Effect of Primary Mitral Regurgitation on Left Ventricular Synchrony

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Mitral regurgitation (MR) promotes left ventricular (LV) dilatation and eccentric remodeling. In the presence of LV dyssynchrony and heart failure, cardiac resynchronization therapy decreases the severity of MR. Whether primary MR can cause LV dyssynchrony is unknown. We investigated whether moderate to severe primary MR causes LV dyssynchrony in the presence of LV dilation and an ejection fraction (EF) >55%. We studied 37 normal subjects and 22 patients with moderate to severe MR and no coronary artery disease. Electrocardiographically gated cine and tagged cardiac magnetic resonance imaging was performed. Two-dimensional, maximum-circumferential shortening strain and time-to-peak strain (TTPS) were computed using harmonic-phase analysis of tagged magnetic resonance imaging. LV dyssynchrony was assessed by comparing TTPS delay of various LV quadrants and TTPS dispersion among the contralateral quadrants in patients with MR and normal subjects. Statistical comparison was done using a generalized linear model for repeated measurements. LV end-diastolic and LV end-systolic volumes were significantly larger in patients with MR versus normal subjects (207 ± 11 vs 130 ± 4 and 73 ± 5 vs 47 ± 2 ml, p <0.001). LVEF did not differ in patients with MR and normal subjects. The difference in the TTPS among various quadrants and the dispersion among the contralateral quadrants of the LV myocardium was similar between patients with MR and normal subjects. In conclusion, moderate to severe MR does not cause LV dyssynchrony in patients with LV dilatation and normal LVEF. Thus, cardiac resynchronization therapy in the absence of LV dyssynchrony may not decrease the severity of MR. **(Am J Cardiol 2007;100:707–711)**

Mitral regurgitation (MR) is a commonly diagnosed clinical entity that is associated with significant morbidity and mortality.[1–3] Cardiac resynchronization therapy (CRT) in patients with heart failure has been shown to decrease the severity of MR.[4,5] This may be due to electrical and mechanical synchronization that causes increased mitral valve leaflet cooptation.[4–6] However, it is unknown if MR on its own contributes to left ventricular (LV) dyssynchrony independent of LV dysfunction. Regional measurements of the timing and magnitude of myocardial shortening using tagged magnetic resonance imaging is an established method for the assessment of LV dyssynchrony.[7] In the present study, patients with moderate to severe MR with eccentric LV remodeling, LV ejection fraction (EF) >55%, and no evidence of myocardial ischemia had cine magnetic resonance imaging and magnetic resonance imaging tissue tagging. We demonstrate that moderate to severe MR with eccentric LV remodeling does not cause LV dyssynchrony in patients with normal LVEF. Thus, CRT in the absence of LV dyssynchrony may not decrease the severity of MR.

Methods

The study was approved by the institutional review board of the University of Alabama at Birmingham and informed consent was obtained from all participants. Normal volunteers (n = 37) with no history of heart disease formed the control cohort. The MR group (n = 22) included patients with moderate to severe MR. MR on echocardiogram was classified as moderate to severe based on the ratio of MR area to left atrial area ≥0.40 (or 40%).[8] The severity of MR was also confirmed by magnetic resonance imaging.[9,10] To exclude any confounding factors of ischemia patients with MR and negative coronary angiographic or nuclear stress testing results were included for the study.

Magnetic resonance imaging was performed on a 1.5-T magnetic resonance imaging scanner (GE, Milwaukee, Wisconsin) optimized for cardiac application. Electrocardio-

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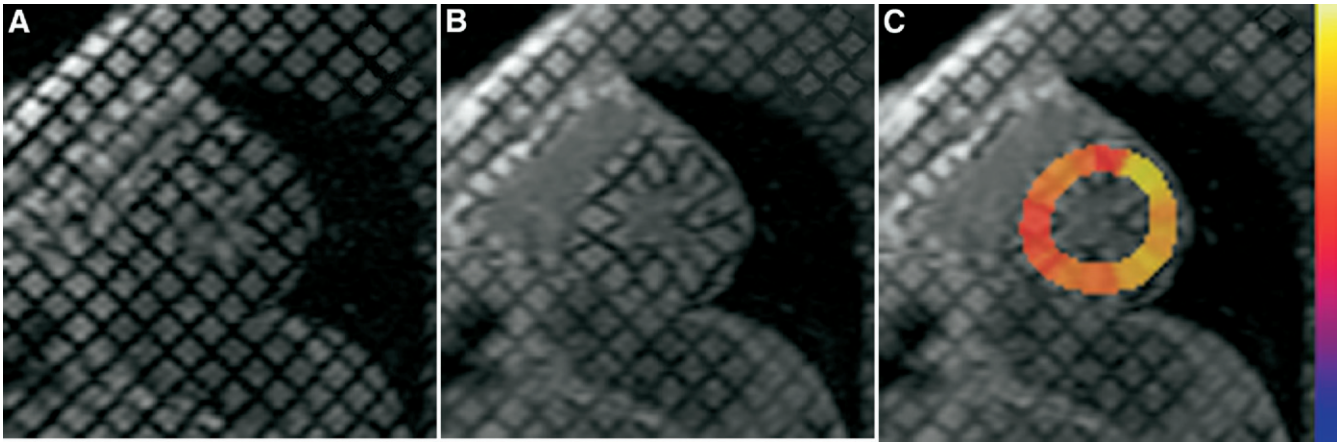

Figure 1. Tagged magnetic resonance images of a normal volunteer at LV midlevel at end-diastole *(A)* and end-systole *(B)*. *(C)* The end-systole image is overlaid with a map of regional maximum shortening (0% shortening is mapped to blue, 25% shortening is mapped to yellow).

Table 1
Baseline parameters in patients with mitral regurgitation and normal subjects

Variable	Normal (n = 37)	MR (n = 22)
Age (yrs)	39 ± 11	53 ± 10
Men	16 (44%)	13 (60%)
Hypertension	1 (3%)	6 (28%)
Diabetes mellitus	0	1 (5%)
Body surface area (m^2)	1.97 ± 0.22	1.84 ± 0.46
Heart rate (beats/min)	73 ± 11	69 ± 13
Mean systolic blood pressure (mm Hg)	125	118
Mean diastolic blood pressure (mm Hg)	75	74

graphically gated breath-hold steady-state free precision technique was used to obtain standard (2-, 3-, and 4-chamber short-axis) views using the following parameters: slice thickness of the imaging planes 8 mm, field of view 44 × 44, scan matrix 256 × 128., flip angle $\alpha = 45°$, repetition/echo times 3.8/1.6). Fast gradient echocardiographic sequence with a 2-dimensional spatial modulation of magnetization tagging preparation was done using exactly the same slice prescription as above. GE Advantage Workstation with Mass Medis 2.0 (Lieden, The Netherlands) software with semiautomated contour detection was used for quantifying LV and right ventricular volumes, LVEF, and right ventricular EF.[11–13] Severity of MR on magnetic resonance images was based on previously published criterion for the intensity and width of the regurgitant jet.[9,10,14,15]

Two-dimensional, maximum-shortening strain was computed in each image using the harmonic-phase analysis.[16,17] Two-dimensional, maximum-shortening strain is the maximum contraction at a given point and is approximately circumferential in orientation. Peak 2-dimensional myocardial strain and time-to-peak strain (TTPS) were computed for each subject. The TTPS was defined as the time at which the peak strain was attained.[16,17] The local strain of tissue is measured based on the spatial frequency of the tag lines as shown in Figure 1. For strain analysis, LV wall contours were semiautomatically drawn using custom-written software on each short-axis slice 2 timeframes before and 2

Table 2
Magnetic resonance imaging parameters in patients with mitral regurgitation and normal subjects

MRI Variable	Normal (n = 37)	MR (n = 22)	p Value
LV end-diastolic volume (ml)	130 ± 4	207 ± 11	<0.001
LV end-systolic volume (ml)	47 ± 2	73 ± 5	<0.001
LV stroke volume (ml)	83 ± 3	134 ± 7	<0.001
Right ventricular end-diastolic volume (ml)	127 ± 5	147 ± 8	NS
Right ventricular end-systolic volume (ml)	59 ± 3	68 ± 5	NS
Right ventricular stroke volume (ml)	70 ± 3	79 ± 5	NS
Right ventricular EF (%)	55 ± 1	54 ± 2	NS
LVEF (%)	64 ± 1	64 ± 1	NS
LV mass (g)	115 ± 6	141 ± 8	0.01
2 × posterior wall thickness/LV end-diastolic dimension	0.32 ± 0.01	0.26 ± 0.0	0.001
LV end-diastolic volume/LV mass (ml/g)	1.21 ± 0.06	1.49 ± 0.0	0.006

MRI = magnetic resonance imaging.

timeframes after the timeframe closest to end-systole. These 5 timeframes around end-systole constituted a search window over which the peak strain and TTPS were computed. The LV wall in each image was divided into 4 sectors starting at the anterior right ventricular insertion point. In each timeframe in the search window, the median 2-dimensional, maximum-shortening strain was computed in each sector over the basal, middle, and apical thirds of the LV. This procedure produced 12 strain values (4 sectors and 3 levels) per timeframe for each subject. In each sector and level, a quadratic polynomial was fitted to the strains versus timeframe data. The peak strain was defined as the maximum magnitude fitted strain. End-systole was determined from cine -magnetic resonance imaging. The raw images were visually inspected before processing and found to have no significant difference in wall motion between the various LV quadrants. Therefore it is unlikely that the true peak strain occurred outside the defined time window for calculating the peak strain.