh, B. J., Kronmal, R. A., Schaff, H. V., Frye, R. L., Ryan, T. J., Mock, M. B., et al. (1985). Comparison of coronary artery bypass surgery and medical therapy in patients 65 years of age or older. A nonrandomized study from the Coronary Artery Surgery Study (CASS) registry. *N. Engl. J. Med.* 313(4):217–224.
- Gradman, A., Deedwania, P., Cody, R., Massie, B., Packer, M., Pitt, B., et al. (1989). Predictors of total mortality and sudden death in mild to moderate heart failure. Captopril-Digoxin Study Group. *J. Am. Coll. Cardiol.* 14(3):564–570.
- Hains, A. D., Al Khawaja I., Hinge, D. A., Lahiri, A., Raftery, E. B. (1987). Radionuclide left ventricular ejection fraction: a comparison of three methods. *Br. Heart. J.* 57(3):242–246.
- Hood, W. P. Jr., Rackley, C. E., Rolett, E. L. (1968). Wall stress in the normal and hypertrophied human left ventricle. *Am. J. Cardiol.* 22(4):550–558.
- Hundley, W. G., Hamilton, C. A., Thomas, M. S., Herrington, D. M., Salido, T. B., Kitzman, D. W., et al. (1999). Utility of fast cine magnetic resonance imaging and display for the detection of myocardial ischemia in patients not well suited for second harmonic stress echocardiography. *Circulation* 100(16):1697–1702.
- Kennedy, J. W., Baxley, W. A., Figley, M. M., Dodge, H. T., Blackmon, J. R. (1966). Quantitative angiocardiology. I. The normal left ventricle in man. *Circulation* 34(2):272–278.
- Kjoller, E., Kober, L., Jorgensen, S., Torp-Pedersen, C. (1999). Long-term prognostic importance of hyperkinesia following acute myocardial infarction. TRACE Study Group. TRAndolapril Cardiac Evaluation. *Am. J. Cardiol.* 83(5):655–659.
- Klein, C., Nekolla, S. G., Bengel, F. M., Momose, M., Sammer, A., Haas, F., et al. (2002). Assessment of myocardial viability with contrast-enhanced magnetic resonance imaging: comparison with positron emission tomography. *Circulation* 105(2):162–167.
- Kuikka, J., Ahonen, A. (1977). A simple and rapid non-invasive radioisotope method to determine ventricular ejection fractions and cardiopulmonary transit times. *Nuklearmedizin* 16(2):57–62.
- Kwong, R. Y., Schussheim, A. E., Rekhraj, S., Aletras, A. H., Geller, N., Davis, J., Christian, T. F., Balaban, R. S., Arai, A. E. (2003). Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. *Circulation* 107:538–544.
- Lee, T. H., Hamilton, M. A., Stevenson, L. W., Moriguchi, J. D., Fonarow, G. C., Child, J. S., et al. (1993). Impact of left ventricular cavity size on survival in advanced heart failure. *Am. J. Cardiol.* 72(9):672–676.
- Longobardi, S., Cuocolo, A., Merola, B., Di Rella, F., Colao, A., Nicolai, E., et al. (1998). Left ventricular function in young adults with childhood and adulthood onset growth hormone deficiency. *Clin. Endocrinol. (Oxf.)* 48(2):137–143.
- Lorenz, C. H., Walker, E. S., Morgan, V. L., Klein, S. S., Graham, T. P. Jr. (1999). Normal human right and left ventricular mass, systolic function, and gender differences by cine magnetic resonance imaging. *J. Cardiovasc. Magn. Reson.* 1(1):7–21.
- Marcus, J. T., Gotte, M. J., DeWaal, L. K., Stam, M. R., Van der Geest, R. J., Heethaar, R. M., et al. (1999). The influence of through-plane motion on left ventricular volumes measured by magnetic resonance imaging: implications for image acquisition and analysis. *J. Cardiovasc. Magn. Reson.* 1(1):1–6.
- McGowan, J. H., Martin, W., Burgess, M. I., McCurrach, G., Ray, S. G., McDonagh, T. A., et al. (2001). Validation of an echocardiographic wall motion index in heart failure due to ischaemic heart disease. *Eur. J. Heart Fail.* 3(6):731–737.
- Moon, J. C., Lorenz, C. H., Francis, J. M., Smith, G. C., Pennell, D. J. (2002). Breath-hold FLASH and FISP cardiovascular MR imaging: left ventricular volume differences and reproducibility. *Radiology* 223(3):789–797.
- Moraski, R. E., Russell, R. O. Jr., Smith, M. K., Rackley, C. E. (1975). Left ventricular function in patients with and without myocardial infarction and one, two or three vessel coronary artery disease. *Am. J. Cardiol.* 35(1):1–10.
- Nagel, E., Lehmkuhl, H. B., Bocksch, W., Klein, C., Vogel, U., Frantz, E., et al. (1999). Noninvasive diagnosis of ischemia-induced wall motion abnormalities with the use of high-dose dobutamine stress MRI: comparison with dobutamine stress echocardiography. *Circulation* 99(6):763–770.
- Nakhjavan, F. K., Natarajan, G., Goldberg, H. (1975). Comparison of ejection fraction and zonal mean velocity of myocardial fiber shortening. *Circulation* 52(2):264–267.
- Oh, J. K., Seward, J. B., Tajik, A. J. (1999). In: Mayo Clinic and Mayo Foundation, ed. *The Echo Manual*. Rochester, Minnesota: Lippincott Williams & Wilkins, pp. 73–90.

**Quantitative and Qualitative Left Ventricular Function**

463

- Passamani, E., Davis, K. B., Gillespie, M. J., Killip, T. (1985). A randomized trial of coronary artery bypass surgery. Survival of patients with a low ejection fraction. *N. Engl. J. Med.* 312(26):1665–1671.
- Pennell, D. J., Underwood, S. R., Manzara, C. C., Swanton, R. H., Walker, J. M., Ell, P. J., et al. (1992). Magnetic resonance imaging during dobutamine stress in coronary artery disease. *Am. J. Cardiol.* 70(1):34–40.
- Pfisterer, M. E., Battler, A., Slutsky, R., Froelicher, V., Ashburn, W. (1980). Differential diagnosis of atypical chest pain syndromes by equilibrium radionuclide angiography during exercise. *Eur. J. Cardiol.* 11(6):425–434.
- Pietras, R. J., Kondos, G. T., Kaplan, D., Lam, W. (1985). Comparative angiographic right and left ventricular volumes. *Am. Heart J.* 109(2):321–326.
- Plein, S., Bloomer, T. N., Ridgway, J. P., Jones, T. R., Bainbridge, G. J., Sivananthan, M. U. (2001). Steady-state free precession magnetic resonance imaging of the heart: comparison with segmented k-space gradient-echo imaging. *J. Magn. Reson. Imaging* 14(3):230–236.
- Plein, S., Smith, W. H., Ridgway, J. P., Kassner, A., Beacock, D. J., Bloomer, T. N., et al. (2001). Qualitative and quantitative analysis of regional left ventricular wall dynamics using real-time magnetic resonance imaging: comparison with conventional breath-hold gradient echo acquisition in volunteers and patients. *J. Magn. Reson. Imaging.* 14(1):23–30.
- Rerkpattanapipat, P., Link, K. M., Hamilton, C. A., Hundley, W. G. (2001). Detecting left ventricular myocardial ischemia during intravenous dobutamine with cardiovascular magnetic resonance imaging (MRI). *J. Cardiovasc. Magn. Reson.* 3(1):21–25.
- van Ruge, F. P., Holman, E. R., van der Wall, E. E., de Roos, A., van der, L. A., Bruschke, A. V. (1993). Quantitation of global and regional left ventricular function by cine magnetic resonance imaging during dobutamine stress in normal human subjects. *Eur. Heart. J.* 14(4):456–463.
- van Ruge, F. P., van der Wall, E. E., Spanjersberg, S. J., de Roos, A., Matheijssen, N. A., Zwinderman, A. H., et al. (1994). Magnetic resonance imaging during dobutamine stress for detection and localization of coronary artery disease. Quantitative wall motion analysis using a modification of the centerline method. *Circulation* 90(1):127–138.
- Sandstede, J. J., Bertsch, G., Beer, M., Kenn, W., Werner, E., Pabst, T., et al. (1999). Detection of myocardial viability by low-dose dobutamine Cine MR imaging. *Magn. Reson. Imaging* 17(10):1437–1443.
- Schiller, N. B., Shah, P. M., Crawford, M., DeMaria, A., Devereux, R., Feigenbaum, H., et al. (1989). Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J. Am. Soc. Echocardiogr.* 2(5):358–367.
- Steele, P., Kirch, D., LeFree, M., Battock, D. (1976). Measurement of right and left ventricular ejection fractions by radionuclide angiocardiology in coronary artery disease. *Chest* 70(1):51–56.
- Wachspress, J. D., Clark, N. R., Untereker, W. J., Kraushaar, B. T., Kurnik, P. B. (1988). Systolic and diastolic performance in normal human subjects as measured by ultrafast computed tomography. *Cathet. Cardiovasc. Diagn.* 15(4):277–283.
- Wackers, F. J., Berger, H. J., Johnstone, D. E., Goldman, L., Reduto, L. A., Langou, R. A., et al. (1979). Multiple gated cardiac blood pool imaging for left ventricular ejection fraction: validation of the technique and assessment of variability. *Am. J. Cardiol.* 43(6):1159–1166.
- Waiter, G. D., McKiddie, F. I., Redpath, T. W., Semple, S. I., Trent, R. J. (1999). Determination of normal regional left ventricular function from cine-MR images using a semi-automated edge detection method. *Magn. Reson. Imaging.* 17(1):99–107.
- Wynne, J., Green, L. H., Mann, T., Levin, D., Grossman, W. (1978). Estimation of left ventricular volumes in man from biplane cineangiograms filmed in oblique projections. *Am. J. Cardiol.* 41(4):726–732.
- Yang, P. C., Kerr, A. B., Liu, A. C., Liang, D. H., Hardy, C., Meyer, C. H., et al. (1998). New real-time interactive cardiac magnetic resonance imaging system complements echocardiography. *J. Am. Coll. Cardiol.* 32(7):2049–2056.
- The Multicenter Postinfarction Research Group. (1983). Risk stratification and survival after myocardial infarction. *N. Engl. J. Med.* 309:331–336.