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Feasibility of Tissue Magnetic Resonance Imaging

A Pilot Study in Comparison With Tissue Doppler Imaging and Invasive Measurement

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OBJECTIVES This research was intended to determine the feasibility of tissue magnetic resonance (MR) imaging in comparison with tissue Doppler imaging and its potential implications for the estimation of filling pressure, in comparison with invasive measurement.

BACKGROUND Evaluation of diastolic function using MR imaging is commonly confined to the study of transmitral flow. However, transmitral flow is unreliable for the estimation of left ventricular (LV) filling pressures in hypertrophy and normal systolic function. Normalizing early mitral velocity (E) for the influence of myocardial relaxation by combining E with early diastolic mitral septal tissue velocity (Ea) provides better Doppler estimates of filling pressures.

METHODS Eighteen patients with hypertensive heart disease (LV mass index: 114 ± 21 g/m^2), absence of valvular regurgitation, and with normal or mildly reduced systolic function (LV ejection fraction: 57.6 ± 6.5%) referred for cardiac catheterization, underwent consecutive measurement of mitral flow and septal tissue velocities with phase-contrast MR and Doppler. These data were compared with mean pulmonary capillary wedge pressure (PCWP).

RESULTS There was a strong relation between MR (11.6 ± 4.3) and Doppler-assessed (12.1 ± 3.5) E/Ea (95% confidence interval of −1.5 to 0.5) ($r = 0.89$, $p < 0.0001$). In addition, E/Ea related strongly to invasively measured PCWP (MR: $r = 0.80$, $p < 0.0001$ and Doppler: $r = 0.85$, $p < 0.0001$).

CONCLUSIONS Tissue MR imaging is a feasible method to assess Ea. Combining E and Ea allowed similar estimation of filling pressure by MR and Doppler, in good agreement with invasive measurement. The potential confounding effect of valvular regurgitation needs further study. (J Am Coll Cardiol 2005;45:1109–16) © 2005 by the American College of Cardiology Foundation

Assessment of left ventricular (LV) filling pressures is important for the interpretation of symptoms, optimization of unloading therapy, and prediction of prognosis in heart disease (1). Doppler echocardiography of the transmitral flow has been used as a noninvasive alternative for determination of LV filling pressures (2,3). Doppler-derived indexes have been correlated with both phase-contrast magnetic resonance (MR) velocity and volumetric measurements of transmitral flow (4–7). Transmitral flow results from the instantaneous atrioventricular pressure gradient and, therefore, reflects the level of left atrial pressure, hence, filling pressure. However, besides dependence on left atrial pressure, transmitral flow is also affected by different degrees of LV elastic recoil, myocardial relaxation, chamber and atrial compliance, and the presence of valvular regurgitation. Therefore, the transmitral filling pattern is a dynamic phenomenon restricting its use as a single parameter, especially in patients with LV hypertrophy (8,9) and normal systolic function (10). Normalizing early mitral velocity (E) for the influence of myocardial relaxation by combining E with early mitral septal tissue velocity (Ea) provides better Doppler estimates of filling pressure (Fig. 1). This method has been successfully applied in subsets of patients including those with normal systolic function and LV hypertrophy (11–15).

Phase-contrast MR allows velocity encoding of flow but also moving structures (tissue MR imaging) in any chosen direction at near echocardiographic frame rates (16). However, MR evaluation of diastolic filling has been limited to the analysis of the transmitral filling pattern only. The purpose of the present study was to determine the feasibility of tissue MR imaging to assess early diastolic septal velocities in comparison with tissue Doppler imaging and its potential implications for the estimation of filling pressures in comparison with invasive measurement. To avoid the confounding influence of valvular regurgitation, only patients without valvular regurgitation were studied.

METHODS

Subjects and study design. Eighteen consecutive patients (11 men and 7 women, 62.2 ± 10.4 years) with hypertension-induced LV hypertrophy (mass index 114 ± 21 g/m^2) (Table 1) referred for clinically indicated heart catheterization were included in the present study. Selection criteria were normal sinus rhythm, LV ejection fraction >45%, absence of valvular disease, and no contraindication for MR. All patients successively underwent an MR and Doppler echocardiographic study (time frame 68 ± 21 min) followed by invasive pressure

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Abbreviations and Acronyms

A	= peak mitral velocity at atrial contraction
CI	= confidence interval
E	= peak mitral velocity in early diastole
Ea	= early diastolic tissue velocity
LV	= left ventricle/ventricular
MR	= magnetic resonance
PCWP	= pulmonary capillary wedge pressure
ROI	= region-of-interest

measurement (time frame 102 ± 37 min). The patients presented in a fasting state, and neither fluid infusion nor sedation was administered during the whole protocol (170 ± 30 min). The study protocol was approved by the medical ethical committee of the University Hospital of Antwerp, Belgium, and all patients gave informed consent before participation.

MR. ACQUISITION TECHNIQUE. Subjects were examined by using a Sonata MR scanner (Siemens, Erlangen, Germany). Data were acquired using a commercially available 12-channel body array surface coil. The entire heart was imaged in the short-axis orientation with breath-hold Truefisp imaging. From the endocardial and epicardial tracings,

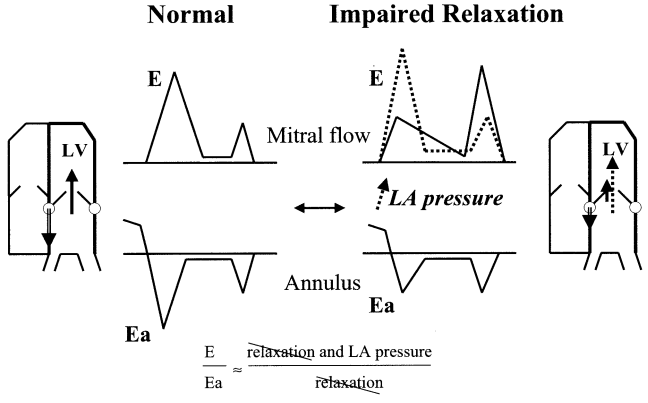

Figure 1. Diagram of mitral filling pattern, mitral annulus velocities, and corresponding four-chamber view during early diastole. **(Left side)** Left ventricular (LV) diastole is characterized by swift myocardial relaxation and elastic recoil. As a result, normal transmitral flow is characterized by a prominent and rapid early (E) filling wave **(arrow)** due to passive suction, and by a diminutive late (A) atrial filling wave due to atrial contraction. During diastole, the LV expands longitudinally resulting in a descent of the mitral valve annulus **(open arrow)** as opposed to the relatively fixed apex. As the velocity of the earliest diastolic motion of the mitral valve annulus (Ea) relates to the rate of myocardial relaxation, Ea is prominent in normal hearts. **(Right side)** When diastolic dysfunction occurs, myocardial relaxation is impaired; LV pressure falls slowly, reducing early transmitral driving pressure. As a result, E is decreased **(arrow)**, and, because of increased atrial preload, A is increased. Due to decreased myocardial relaxation velocity, Ea is reduced **(open arrow)**. As disease progresses, LV compliance also becomes impaired, and LV filling becomes dependent on increased left atrial (LA) or filling pressure **(dashed arrow)**. This results in an increased E. As the underlying impaired relaxation is masked and because the pattern resembles the normal filling pattern, it is called pseudonormalized pattern. Combining E, which is dependent on both filling pressure and myocardial relaxation, with Ea, which is mainly dependent on myocardial relaxation, allows differentiation of a normal from a pseudonormal signal and better evaluation of filling pressures (see equation). E = peak mitral velocity in early diastole; Ea = early diastolic tissue velocity.

Table 1. Baseline Characteristics

Parameter	(n = 18)
Gender (M/F)	11/7
Age (yrs)	62.2 ± 10.4
LV mass (g)	211 ± 44
LV mass index (g/m^2)	114 ± 21
LV end-diastolic volume (ml)	148 ± 35
LV end-systolic volume (ml)	63 ± 20
LV stroke volume (ml)	84 ± 21
Cardiac output (l/min)	6.7 ± 2.4
Cardiac index (l/min/m^2)	3.6 ± 1.1
LV ejection fraction (%)	57.6 ± 6.5
Left atrial volume/BSA (ml/m^2)	41 ± 12

All values are mean ± SD. Parameters of left ventricular (LV) dimensions and function were determined by magnetic resonance (MR).
BSA = body surface area.

LV end-diastolic volume, end-systolic volume, stroke volume, ejection fraction, mass, and mass-index were calculated using MASS analytical software package (Medis, Leiden, the Netherlands) as described previously (17).

Transmitral flow was measured using a retrospectively electrocardiographically triggered Flash phase-contrast MR technique with a velocity sensitivity of 130 cm/s (18). The center of the slice was positioned in the middle of the mitral valve at the level of the valve tips during early diastole with the imaging plane perpendicular to mitral inflow, using both two-chamber and four-chamber images (Fig. 2A, upper panel). In order to cover late diastolic filling, acquisition was performed throughout the cardiac cycle with a retrospective period of 1.2. Imaging parameters included the following: 30/3.2 (repetition time ms/echo-time ms), 5-mm section thickness, 240 × 256 matrix, 380 × 380 mm field of view, 1.6 × 1.5 mm in-plane spatial resolution and 30-degree flip angle. Two signals were averaged, and temporal resolution was 16 to 18 ms.

Myocardial tissue velocities were measured by repeating this phase-contrast MR sequence with velocity encoding of 30 cm/s and a different image slice position. The image slice was positioned at two-thirds of the long axis, planned on early diastolic two- and four-chamber images, perpendicular to the interventricular septum (Fig. 2A, lower panel).

IMAGE ANALYSIS. Analysis was done offline by tracing a region-of-interest (ROI) on the modulus images and transferring this ROI to the paired phase images, using the FLOW analytical software package (Medis, Leiden, the Netherlands).

For assessment of transmitral flow, tracings were performed manually on the images acquired with a velocity encoding of 130 cm/s along the borders of the mitral valve from opening to closing. From the reconstructed velocity versus time curves of LV filling, peak velocity in early diastole (E) and peak velocity at atrial contraction (A) were determined (18). From these peak velocities, the ratio E/A was calculated.

In order to define the most optimal ROI for assessment of tissue velocities, a standardized circular ROI of 20 pixels was

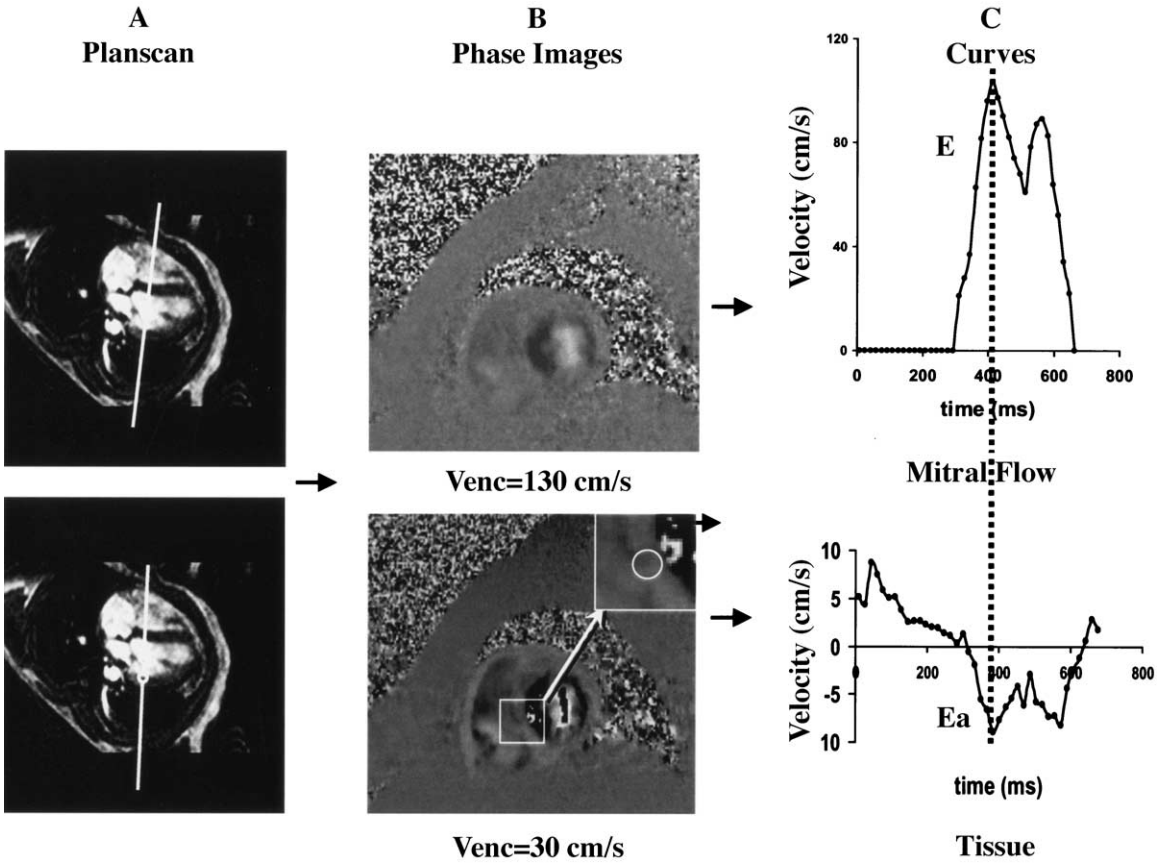

Figure 2. **(A)** Planscan for acquisition of transmitral flow and tissue velocities. To assess transmitral flow, a phase-contrast magnetic resonance (MR) sequence was used, with a velocity encoding of 130 cm/s and the center of the slice positioned perpendicular to mitral inflow, at early diastole **(upper panel)**. To assess tissue MR velocities, phase-contrast MR was repeated with a velocity encoding of 30 cm/s, and the image slice positioned at two-thirds of the long axis, planned on early diastolic two- and four-chamber images, perpendicular to the interventricular septum **(lower panel)**. **(B)** Velocity-encoded images of transmitral flow **(upper panel)** and tissue velocities **(lower panel)**. The tissue velocities are measured from a circular region-of-interest of 20 pixels in the posteroseptal region. **(C)** Corresponding velocity versus time curves. From these curves, peak mitral velocity in early diastole (E) = 103 cm/s, early diastolic posteroseptal tissue velocity Ea = 8.9 cm/s and E/Ea = 11.6 were derived. Ea = early diastolic tissue velocity; Venc = velocity encoding.

placed at different locations in the LV myocardium (Fig. 3). For each ROI, peak early diastolic velocity (Ea) was measured, and E/Ea calculated (Fig. 2C). From these measurements, one optimal ROI was selected for comparison with invasive mean pulmonary capillary wedge pressure (PCWP) and Doppler.

All tracings were performed blinded to invasive and Doppler data in random order by one observer (B.P.P.) and repeated in the posteroseptal region in the first 10 consecutive patients by the same observer (B.P.P.) and by a second independent observer (D.D.) at an interval of more than one month blinded to previous data.

Doppler echocardiography. Doppler echocardiography was performed with a Hewlett Packard Agilent Sonos 5500 phased-array scanner (Andover, Massachusetts) with a 2.5-MHz transducer. A single investigator (B.P.P.), who had achieved level 3 training in echocardiography (19), performed all Doppler studies. Recordings of transmitral flow and septal mitral annulus velocities were obtained during relaxed end-expiration with the patient lying in supine left lateral decubitus as previously described (20). Three consecutive cardiac cycles were acquired and stored for each parameter.

Offline analysis was performed blinded to MR and hemodynamic data using the dedicated software of the ultrasound machine. For the transmitral flow, peak velocities in early diastole (E) and at atrial contraction (A) were measured, and their ratio (E/A) was calculated. From the tissue-Doppler recordings, early diastolic peak velocity (Ea) was measured.

Measurements of E and Ea were repeated in random order in the first 10 consecutive patients by the same observer (B.P.P.) and by a second independent observer (D.D.) at an interval of more than one month blinded to previous data.

Invasive measurement. Mean pulmonary capillary wedge pressure has been shown to accurately reflect LV filling pressure (21). Under fluoroscopic guidance, a 7-F balloon-tipped pulmonary artery catheter was placed in pulmonary wedge position after inflation with 1 ml of air. PERCEPTOR transducers (Boston Scientific Scimed, Boston, Massachusetts, natural frequency: 225 MHz) were balanced before acquisition of hemodynamic data with zero level at midaxillary line. Mean pulmonary capillary wedge pressure was measured automatically by the monitoring system

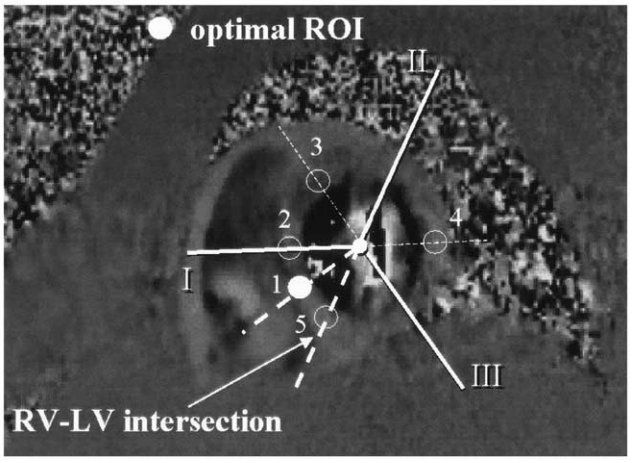

Figure 3. A standardized circular region of interest (ROI) of 20 pixels was placed at different locations around the circumference of the heart. A reference line **(II)** was traced through the center of the left ventricle (LV), and the intersection of the posterior LV with the right ventricle (RV). Based on this reference line, the LV myocardium was divided into three equal triangular regions, corresponding with the coronary artery territories; ROIs were placed in the center of the myocardium at the following locations: posteroseptal **(1)**, midseptal **(2)**, anteroseptal **(3)**, lateral **(4)**, and inferior **(5)**. The posteroseptal ROI was positioned at 30 degrees posterior to line **I**.

(Cathcor Siemens, Erlangen, Germany) after confirmation of wedge position by observing a phasic change in waveform and a decrease of at least 5 mm Hg from mean pulmonary artery pressure. All measurements were made online by averaging three consecutive cycles at end-expiration by an observer (J.M.B.) blinded to previous data. An elevated PCWP was defined clinically relevant if >15 mm Hg.

Statistical analysis. Hemodynamic data during different imaging modalities were tested by repeat measurements analysis of variance (ANOVA) after testing for normality of distribution using the Kolmogorov-Smirnov test.

A paired sample two-tailed Student *t* test was used to compare, and 95% confidence intervals (CI) were calculated to compare MR with Doppler-measured parameters. Linear regression was used to assess whether selected variables were associated with invasive measurements. We estimated a correlation coefficient between MR-measured E/Ea and PCWP of 0.8, with a power of 0.9 at alpha = 0.01. Accordingly, yielding a sample size of 16 with 2 extra patients was adequate to detect such a relation. Analysis of the limits of agreement between MR and Doppler-measured E/Ea and between MR phase-contrast-estimated pressures and catheter-measured pressures was evaluated in accordance with the analysis advocated by Bland and Altman (22). Intraobserver (B.P.P.) variability in MR-measured E/Ea was calculated as the absolute difference in E/Ea between two analyses and divided by the mean E/Ea of both analyses and depicted on a Bland-Altman plot. The same calculation was done for analyses by a second observer (D.D.) to assess MR interobserver variability. Significance was set at $p < 0.05$.

RESULTS

The Kolmogorov-Smirnov test indicated no significant deviation from normality of heart rate (MR p = 0.9, Doppler p = 0.906, invasive p = 0.930), systolic blood pressure (MR p = 0.905, Doppler p = 0.975, invasive p = 0.766), and diastolic blood pressure (MR p = 0.946, Doppler p = 0.998, invasive p = 0.898) measured during three imaging modalities. Overall, heart rate was similar during all acquisitions with different imaging modalities (MR 64 ± 11 beats/min, Doppler 63 ± 10 beats/min, invasive 65 ± 11 beats/min, p = 0.101) as determined by repeat measurements ANOVA. The same was true for systolic (MR 159 ± 17 mm Hg, Doppler 156 ± 14 mm Hg, invasive 162 ± 20 mm Hg, p = 0.272) and diastolic blood pressure (MR 76 ± 10 mm Hg, Doppler 77 ± 10 mm Hg, invasive 74 ± 8 mm Hg, p = 0.302).

The time necessary for offline analysis was, on average, 1 min for Doppler measurements and 10 min for MR tracings and measurements in each patient.

Correlation between MR and Doppler. Magnetic-resonance-assessed E/Ea varied at different locations in the LV myocardium (Table 2). Although significant correlations in all interventricular septum ROI with Doppler were present, best correlations were found with MR-assessed posteroseptal E/Ea ($r = 0.89$, $p < 0.0001$). Magnetic resonance and Doppler parameters of LV filling are presented in Table 3. There was a strong relation between posteroseptal MR (11.6 ± 4.3) and Doppler-assessed (12.1 ± 3.5) E/Ea (95% CI −1.5 to 0.5) ($r = 0.89$, $p < 0.0001$). Results of Bland-Altman analysis revealed good agreement between posteroseptal MR and Doppler E/Ea (Figs. 4A and 4B). Although measurements of A with the two techniques were closely related, MR had a tendency to underestimate A (mean difference −12.1 ± 25.7 cm/s with a 95% CI of −24.9 to 0.7; p = 0.063). Therefore, MR-assessed E/A was higher than Doppler (mean difference 0.3 ± 0.3 with a 95% CI of 0.2 to 0.5; p = 0.001). For both techniques, correlations between invasive PCWP and E/Ea were strong (MR: $r = 0.80$, $p < 0.0001$ and Doppler: $r = 0.85$, $p < 0.0001$).

Correlation between MR and invasive pressure. Figure 5 shows the correlation between MR flow parameters and invasive PCWP. Neither E nor E/A ratio correlated with invasive PCWP (Fig. 5A).

Although significant correlations in all interventricular septum ROI with PCWP were present (Table 2), best correlations were found with MR-assessed posteroseptal E/Ea ($r = 0.80$, $p < 0.0001$) (Fig. 5B). In the further analysis, therefore, posteroseptal E/Ea was used; E/Ea was tested to determine the accuracy in identifying PCWP >15 mm Hg; E/Ea <8 had 100% positive predictive value for PCWP ≤15 mm Hg, and E/Ea >15 had a 100% positive predictive value for PCWP >15 mm Hg.

For the estimation of PCWP, a linear regression analysis was performed. Results of Bland-Altman analysis showed

Table 2. MR Determined Regional E/Ea

Region of Interest (n)	E/Ea	Mean Difference Posteroseptal and Regional E/Ea (95% Confidence Interval)	Correlation With Invasive PCWP r	Correlation With Doppler Posteroseptal E/Ea r
Posteroseptal (1)	11.6 ± 4.3	NA	0.80†	0.89†
Midseptal (2)	8.6 ± 3.2	3.0 (1.4, 4.6)*	0.64†	0.59†
Anteroseptal (3)	11.4 ± 2.8	0.2 (−1.4, 1.8)	0.52†	0.66†
Lateral (4)	7.1 ± 2.9	4.5 (2.3, 6.7)*	0.08	0.38
Inferior (5)	9.1 ± 3.5	2.5 (0.7, 4.3)*	0.55†	0.66†

Values are mean ± SD. *$p < 0.05$ paired sample two-tailed Student t test regional E/Ea versus posteroseptal E/Ea; †Significance of correlation $p < 0.05$.
E = peak mitral velocity in early diastole; Ea = early diastolic tissue velocity; NA = not applicable; PCWP = mean pulmonary capillary wedge pressure.

good agreement between MR-estimated and catheter-measured PCWP (Fig. 5C).

Reproducibility. Both intra- and interobserver variability of MR and Doppler analyses were comparable. The mean intraobserver difference in MR-measured E/Ea was 0.5 ± 1.7 (95% CI of −0.7 to 1.7) ($p = 0.374$) and in Doppler-measured E/Ea −0.4 ± 0.9 (95% CI of −1.1 to 0.2) ($p = 0.183$). The mean interobserver difference in MR-measured E/Ea was 1.1 ± 2.3 (95% CI of −0.6 to 2.8) ($p = 0.168$) and in Doppler-measured E/Ea −0.4 ± 0.8 (95% CI of −1.0 to 0.1) ($p = 0.118$). Results of Bland-Altman analysis also revealed good intra- and interobserver agreement for tissue MR imaging (Fig. 6).

DISCUSSION

The present study demonstrates that tissue MR imaging is a feasible method to assess early diastolic septal velocities similar to tissue Doppler imaging.

Transmitral parameters alone do not correlate with LV filling pressure in patients with preserved systolic function and LV hypertrophy. Transmitral flow is affected by multiple interrelated factors as filling pressure, LV elastic recoil, myocardial relaxation, atrial and chamber compliance, as well as the presence of valvular regurgitation. Estimation of filling pressure can be improved by the analysis of the pulmonary venous flow including systolic, diastolic, and atrial reversal velocities and duration (2,3), by altering preload (e.g., Valsalva maneuver, nitroglycerin administration) (23,24) and by identifying underlying impaired relaxation by recording the flow propagation velocity of early LV filling with color M-mode echocardiography (25). Phase-contrast MR studies have included analysis of pulmonary vein flow (4,26,27). Recently, tissue Doppler measurement of the velocity of the earliest diastolic motion of the mitral annulus (Ea) has been proposed as a better predictor of LV filling pressure (11–15). Phase-contrast MR allows velocity encoding of moving structures in any chosen direction at near echocardiographic frame rates (16). However, MR evaluation of filling pressures has not included Ea measurements, but has commonly been limited to analysis of transmitral filling pattern only. Therefore, the use of tissue MR imaging is a new tool for the estimation of filling pressures. To eliminate possible confounding effects of valvular regurgitation, patients with valvular disease were not included in the study.

Correlation between MR and Doppler. Magnetic resonance and Doppler measurements of transmitral flow (E and A) and Ea did relate closely. Because the sample volume of tissue Doppler imaging is located in the posteroseptal mitral annulus, the MR-assessed posteroseptal E/Ea, as compared with neighboring LV myocardial ROIs, had the strongest correlation with Doppler-assessed E/Ea. As compared with Doppler, the A-wave values as measured by MR tended to be lower. Consequently, the E/A ratio was higher as measured by MR versus measured by Doppler. Similar observations were reported by Karwatowski et al. (6). The higher variability of A and Ea values, as measured by MR, may be related to technical differences in measurements by MR versus Doppler. Doppler measures velocities by assessing Doppler shifts that are displayed after fast Fourier transform as a real-time spectral Doppler pattern. Phase-contrast MR, on the other hand, measures velocities by the

Table 3. MR and Doppler Parameters of LV Filling

	MR	Doppler	Mean Difference MR and Doppler (95% Confidence Interval)	r
E (cm/s)	74.5 ± 16.8	75.9 ± 19.1	−1.4 (−9.9, 7.0)	0.56†
A (cm/s)	65.4 ± 31.7	77.5 ± 14.4	−12.1 (−24.9, 0.7)	0.60†
E/A	1.3 ± 0.5	1.0 ± 0.3	0.3 (0.2, 0.5)*	0.71†
Ea (cm/s)	7.2 ± 5.4	6.4 ± 1.1	0.8 (−0.5, 2.1)	0.49†
E/Ea	11.6 ± 4.3	12.1 ± 3.5	−0.5 (−1.5, 0.5)	0.89†

Values are mean ± SD. *$p < 0.05$ paired sample two-tailed Student t test magnetic resonance (MR) versus Doppler; †Significance of correlation $p < 0.05$.
A = peak mitral velocity at atrial contraction; E = peak mitral velocity in early diastole; Ea = early diastolic posteroseptal tissue velocity; LV = left ventricular; PCWP = mean pulmonary capillary wedge pressure.

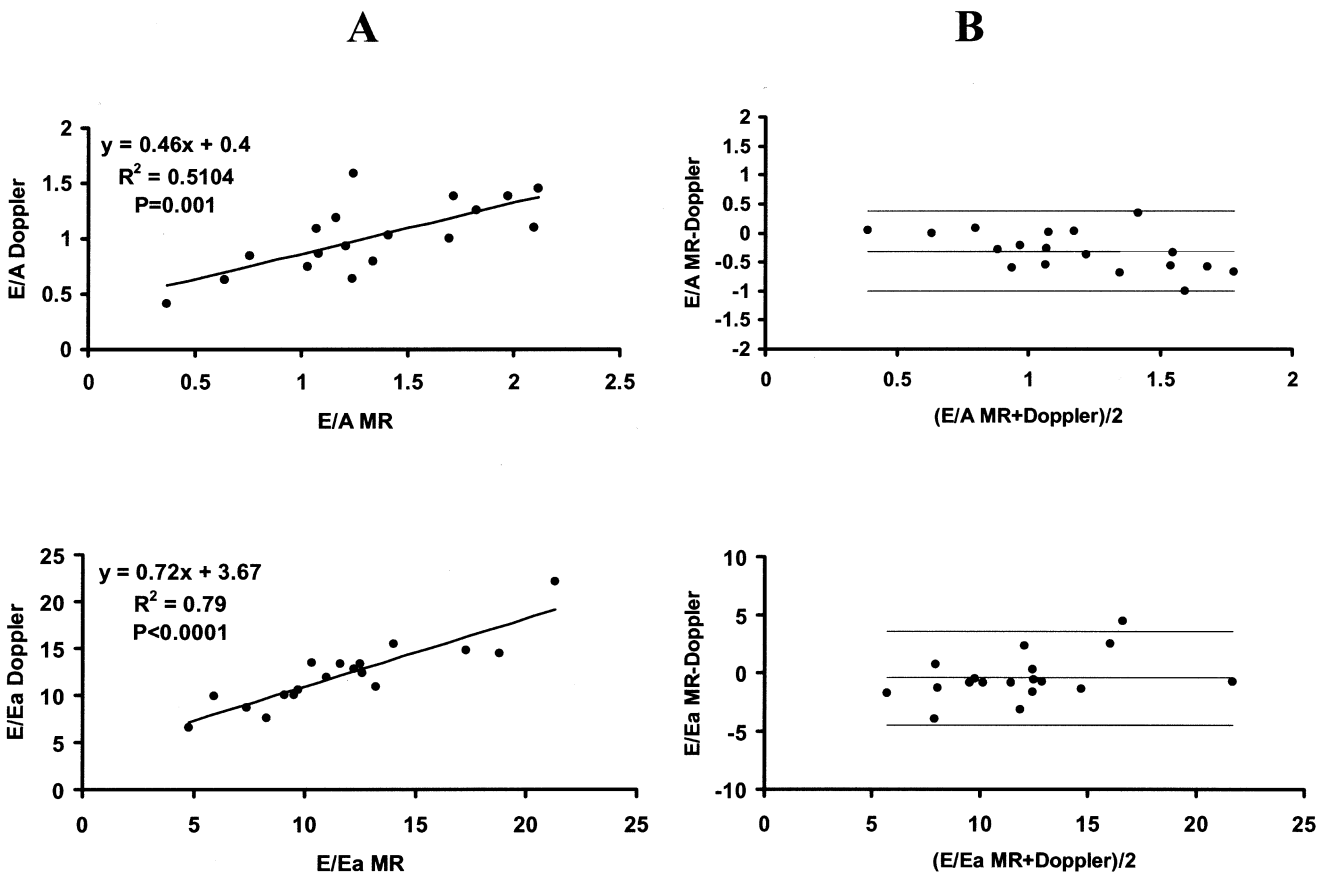

Figure 4. (A) Correlation of magnetic resonance and Doppler-measured E/A and E/Ea. **(B)** Bland-Altman plot of the difference between magnetic resonance (MR) and Doppler-measured E/A and between posteroseptal MR and Doppler-measured E/Ea. **Horizontal lines** show the mean difference between two methods ± 2 SDs. A = peak mitral velocity at atrial contraction; E = peak mitral velocity in early diastole; Ea = early diastolic tissue velocity.

spin-phase shift principle that typically requires 2 to 3 min of acquisition. The measured velocities represent the mean velocities during the acquisition period in a defined ROI. With Doppler, the sample volume to measure flow and/or velocity is markedly smaller than with MR, which measures flow through the whole orifice.

These issues may contribute to the observed differences between measurements with MR versus Doppler. However, despite the variability in measurements (as performed by MR and Doppler), there were no statistically significant differences between parameters as measured by MR and Doppler.

Correlation between MR and invasive pressure. The transmitral filling pattern has a limited clinical value because both filling pressure and myocardial relaxation rate influence transmitral flow. In LV hypertrophy, impaired relaxation dominates the transmitral filling pattern. Therefore, transmitral flow parameters (E and E/A) alone do not correlate with LV filling pressure in these patients.

However, when combining E and posteroseptal Ea, a strong correlation was seen with LV filling pressure. Magnetic resonance provided excellent estimates of filling pressure when E was normalized for the influence of myocardial relaxation by E/Ea. These observations are in close agreement with reports on Doppler (8,9); Ea represents the velocity changes of the heart base during early diastole in LV long-axis dimension and reflects the rate of myocardial relaxation; Ea has been shown to be relatively independent of left atrial pressure (9,28,29) and is not influenced by systolic function (11).

The E/Ea did correlate strongly with PCWP in both techniques. Combining both transmitral flow and mitral annular velocities, MR provided similar prediction of filling pressures as compared to Doppler echocardiography; E/Ea <8 accurately identified patients with a normal and E/Ea >15 patients with an elevated PCWP. In patients with intermediate values (<8 and >15), PCWP did vary widely and was similar for Doppler and MR estimates. These cutoff values have been used previously in echocardiographic studies (15). Although Doppler studies have shown that E/Ea improves evaluation of filling pressures, additional analysis of E/A ratio before and during Valsalva (24) and assessment of pulmonary venous flow (15) could have helped in classifying the patients with intermediate E/Ea values. However, the present study was designed as a feasibility study of tissue MR imaging; therefore further

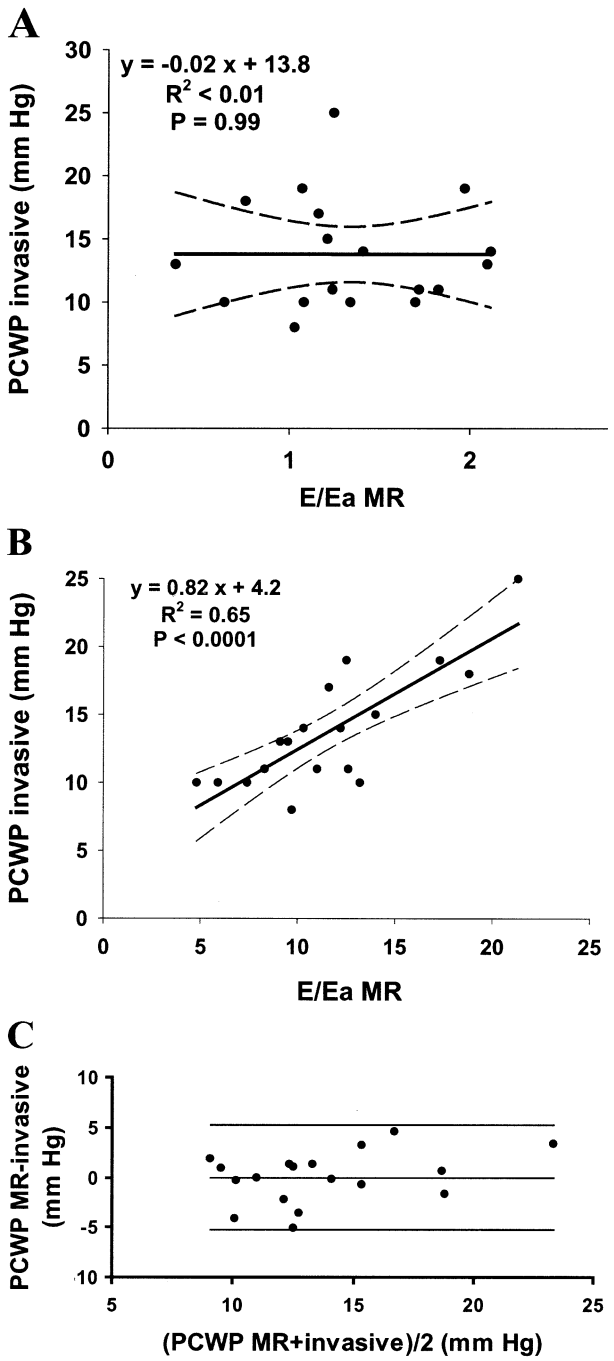

Figure 5. (A) Correlation between magnetic resonance (MR)-measured E/A and invasive mean pulmonary capillary wedge pressure (PCWP). Note absence of correlation ($p = 0.99$). **(B)** Correlation between posteroseptal MR-measured E/Ea and invasive PCWP ($R^2 = 0.65$, $p < 0.0001$). **(C)** Bland-Altman plot of the difference between MR-estimated and catheter-measured PCWP. **Horizontal lines** show the mean difference between two methods ± 2 SDs. A = peak mitral velocity at atrial contraction; E = peak mitral velocity in early diastole; Ea = early diastolic tissue velocity.

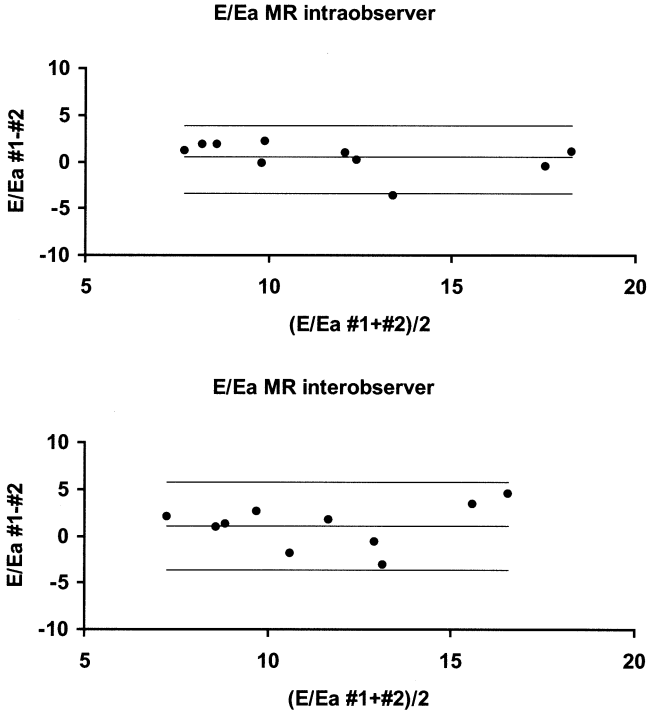

Figure 6. Bland-Altman plots illustrating good intraobserver and interobserver variability for posteroseptal magnetic resonance (MR)-measured E/Ea. **Horizontal lines** show the mean difference between two analyses ± 2 SDs. E = peak mitral velocity in early diastole; Ea = early diastolic tissue velocity.

classification of filling pressures in patients with intermediate E/Ea was not currently performed. Magnetic resonance displayed minimal intraobserver and interobserver variability.

Study limitations. The order of imaging was the same in all subjects, because of practical aspects, mainly the clinical availability of imaging modalities. Consequently, there is a theoretical possibility that results may be influenced by this imaging strategy. Although the study was carried out within a relatively short time interval while care was taken to avoid any fluid infusions, measurements could not be performed simultaneously, introducing the potential for changes in physiological state. However, as apparent from hemodynamic data, no changes were observed during measurements.

Magnetic resonance phase-contrast measurement usually has a duration of 2 to 3 min, and the result represents the average flow during the acquisition period. Retrospective electrocardiographic triggering is needed to acquire atrial contribution to LV filling. In this technique, images are acquired irrespective of the electrocardiogram, while the electrocardiogram is recorded in parallel. The computer retrospectively calculates the appropriate cardiac phases based on the stored electrocardiogram. Therefore, in contrast to Doppler, this sequence cannot be used, with the presence of beat-to-beat variation in R-R interval and ectopy. However, technical progress may allow the capture of beat-to-beat variation using MR. For these reasons, the use of MR remains confined to stable patients who do not have a contraindication for an MR study. In addition, MR needs time-consuming offline analysis.

Because myocardial velocities differ among the myocardium, the position of the ROI could influence the variability of measurements. Therefore, the position of the ROI was standardized based on the position of the center of the LV, and a reference line through the RV-LV intersection (Fig. 3). In addition, the ROI position was adjusted to in-plane rotational

motion throughout the cardiac cycle. Finally, respiratory motion may have influenced the measurements. However, these problems also occur with Doppler. In the future, it may be possible to correct for breathing motion by using tissue MR imaging combined with respiratory navigator gating.

The present study was designed as a feasibility study, and the data have been acquired from a small set of patients. The patients had only mild LV hypertrophy, and only five patients had a PCWP of more than 15 mm Hg. One patient had an LV ejection fraction of <50%. Therefore, a much larger prospective study is needed to assess if tissue MR imaging is reproducible and clinically applicable in broad and different groups of patients, including those with depressed systolic LV function and tachycardia. Further research is needed to classify the observed estimation of filling pressure and to compare with echocardiographic approaches, such as pulmonary venous flow and altered preload, in patients with intermediate E/Ea values (<8 and >15).

Conclusions. Tissue MR imaging is a feasible method to assess early diastolic septal velocities (Ea). In addition, combining early mitral velocity (E) and Ea allowed similar estimation of filling pressure by MR and Doppler in patients with hypertensive heart disease and absence of valvular regurgitation, in good agreement with invasive measurement. The potential confounding effect of valvular regurgitation needs further study.

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