

# Speckle-Tracking Echocardiography for Predicting Outcome in Chronic Aortic Regurgitation During Conservative Management and After Surgery

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**OBJECTIVES** The aim of this study was to test myocardial deformation imaging using speckle-tracking echocardiography for predicting outcomes in chronic aortic regurgitation.

**BACKGROUND** In chronic aortic regurgitation, left ventricular (LV) dysfunction must be detected early to allow timely surgery. Speckle-tracking echocardiography has been proposed for this purpose, but the clinical value of this method in aortic regurgitation has not been established.

**METHODS** A longitudinal study was performed in 64 patients with moderate to severe aortic regurgitation. Thirty-five patients were managed conservatively with frequent clinical visits and sequential echocardiography and followed for an average of  $19 \pm 8$  months, while 29 patients underwent surgery for the valve lesion and were followed for 6 months post-operatively. Baseline LV function by speckle-tracking and conventional echocardiography was compared with impaired outcome after surgery (defined as persisting symptoms or persisting LV dilation [LV end-diastolic volume index  $\geq 87$  ml/m<sup>2</sup>] or dysfunction [LV ejection fraction  $< 50\%$ ]) and with disease progression during conservative management (defined as development of symptoms, increase in LV volume  $> 15\%$ , or decrease in LV ejection fraction  $> 10\%$ ).

**RESULTS** Reduced myocardial systolic strain, systolic strain rate, and early diastolic strain rate by speckle-tracking echocardiography was associated with disease progression during conservative management ( $-16.3\%$  vs.  $-19.0\%$ ,  $p = 0.02$ ;  $-1.04$  vs.  $-1.19$  s<sup>-1</sup>,  $p = 0.02$ ; and  $1.20$  vs.  $1.60$  s<sup>-1</sup>,  $p = 0.002$ , respectively) and with impaired outcome after surgery ( $-11.5\%$  vs.  $-15.6\%$ ,  $p = 0.01$ ;  $-0.88$  vs.  $-1.01$  s<sup>-1</sup>,  $p = 0.04$ ; and  $0.98$  vs.  $1.33$  s<sup>-1</sup>,  $p = 0.01$ , respectively). Conventional parameters of LV function and size (LV ejection fraction and LV end-diastolic volume index) were associated with outcome after surgery ( $p = 0.04$  and  $p = 0.01$ , respectively) but not with outcome during conservative management ( $p = 0.57$  and  $p = 0.39$ , respectively).

**CONCLUSIONS** Speckle-tracking echocardiography is useful for the early detection of LV systolic and diastolic dysfunction in chronic aortic regurgitation. (J Am Coll Cardiol Img 2011;4:223–30) © 2011 by the American College of Cardiology Foundation

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Chronic aortic regurgitation (AR) leads to left ventricular (LV) enlargement and, if not surgically corrected, can lead to LV dysfunction, heart failure, and death (1). If surgery is performed too late, the left ventricle may have been irreversibly damaged (2,3). It is therefore recommended to perform surgery to correct regurgitation as soon as the disease becomes symptomatic or, in asymptomatic patients, when the LV end-systolic diameter has increased beyond 55 mm (or 25 mm/m<sup>2</sup>) or the LV ejection fraction (LVEF) has decreased below 50% (4,5).

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However, LV dilation and decrease in LVEF of this magnitude are often seen only late in the disease, and a large subset of patients develop symptoms requiring surgery before developing detectable LV dysfunction (6,7). A more sensitive parameter of LV dysfunction than LV diameter and LVEF would be of considerable clinical value, as it would allow clinicians to detect early abnormalities, assist in the evaluation of symptoms, and indicate the need for vigilant observation, and possibly earlier surgery.

Studies have suggested newer echocardiographic measures of systolic function to be of value in AR, using either measures of absolute cardiac motion or of myocardial deformation: longitudinal basal velocities (8–11) by tissue Doppler echocardiography, myocardial strain or strain rate (12) by tissue Doppler, and myocardial strain (13) or strain rate after

exercise (14) by speckle-tracking echocardiography have been examined. The relative values of these methods and their possible clinical role have not been established.

This study was performed to test if deformation imaging by speckle-tracking echocardiography adds clinical value in the evaluation of patients with chronic AR. We hypothesized that myocardial systolic and diastolic deformation rate would be impaired in patients that experienced disease progression during conservative management and would be further impaired in patients who did not recover fully after having surgery for AR. We sought to compare the performance of speckle-tracking deformation imaging with conventional measures and with tissue Doppler measures of LV longitudinal motion.

## METHODS

**Study population and design.** Study participants were recruited from patients seen at our outpatient

echocardiography clinic. Prospective recruitment to both conservative and surgical groups occurred from May 2006 to March 2008 and was supplemented by the identification of all patients who underwent surgery for AR and fulfilled the enrollment criteria from patient records starting in July 2005.

Inclusion criteria for the study were moderate or severe AR according to European Society of Cardiology guidelines (5) and age >18 years. Exclusion criteria were acute AR, previous heart surgery or valve implantation, aortic stenosis (mean gradient >20 mm Hg), mitral valve disease beyond mild mitral regurgitation, previous revascularization or previous myocardial infarction, compromised LV function of known other reason than AR, and permanent atrial fibrillation.

Conservatively managed patients were seen at 6-month or 12-month intervals, at the discretion of the attending cardiologist. The last visit before July 1, 2009, was defined as the final follow-up visit. After surgery, patients were seen at 3 and 6 months after surgery.

### Outcome measure in conservatively managed patients.

The aim of conservative follow-up in patients with chronic AR is to detect the development of symptoms or deterioration of LV size or function. For this study, a patient exhibiting 1) the development of symptoms warranting referral to aortic valve replacement; 2) a relative increase in left ventricular end-diastolic volume index (LVEDVI) >15%; or 3) a relative decrease in LVEF >10% was classified as exhibiting “progression;” otherwise, the patient was considered “stable.”

### Outcome measure in the post-surgery group.

Surgery in AR is performed to avoid heart failure and LV dysfunction. If a patient 6 months after aortic valve replacement had either 1) symptoms of heart failure (New York Heart Association functional class  $\geq$  II); 2) a more than mildly dilated left ventricle (15) (LVEDVI  $\geq$  87 ml/m<sup>2</sup>); or 3) subnormal LV function (LVEF < 50%), this was considered an “impaired outcome;” otherwise, the patient was considered to have a “good outcome.”

**Echocardiography.** Figure 1 shows examples of the imaging modalities used. Echocardiographic examinations were performed using Vivid 7 and Vivid 7 Dimension machines (GE Vingmed Ultrasound AS, Horten, Norway). Blinded offline analysis was performed using EchoPAC PC version 6.1.1 (GE Vingmed Ultrasound AS). For all measurements, the average of 3 heart cycles was used. LV volumes and LVEF were assessed using Simpson’s method of discs on the 4- and 2-chamber apical views. Vena contracta width was measured as previously de-

## ABBREVIATIONS AND ACRONYMS

**AR** = aortic regurgitation

**AUC** = area under the curve

**$\epsilon_{sys}$**  = total systolic strain

**LV** = left ventricular

**LVEDVI** = left ventricular end-diastolic volume index

**LVEF** = left ventricular ejection fraction

**$SR_{dia}$**  = peak early diastolic strain rate

**$SR_{sys}$**  = peak systolic strain rate

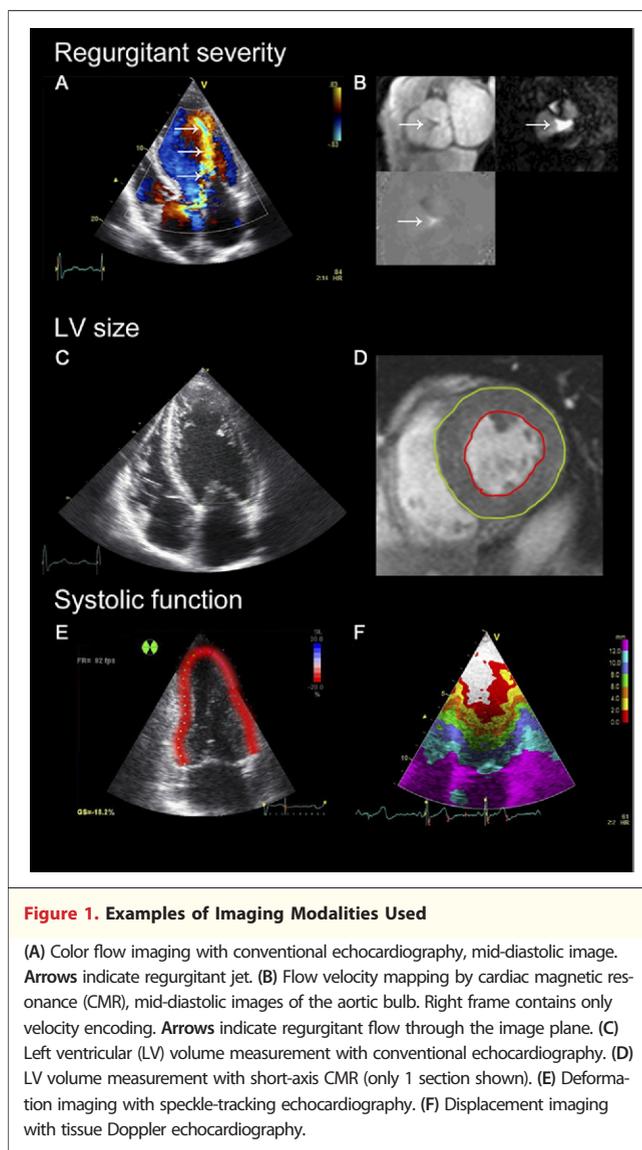
scribed (16). Longitudinal deformation was analyzed on 2-dimensional grayscale loops using the 2-dimensional strain modality of the EchoPAC software (GE Vingmed Ultrasound AS). Meridional end-systolic strain was calculated in grams per square centimeter as  $1.35 \times \text{systolic blood pressure (mm Hg)} \times b/2b/(1 + b/2b)$ , where  $b$  is systolic LV cavity radius, and  $h$  is systolic wall thickness.

Global measures of total systolic strain ( $\epsilon_{\text{sys}}$ ), peak systolic strain rate ( $\text{SR}_{\text{sys}}$ ), and peak early diastolic strain rate ( $\text{SR}_{\text{dia}}$ ) were calculated as averages of the values in all correctly tracked segments in an 18-segment model. Color tissue Doppler studies were performed in apical views at a frame rate  $> 150 \text{ s}^{-1}$ . Total systolic longitudinal displacement, peak systolic velocity, and peak early diastolic velocity were measured in the basal segments of all 6 walls, and the average was used.

**Cardiac magnetic resonance.** Patients were examined using a 3.0-T Achieva scanner (Philips Medical Systems, Best, the Netherlands) with a 6-channel cardiac coil. Short-axis cine images of the left ventricle were analyzed using dedicated software (ViewForum, version 5.1, Philips Medical Systems). Phase velocity mapping was performed in a section perpendicular to the ascending aorta, at the mid-level of the aortic bulb (phase-contrast turbo field echo sequence, velocity encoding 200 cm/s). The integral of flow rate was calculated for forward flow through the image plane during systole (total stroke volume) and backward flow during diastole (regurgitant volume). Regurgitant fraction was calculated as regurgitant volume/total stroke volume.

**Statistical analysis.** All p values are 2 tailed, and a significance level of 0.05 was used. Summary statistics are given as mean  $\pm$  SD unless stated otherwise. For comparisons,  $t$  tests and Fisher exact tests were used. Prediction of outcome was tested with logistic regression using likelihood ratio tests, and standardized odds ratios are reported for predictive variables. Receiver-operator characteristic curve analyses were performed to provide the area under the curve (AUC) for each variable, and optimal cutoffs were selected by optimizing sensitivity plus specificity. For reproducibility analysis, the coefficient of variation was calculated as the SD of the difference between repeated measurements divided by the mean value. All analyses were performed using SAS for Windows release 9.1 (SAS Institute Inc., Cary, North Carolina).

**Ethics.** Prospectively recruited participants gave written informed consent. The study protocol was approved



**Figure 1. Examples of Imaging Modalities Used**

(A) Color flow imaging with conventional echocardiography, mid-diastolic image. Arrows indicate regurgitant jet. (B) Flow velocity mapping by cardiac magnetic resonance (CMR), mid-diastolic images of the aortic bulb. Right frame contains only velocity encoding. Arrows indicate regurgitant flow through the image plane. (C) Left ventricular (LV) volume measurement with conventional echocardiography. (D) LV volume measurement with short-axis CMR (only 1 section shown). (E) Deformation imaging with speckle-tracking echocardiography. (F) Displacement imaging with tissue Doppler echocardiography.

by the regional Committee on Biomedical Research Ethics (registration number KA - 20 060 049).

## RESULTS

**Patient characteristics and outcomes.** Sixty-four patients were included in the analysis. Twenty-nine patients had indications for surgery at baseline and were included in the post-surgical group. Thirty-five patients did not have indications for surgery and were included in the follow-up group. Table 1 lists baseline clinical characteristics of the study participants.

Of the 35 patients who were managed conservatively, 2 failed to appear for further visits and were excluded. The remaining 33 patients were followed for an average of  $19 \pm 8$  months. Three patients (9%) developed symptoms and were referred to surgery;

**Table 1. Clinical Data**

Variable	All Patients (n = 64)	Conservative Management (n = 35)	Surgery* (n = 29)
Age (yrs)	57 ± 13	56 ± 14	57 ± 13
Men	46 (72%)	21 (60%)	25 (86%)†
NYHA functional class ≥ II	26 (39%)	2 (6%)	24 (83%)†
Hypertension	37 (58%)	22 (63%)	15 (52%)
Diabetes	1 (2%)	1 (3%)	0 (0%)
BMI (kg/m <sup>2</sup> )	24.7 ± 3.3	24.7 ± 3.7	24.7 ± 2.8
Systolic blood pressure (mm Hg)	140 ± 20	138 ± 20	143 ± 19
Diastolic blood pressure (mm Hg)	76 ± 12	80 ± 11	71 ± 13†
Heart rate (beats/min)	69 ± 11	68 ± 11	71 ± 10
Medical therapy			
Beta-blockers	10 (16%)	5 (14%)	5 (17%)
Calcium antagonists	16 (25%)	13 (37%)	3 (10%)†
ACE inhibitors	18 (18%)	8 (25%)	10 (34%)
ARII antagonists	8 (13%)	6 (17%)	2 (7%)
Diuretic agents	19 (30%)	9 (26%)	10 (34%)

Data are expressed as mean ± SD or as n (%). \*Twelve patients received mechanical valve (St. Jude, sizes 23 to 27), 10 patients received biological valves (sizes 21 to 27), 5 patients received composite grafts, and 2 patients had the regurgitant lesion corrected by aortic repair only. Four patients had concomitant coronary artery bypass grafting performed. †p < 0.05.  
ACE = angiotensin-converting enzyme; ARII = angiotensin II receptor; BMI = body mass index; NYHA = New York Heart Association.

these patients had been followed for 0.4, 0.5, and 1.0 years at that time. No patients in the follow-up group were referred to surgery for asymptomatic LV dilation or dysfunction. At final follow-up, 4 patients (12%) had relative increases in LVEDVI >15%, and 2 patients (6%) had relative decreases in LVEF >10%. In total, 8 patients (24%) had the combined end point of development of symptoms warranting surgery, a relative increase in LVEDVI >15%, or a relative decrease in LVEF >10%.

The post-surgical population included 3 patients referred to surgery from the conservatively managed group. Three patients were lost to follow-up after surgery (2 patients had surgery at another hospital and 1 patient did not show up for post-surgical visits). A total of 29 patients were thus included in the post-surgical outcome analysis. At 6 months, 5 patients (17%) had symptoms of heart failure (all New York Heart Association functional class II; none of these patients were asymptomatic at baseline), 4 patients had more than mild dilation of the left ventricle (post-surgical LVEDVI ≥87 ml/m<sup>2</sup>), and 8 patients had post-surgical LVEF <50%. In total, 11 patients (38%) had the combined end point of symptoms, LV dilation, or LV dysfunction. **Baseline echocardiography.** Table 2 lists baseline measurements from echocardiography and cardiac magnetic resonance. Surgical patients had larger left ventricles, more severe regurgitation, and evidence of LV dysfunction by both conventional and speckle-tracking echocardiography compared with

conservatively managed patients, but tissue Doppler measurements were similar in the 2 groups. Accordingly, when patients were divided on the basis of the presence of symptoms of heart failure, the speckle-tracking parameters  $\epsilon_{\text{sys}}$ ,  $\text{SR}_{\text{sys}}$ , and  $\text{SR}_{\text{dia}}$  were lower in patients with symptoms ( $-14.2 \pm 4.1\%$  vs.  $-18.3 \pm 3.2\%$ ,  $p < 0.001$ ;  $-1.01 \pm 0.21 \text{ s}^{-1}$  vs.  $-1.13 \pm 0.19 \text{ s}^{-1}$ ,  $p = 0.02$ ; and  $1.22 \pm 0.35 \text{ s}^{-1}$  vs.  $1.51 \pm 0.34 \text{ s}^{-1}$ ,  $p = 0.005$ , respectively), while tissue Doppler measurements (total systolic longitudinal displacement, peak systolic velocity, and peak early diastolic velocity) were not associated with symptoms ( $10.5 \pm 2.6 \text{ mm}$  vs.  $11.1 \pm 1.9 \text{ mm}$ ,  $p = 0.60$ ;  $5.6 \pm 1.1 \text{ cm/s}$  vs.  $5.8 \pm 1.0 \text{ cm/s}$ ,  $p = 0.71$ ; and  $-6.0 \pm 2.5 \text{ cm/s}$  vs.  $-6.2 \pm 2.0 \text{ cm/s}$ ,  $p = 0.78$ , respectively).

With increasing LV size, LVEF and speckle-tracking deformation parameters were found to decrease ( $p < 0.001$  for all). In contrast, for tissue Doppler parameters of basal LV motion, there was a biphasic relationship with LV size: the highest values of basal displacement and velocity were seen in patients with mildly to moderately enlarged left ventricles, while patients with nondilated or with severely dilated ventricles had lower values (Fig. 2).

End-systolic wall stress was higher in surgical and in symptomatic patients. There was a significant association between increased systolic wall stress and decreased systolic function measures LVEF,  $\epsilon_{\text{sys}}$ , and  $\text{SR}_{\text{sys}}$  ( $r = -0.54$ ,  $p < 0.001$ ;  $r = 0.55$ ,  $p < 0.001$ ;

**Table 2. Baseline Conventional Echocardiographic, Speckle-Tracking, Tissue Doppler, and CMR Data**

Measurement	All Patients (n = 64)	Conservative Management (n = 35)	Surgery (n = 29)	p*
<b>Conventional echocardiography</b>				
LVEF (%)	54.6 ± 9.1	58.2 ± 5.1	50.3 ± 10.9	<0.001
LVEDVI (ml/m <sup>2</sup> )	80.1 ± 32.7	59.7 ± 17.2	104.8 ± 29.8	<0.001
LVESVI (ml/m <sup>2</sup> )	38.0 ± 22.4	24.9 ± 7.7	53.7 ± 24.2	<0.001
Wall thickness (cm)	1.06 ± 0.19	0.99 ± 0.16	1.15 ± 0.20	<0.001
AR vena contracta (mm)	7.1 ± 2.8	5.4 ± 1.7	9.3 ± 2.5	<0.001
ESS (g/cm <sup>2</sup> )	95.8 ± 31.0	83.9 ± 21.3	111.2 ± 34.9	<0.001
<b>Speckle tracking</b>				
ε <sub>sys</sub> (%)	-16.3 ± 4.1	-18.3 ± 2.9	-14.0 ± 4.2	<0.001
SR <sub>sys</sub> (s <sup>-1</sup> )	-1.06 ± 0.20	-1.15 ± 0.18	-0.96 ± 0.19	<0.001
SR <sub>dia</sub> (s <sup>-1</sup> )	1.36 ± 0.37	1.49 ± 0.34	1.21 ± 0.35	0.002
<b>Tissue Doppler</b>				
LD <sub>sys</sub> (mm)	10.7 ± 2.3	11.0 ± 1.9	10.4 ± 2.7	0.39
s' (cm/s)	5.7 ± 1.0	5.8 ± 1.0	5.5 ± 1.0	0.16
e' (cm/s)	-6.1 ± 2.1	-6.2 ± 2.0	-5.9 ± 2.2	0.62
E/e'	12.2 ± 4.9	11.9 ± 5.1	12.5 ± 4.7	0.60
<b>CMR</b>				
LV mass index (g/m <sup>2</sup> )	91.8 ± 34.0	78.2 ± 22.9	121.2 ± 36.1	<0.001
Regurgitant volume (ml)	32.2 ± 40.5	16.2 ± 13.9	66.7 ± 56.1	<0.001
Regurgitant fraction (%)	22.4 ± 17.8	15.9 ± 10.5	36.4 ± 22.3	<0.001

Data are expressed as mean ± SD. \*For difference between surgery and conservative groups.

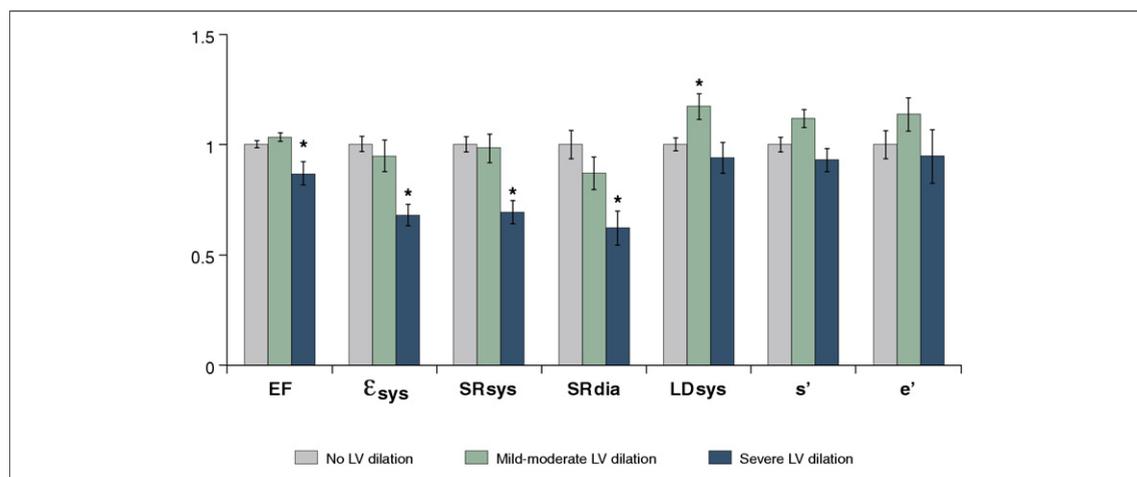
AR = aortic regurgitation; CMR = cardiac magnetic resonance; e' = peak early diastolic velocity; ε<sub>sys</sub> = total systolic strain; ESS = meridional end-systolic stress; LD<sub>sys</sub> = total systolic longitudinal displacement; LV = left ventricular; LVEDVI = left ventricular end-diastolic volume index; LVEF = left ventricular ejection fraction; LVESVI = left ventricular end-systolic volume index; s' = peak systolic velocity; SR<sub>dia</sub> = peak early diastolic strain rate; SR<sub>sys</sub> = peak systolic strain rate.

and  $r = 0.46$ ,  $p < 0.001$ , respectively), while there was only a weak association between systolic wall stress and SR<sub>dia</sub> ( $r = -0.25$ ,  $p = 0.05$ ).

**LV response after surgery.** The post-surgical changes in LV size and function are shown in Figure 3. LV

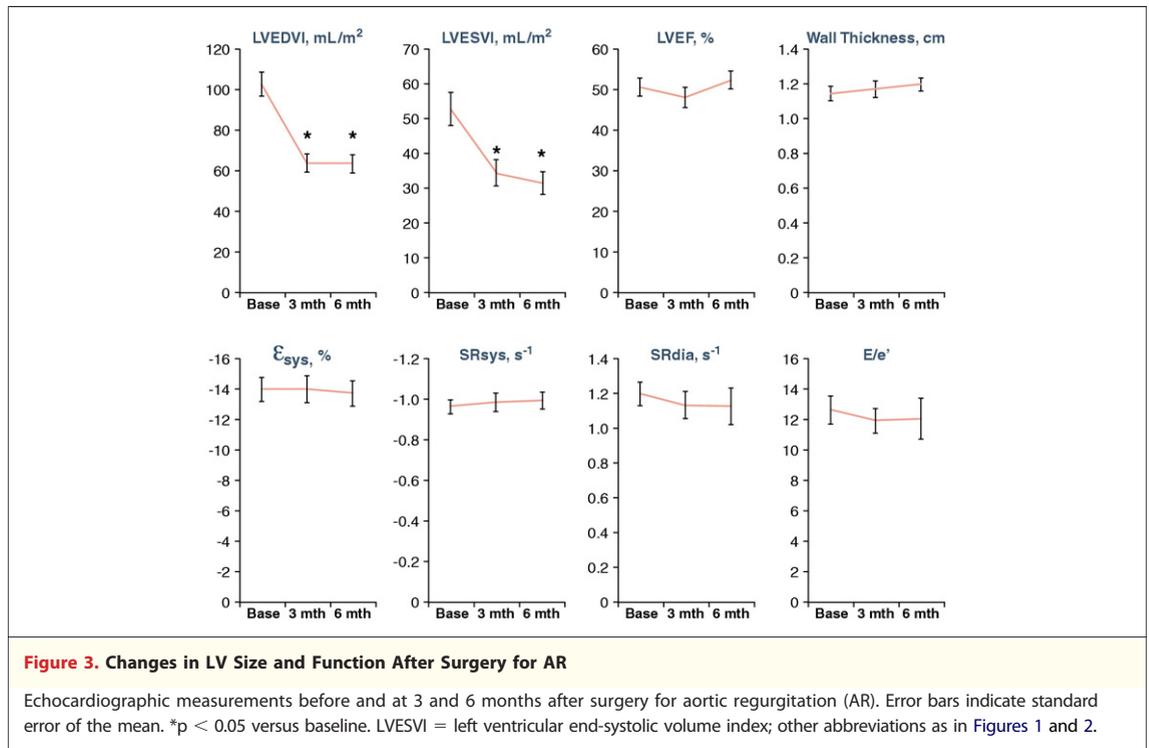
size decreased markedly after surgery, while neither LVEF nor speckle-tracking measures of LV systolic and diastolic function improved significantly.

**Predictors of outcome.** Baseline clinical characteristics did not differ between stable patients and



**Figure 2. LV Size and Echocardiographic Measures of LV Function**

All measurements are scaled. The group without LV dilation is used as a reference (value of 1). Lower values imply impaired function. No LV dilation: LV end-diastolic volume index (LVEDVI) <76 ml/m<sup>2</sup>; mild to moderate LV dilation: LVEDVI 76 to 97 ml/m<sup>2</sup>; severe LV dilation: LVEDVI > 97 ml/m<sup>2</sup>. \* $p < 0.05$  versus no LV dilation. e' = peak early diastolic velocity; EF = ejection fraction; ε<sub>sys</sub> = total systolic strain; LD<sub>sys</sub> = total systolic longitudinal displacement; s' = peak systolic velocity; SR<sub>dia</sub> = peak early diastolic strain rate; SR<sub>sys</sub> = peak systolic strain rate; other abbreviation as in Figure 1.



patients with disease progression during conservative management or between post-surgical patients with good outcomes and those with impaired outcomes. End-systolic wall stress was not associated with outcome in either group. Type of surgery or concurrent coronary artery bypass grafting had no impact on post-surgical outcome.

Table 3 lists the relationships between baseline echocardiographic measurements and outcomes. All speckle-tracking measures ( $\epsilon_{\text{sys}}$ ,  $\text{SR}_{\text{sys}}$ , and  $\text{SR}_{\text{dia}}$ ) were

significantly associated with outcome both during conservative management and after surgery, while conventional measures and tissue Doppler measures were associated with outcome only after surgery.

The best cutoffs for discriminating between patients with disease progression and stable patients during conservative management were  $-18\%$  for  $\epsilon_{\text{sys}}$  (AUC: 0.72; sensitivity, 88%; specificity, 60%),  $-1.1 \text{ s}^{-1}$  for  $\text{SR}_{\text{sys}}$  (AUC: 0.76; sensitivity, 75%; specificity, 76%), and  $1.2 \text{ s}^{-1}$  for  $\text{SR}_{\text{dia}}$  (AUC: 0.81;

**Table 3. Association Between Echocardiography and Outcome**

Baseline Measurement	Outcome During Conservative Management (n = 33)				Outcome After Surgery (n = 29)			
	Stable (n = 25)	Progression (n = 8)	OR (95% CI)	p Value	Good (n = 18)	Impaired (n = 11)	OR (95% CI)	p Value
Conventional echocardiography								
LVEF (%)	58.7 ± 5.4	57.6 ± 3.6	1.3 (0.6–3.0)	0.57	53.9 ± 9.8	45.2 ± 11.8	2.3 (1.1–6.1)	0.04
LVEDVI (ml/m <sup>2</sup> )	58.9 ± 16.4	64.9 ± 21.1	1.4 (0.6–3.5)	0.39	92.2 ± 24.8	119.7 ± 33.4	3.0 (1.2–10.7)	0.01
LVESVI (ml/m <sup>2</sup> )	24.2 ± 7.1	27.8 ± 10.2	1.6 (0.7–4.0)	0.26	43.6 ± 18.8	67.5 ± 27.7	3.2 (1.3–10.5)	0.01
Speckle tracking								
$\epsilon_{\text{sys}}$ (%)	-19.0 ± 2.6	-16.3 ± 3.3	3.2 (1.2–13.8)	0.02	-15.6 ± 2.3	-11.5 ± 4.3	3.7 (1.4–14.4)	0.006
$\text{SR}_{\text{sys}}$ (s <sup>-1</sup> )	-1.19 ± 0.17	-1.04 ± 0.14	3.3 (1.2–13.4)	0.02	-1.01 ± 0.17	-0.88 ± 0.19	2.6 (1.0–9.0)	0.04
$\text{SR}_{\text{dia}}$ (s <sup>-1</sup> )	1.60 ± 0.30	1.20 ± 0.34	4.6 (1.6–18.8)	0.002	1.33 ± 0.36	0.98 ± 0.21	4.0 (1.4–16.3)	0.005
Tissue Doppler								
$\text{LD}_{\text{sys}}$ (mm)	11.2 ± 1.8	10.7 ± 2.1	1.4 (0.6–3.3)	0.45	11.2 ± 2.4	8.9 ± 2.5	2.8 (1.2–8.0)	0.02
$s'$ (cm/s)	6.0 ± 1.1	5.5 ± 0.6	1.9 (0.8–5.4)	0.14	5.8 ± 0.8	4.9 ± 1.2	2.9 (1.2–9.4)	0.02
$e'$ (cm/s)	-6.5 ± 2.1	-5.9 ± 1.8	1.4 (0.6–3.4)	0.46	-6.2 ± 2.4	-5.0 ± 2.0	1.8 (0.8–4.9)	0.17

Data are expressed as mean ± SD.

CI = confidence interval; OR = odds ratio associated with 1 SD of worsening in predictive measure; other abbreviations as in Table 2.

sensitivity, 75%; specificity, 92%). The best cutoffs for predicting post-surgical outcome were  $-14\%$  for  $\epsilon_{\text{sys}}$  (AUC: 0.77; sensitivity, 82%; specificity, 72%),  $-1.0 \text{ s}^{-1}$  for  $\text{SR}_{\text{sys}}$  (AUC: 0.71; sensitivity, 82%; specificity, 61%), and  $1.0 \text{ s}^{-1}$  for  $\text{SR}_{\text{dia}}$  (AUC: 0.77; sensitivity, 64%; specificity, 78%).

**Reproducibility.** Echocardiographic measurements were repeated in 15 randomly selected patients for each modality. For  $\epsilon_{\text{sys}}$ ,  $\text{SR}_{\text{sys}}$ , and  $\text{SR}_{\text{dia}}$ , the mean differences were  $0.1 \pm 1.6\%$ ,  $0.01 \pm 0.15 \text{ s}^{-1}$ , and  $-0.02 \pm 0.11 \text{ s}^{-1}$ , respectively, corresponding to coefficients of variation of 10.6%, 14.6%, and 8.9%. For total systolic longitudinal displacement, peak systolic velocity, and peak early diastolic velocity, the mean differences were  $0.25 \pm 0.41 \text{ mm}$ ,  $0.04 \pm 0.27 \text{ cm/s}$ , and  $0.01 \pm 0.31 \text{ cm/s}$ , respectively, corresponding to coefficients of variation of 4.3%, 4.9%, and 4.9%.

## DISCUSSION

In this longitudinal study of 64 patients with chronic AR, decreased deformation and deformation rate by speckle-tracking echocardiography were found to predict persisting symptoms or LV dysfunction after surgery and to predict the development of symptoms or worsening LV function during conservative management. In contrast, conventional measures of LV size and function and tissue Doppler measurements of LV basal motion predicted outcomes only in patients treated with surgery, not in the less diseased population that was managed conservatively.

Our analysis indicates that both systolic and early diastolic myocardial deformation are impaired early in the disease course in AR, and the strong relationship with reduced functional status shows that the impairment is clinically relevant. We found absolute measures of basal motion to be less suited for the early detection of LV dysfunction, as they seemed useful only in patients with more severe disease, most likely because of the dependency between basal motion and LV size (Fig. 2), which is particularly problematic in volume-overload states. Myocardial deformation imaging with speckle tracking does not suffer from this limitation.

The present study is the first to comprehensively compare newer echocardiographic modalities for measuring LV dysfunction in chronic AR. Our findings are in agreement with those of 2 recent studies (13,14) that also demonstrated benefits from speckle-tracking echocardiography, and also with the findings of Marciniak et al. (12), who used the

strain rate modality of tissue Doppler to measure LV longitudinal deformation. Interestingly, in a new study, Onishi et al. (17) found LV radial systolic strain rate by tissue Doppler to be predictive of post-surgical LVEF in AR. A number of studies on the use of tissue velocity and displacement in AR (8–11) have suggested this modality to be of value. In these studies, patients presumably had more severe disease than the conservatively managed group in the present study, which would place these patients on the “descending slope” of the biphasic relationship between LV remodeling and basal motion.

**Etiology of impaired deformation in AR.** Systolic phase indexes are important measures of dysfunction in AR because of their ability to detect afterload mismatch at the point at which myocardial reserve mechanisms are exhausted (18,19). Speckle-tracking echocardiography detected this expected decrease in systolic function in patients with AR, and we demonstrated its relation with increased afterload. It is interesting that we also found early diastolic strain rate to be a sensitive marker of LV dysfunction. Reduced diastolic deformation rate cannot be attributed to afterload mismatch; instead, it might be caused by changes to the extracellular matrix, which increases in quantity in AR, especially because of an increased amount of noncollagen constituents (20,21). A subsequent change in myocardial passive properties is the probable explanation for the observed diastolic abnormalities.

**Perspectives.** Speckle-tracking deformation imaging may in the future become part of the recommended echocardiographic examinations in patients with chronic AR. Signs of myocardial dysfunction could presumably be picked up earlier with this technique, which should then prompt increased vigilance, including more frequent follow-up in individual patients. It is possible that the implementation of deformation imaging in this way would allow more patients to have surgery performed before the occurrence of irreversible myocardial damage, even without changing the current indications for surgery.

**Study limitations.** The small sample size limited our ability to perform more detailed multivariate and subgroup analyses. As a consequence, uncontrolled confounding is a possibility, and the results should be interpreted accordingly. The sample size necessitated the use of combined end points, so confirmation of our findings should be sought in longer running studies with all-clinical end points. Follow-up in the conservatively managed group also differed somewhat in frequency and duration, as

decisions regarding follow-up intervals were left to the discretion of the attending cardiologist, but no patients were followed at intervals longer than 1 year. Changes in LV volume during follow-up might have been determined with higher precision if repeat cardiac magnetic resonance had been used for this purpose instead of echocardiography.

## CONCLUSIONS

Echocardiographic analysis of LV longitudinal deformation and deformation rate with speckle-tracking echocardiography is useful for the detec-

tion of clinically relevant LV systolic and diastolic dysfunction in patients with chronic, isolated AR. Impaired longitudinal myocardial deformation seems a valuable indicator of early LV dysfunction in AR, and speckle-tracking echocardiography has the potential to improve the management of patients with chronic AR.

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**Key Words:** aortic regurgitation ■ echocardiography ■ heart failure ■ speckle tracking ■ tissue Doppler.