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Mechanical Dispersion Assessed by Myocardial Strain in Patients After Myocardial Infarction for Risk Prediction of Ventricular Arrhythmia

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OBJECTIVES The aim of this study was to investigate whether myocardial strain echocardiography can predict ventricular arrhythmias in patients after myocardial infarction (MI).

BACKGROUND Left ventricular (LV) ejection fraction (EF) is insufficient for selecting patients for implantable cardioverter-defibrillator (ICD) therapy after MI. Electrical dispersion in infarcted myocardium facilitates malignant arrhythmia. Myocardial strain by echocardiography can quantify detailed regional and global myocardial function and timing. We hypothesized that electrical abnormalities in patients after MI will lead to LV mechanical dispersion, which can be measured as regional heterogeneity of contraction by myocardial strain.

METHODS We prospectively included 85 post-MI patients, 44 meeting primary and 41 meeting secondary ICD prevention criteria. After 2.3 years (range 0.6 to 5.5 years) of follow-up, 47 patients had no and 38 patients had 1 or more recorded arrhythmias requiring appropriate ICD therapy. Longitudinal strain was measured by speckle tracking echocardiography. The SD of time to maximum myocardial shortening in a 16-segment LV model was calculated as a parameter of mechanical dispersion. Global strain was calculated as average strain in a 16-segment LV model.

RESULTS The EF did not differ between ICD patients with and without arrhythmias occurring during follow-up (34 ± 11% vs. 35 ± 9%, $p = 0.70$). Mechanical dispersion was greater in ICD patients with recorded ventricular arrhythmias compared with those without (85 ± 29 ms vs. 56 ± 13 ms, $p < 0.001$). By Cox regression, mechanical dispersion was a strong and independent predictor of arrhythmias requiring ICD therapy (hazard ratio: 1.25 per 10-ms increase, 95% confidence interval: 1.1 to 1.4, $p < 0.001$). In patients with an EF >35%, global strain showed better LV function in those without recorded arrhythmias (−14.0% ± 4.0% vs. −12.0 ± 3.0%, $p = 0.05$), whereas the EF did not differ (44 ± 8% vs. 41 ± 5%, $p = 0.23$).

CONCLUSIONS Mechanical dispersion was more pronounced in post-MI patients with recurrent arrhythmias. Global strain was a marker of arrhythmias in post-MI patients with relatively preserved ventricular function. These novel parameters assessed by myocardial strain may add important information about susceptibility for ventricular arrhythmias after MI. (J Am Coll Cardiol Img 2010;3: 247–56) © 2010 by the American College of Cardiology Foundation

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The implantable cardioverter-defibrillator (ICD) is an important innovation in the treatment of sudden cardiac death (1–3), but significant questions remain unanswered. Currently, left ventricular (LV) ejection fraction (EF) is the primary parameter used to select patients for ICD therapy. Impaired EF is shown to be a marker of increased cardiovascular mortality and sudden cardiac death (4,5), but has relatively low sensitivity for detecting arrhythmia risk (6). There is emerging awareness of the limitations of using EF as the main risk stratification tool for ICD therapy (6–8). Sudden cardiac arrest accounts for a smaller proportion of deaths in patients with lowest EFs than in patients with relatively preserved ventricular function (9). A variety of diagnostic tests have been proposed to improve the accuracy of selection of patients who need ICD therapy. Currently available data, however, do not support additional risk-stratification methods for the selection of patients for ICD therapy (7).

ABBREVIATIONS AND ACRONYMS

CI = confidence interval
ECG = electrocardiogram
EF = ejection fraction
ICD = implantable cardioverter-defibrillator
LQTS = long QT syndrome
LV = left ventricular
MI = myocardial infarction
nsVT = nonsustained ventricular tachycardia
VF = ventricular fibrillation
VT = ventricular tachycardia

The presence of myocardial scar forms the substrate for malignant arrhythmias (10). Heterogeneity in scar tissue creates areas of slow conduction that generate the substrate for ventricular arrhythmia after myocardial infarction (MI) (11,12). Electrical dispersion, including both activation time and refractoriness, in infarcted tissue is a known arrhythmogenic factor (13,14). Electrical abnormalities may lead to distorted myocardial function (15,16). Therefore, regional differences in electrical properties may cause heterogeneity of myocardial contraction and may be recognized as mechanical dispersion. Subtle contraction heterogeneity can be demonstrated by myocardial strain echocardiography, which can accurately quantify timing and regional myocardial function (17,18). We recently demonstrated the heterogeneity of systolic contraction by echocardiography as mechanical dispersion, presumably as a consequence of electrical dispersion in patients with long QT syndrome (LQTS). In these patients, mechanical dispersion was associated with ventricular arrhythmias (16).

We hypothesized that post-MI patients at risk of cardiac arrhythmias have increased myocardial mechanical dispersion due to tissue heterogeneity between infarcted and normal myocardium. We aimed to investigate whether mechanical dispersion and myocardial function by strain echocardiography in post-MI patients might serve as risk markers for cardiac arrhythmias.

METHODS

Study population. A total of 85 post-MI patients fulfilling indications for ICD therapy were recruited from 4 university hospitals (St. Olavs Hospital, Trondheim, Norway; Ullevål University Hospital, Oslo, Norway; University Hospital Gasthuisberg, Leuven, Belgium; and Rikshospitalet University Hospital, Oslo, Norway). Written informed consent was given by all participants. The study was approved by the Regional Committee for Medical Research Ethics. All patients were included prospectively with echocardiographic examination usually performed during the hospitalization for ICD implantation (median 0 days [range −175 to 84 days]). Inclusion criteria were previous hospitalization for MI and indication for ICD therapy according to primary or secondary prevention criteria. Primary prevention criteria (44 patients) included patients with an EF <35% at least 40 days after MI or <40% and nonsustained ventricular tachycardia (nsVT) and sustained arrhythmia inducible by an electrophysiology study. Secondary prevention criteria (41 patients) included cardiac arrest survivors and patients with sustained ventricular tachycardia (VT) (3). In secondary prevention patients, the arrhythmia (VT or ventricular fibrillation [VF]) that provided the indication for ICD therapy was defined as the index arrhythmia. Medical treatment and revascularization therapy were recorded. Exclusion criteria were atrial fibrillation, left bundle branch block, previous coronary artery bypass graft surgery, and valve regurgitations greater than moderate. No patients had more than mild valvular stenoses. Arrhythmic events during follow-up were defined as ventricular arrhythmias that required appropriate antitachycardia pacing or shock from the ICD. The time from ICD implantation to the first arrhythmic event during follow-up was recorded. Follow-up time after ICD implantation was a minimum of 300 days.

All 85 ICD patients underwent coronary angiography before ICD implantation. Percutaneous coronary intervention was performed in 49 patients. Four patients underwent coronary artery bypass graft surgery after inclusion and ICD implantation. One patient had received thrombolytic therapy for MI and had no significant stenoses revealed on coronary angiography. In 31 patients, the coronary lesions were ineligible for revascularization.

Control groups. From our outpatient clinic, we recruited 20 patients with previous hospitalization for MI. Exclusion criteria were identical to those for the study population. None of the group experienced arrhythmic events.

The control group consisted of 23 healthy individuals recruited from the hospital staff. All had a normal electrocardiogram (ECG) and echocardiogram.

ECG. A 12-lead ECG was obtained in all participants. The QT interval was heart rate corrected with Bazett's formula (19).

Echocardiography. The echocardiographic studies were performed using Vivid 7 (GE, Horten, Norway) and analyzed with EchoPAC software (GE). The LVEF was assessed according to Simpson's biplane method. Myocardial strain measurements were performed using speckle tracking echocardiography (20). Longitudinal strain was obtained from all apical views at 63 ± 23 frames/s. Global LV longitudinal strain was obtained by averaging the maximum systolic shortening in a 16-segment model (Fig. 1). Post-systolic shortening was not included in the global strain analyses. The maximum systolic lengthening was recorded in segments in which no shortening was present (21).

Myocardial mechanical dispersion. The time to maximum myocardial shortening, including post-systolic shortening, if present, was measured from the ECG onset Q/onset R-wave in 16 LV segments (Fig. 1). Inclusion of an infarcted segment in time analyses required approval from the automated software. The maximum myocardial shortening from a representative strain curve with a shortening duration of a minimum of 50 ms was used in the time analyses. Segments in which no shortening was present were excluded.

To quantify LV mechanical dispersion, we used the SD of the 16 different time intervals to maximum myocardial shortening in each participant; this parameter was defined as mechanical dispersion. An alternative measure for mechanical dispersion was the difference between the longest and shortest time interval from ECG onset Q/onset R-wave to the maximum myocardial shortening in each individual. This parameter was defined as the delta contraction duration.

Strain parameters could be assessed in 95% of the myocardial segments in the study group and in 91% of the subjects in the control group. Time measurements included 88% of the segments in the infarcted patients with ICD. The intraobserver analysis was performed blinded to patients' arrhythmia outcome status.

Statistical analyses. Data are presented as mean ± SD or as median (range). Comparisons of means were analyzed by analysis of variance with the Bonferroni correction for multiple comparisons (SPSS version 15.0, SPSS Inc., Chicago, Illinois). The Kruskal-Wallis test was performed for non-parametric variables. Proportions were compared using a chi-square test. Cox regression analysis was

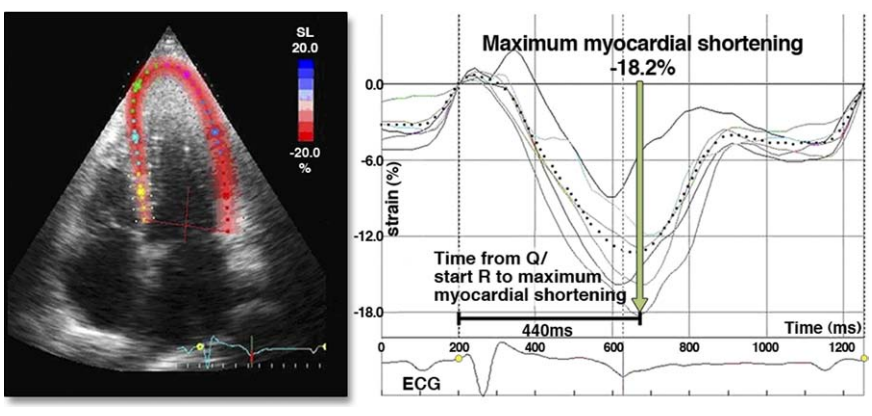

Figure 1. Global Strain, Mechanical Dispersion, and Delta Contraction Duration

Speckle tracking echocardiography longitudinal strain curves in a 4-chamber view from a post–myocardial infarction patient. Maximum myocardial shortening in the septal apical segment is indicated **(green arrow)** as well as the time from electrocardiogram (ECG) onset Q/onset R-wave to maximum myocardial shortening **(time line)**. Global strain: average value of the maximum myocardial shortening in 16 left ventricular segments; mechanical dispersion: SD of the time interval from ECG onset Q/onset R-wave to maximum myocardial shortening in 16 left ventricular segments; delta contraction duration: difference between the segments with the longest and shortest time interval from ECG onset Q/onset R-wave to maximum myocardial shortening.

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used in the patient population to identify predictors of the outcome of arrhythmia requiring appropriate ICD treatment. Patients with ICD meeting primary and secondary prevention criteria were analyzed separately. Hazard ratios and 95% confidence intervals (CIs) were calculated. The multivariate analysis was performed by including significant variables from the univariate model ($p < 0.05$) in addition to age and EF, which were forced in. A close relationship was observed between mechanical dispersion and delta contraction duration, and therefore only mechanical dispersion was included in the multivariate analysis. Kaplan-Meier analysis was used to create freedom-from-arrhythmia survival curves. The value closest to the upper left corner of the receiver-operator characteristic curve determined optimal sensitivity and specificity for the ability of mechanical dispersion to identify arrhythmic events. Reproducibility was expressed as an intraclass correlation coefficient. p Values <0.05 were considered significant.

RESULTS

Clinical findings. Clinical data are presented in Table 1. Indications for ICD therapy according to primary prevention criteria were present in 44 patients and according to secondary prevention criteria in 41 patients. Thirty-eight ICD patients experienced 1 or more episodes with sustained VT or VF requiring appropriate ICD therapy (antitachycardia pacing or shock), whereas 47 ICD patients had no sustained arrhythmia during 2.3 years (range 0.6 to 5.5 years) of follow-up.

The QRS and QTc duration and the use of medication were similar in the 2 ICD groups (Table 1). The median time from ICD implantation to first ICD therapy was 239 days (range 2 to 1,529 days).

Among the 38 patients with recorded arrhythmias occurring during follow-up, 30 received ICD therapy for VT, 5 for VF, and 3 for unknown reasons. Coronary angiography was performed in 4 of 5 patients with VF occurring during follow-up, and 3 required a percutaneous intervention due to new coronary lesions. Arrhythmias occurred later during follow-up in patients with ICD therapy for VF compared with those with VT (2.6 years vs. 1.0 years, $p = 0.02$). There were no differences in QRS and QTc duration or in echocardiographic parameters between patients with VF or VT occurring during follow-up.

No differences were found between the revascularized and nonrevascularized patients regarding incidence or modality of arrhythmia (VT or VF) as recorded by the ICD device ($p = 0.70$). Revascularized patients had a significantly better EF compared with nonrevascularized patients (EF 37 ± 11% vs. 32 ± 8%, respectively; $p = 0.04$).

PRIMARY PREVENTION PATIENTS. In the 44 patients meeting primary prevention criteria, 12 underwent implantation based on an EF <35% and 32 had an EF <40% and nsVT and were inducible by electrophysiology study. Of the 32 patients with nsVT, 15 had an EF <35%. During follow-up, there were significantly more arrhythmic events in those with an EF <40% and nsVT/inducible (18 of 32 patients) compared with those with an EF <35%

Table 1. Clinical Characteristics in 85 Patients With an ICD, 20 Control Patients With a Previous MI, and 23 Healthy Individuals

	Healthy Individuals (n = 23)	Control Patients With Previous MI (n = 20)	ICD Patients Without Arrhythmic Events During Follow-Up (n = 47)	ICD Patients With Arrhythmic Events During Follow-Up (n = 38)	p Value*
Age (yrs)	62 ± 10	62 ± 13	62 ± 10	65 ± 10	0.53
Heart rate (beats/min)	65 ± 11	64 ± 12	68 ± 13	63 ± 13	0.36
No. (%) of women	7 (30)	3 (15)	10 (21)	3 (8)	0.04
Median time (range) from MI (yrs)		4.5 (2.0–30.0)	6.2 (0.4–29.9)	5.9 (0.6–35.8)	0.98
QRS duration (ms)		100 ± 15	100 ± 15	100 ± 25	0.93
QTc (ms)		420 ± 25	450 ± 45	440 ± 40	0.23
Amiodarone, no. (%)		0	10 (21)	8 (21)	0.07
Beta-blocker, no. (%)		19 (95)	43 (91)	35 (92)	0.93
ACE/AT II inhibitor, no. (%)		14 (70)	40 (85)	32 (84)	0.42
Revascularization therapy, no. (%)		13 (65)	29 (62)	25 (66)	0.92
ICD primary prevention, no. (%)			24 (51)	20 (53)	0.89
ICD secondary prevention, no. (%)			23 (49)	18 (47)	0.89

Values are mean ± SD unless otherwise indicated. *p Values for analysis of variance *F* test, Kruskal-Wallis test, and chi-square test.
ACE = angiotensin-converting enzyme; AT II = angiotensin II; ICD = implantable cardioverter-defibrillator; MI = myocardial infarction.

Table 2. Echocardiographic Findings in 85 Patients With an ICD, 20 Control Patients With a Previous MI, and 23 Healthy Individuals

	Healthy Individuals (n = 23)	Control Patients With Previous MI (n = 20)	ICD Patients Without Arrhythmic Events During Follow-Up (n = 47)	ICD Patients With Arrhythmic Events During Follow-Up (n = 38)	p Value*
EF (%)	62 ± 7	55 ± 9	34 ± 11†	35 ± 9†	<0.001
EF >35%, no. (%)	23 (100)	20 (100)	21 (45)†	22 (58)†	<0.001
LVEDV (ml)	107 ± 28	110 ± 26	188 ± 68†	202 ± 86†	<0.001
LVESV (ml)	42 ± 13	51 ± 19	126 ± 59†	132 ± 66†	<0.001
Global strain (%)	−21.6 ± 2.8	−15.9 ± 2.5‡	−11.2 ± 4.0†	−10.0 ± 3.7†	<0.001
Mechanical dispersion (ms)	22 ± 10	45 ± 15§	56 ± 13§	85 ± 29‡	<0.001
Delta contraction duration (ms)	70 ± 33	145 ± 55§	195 ± 65§	335 ± 115‡	<0.001

Values are mean ± SD unless otherwise indicated. Multiple comparisons are obtained with the Bonferroni post hoc test. *p Values for analysis of variance, *F* test, and chi-square test, †p < 0.05 compared with healthy individuals and control patients with previous MI, ‡p < 0.001 compared with all other groups, §p < 0.001 compared with healthy individuals. Global strain: average value of the maximum myocardial shortening in 16 left ventricular (LV) segments; mechanical dispersion: SD of time interval from electrocardiogram (ECG) onset Q/onset R-wave to maximum myocardial shortening in 16 LV segments; delta contraction duration: difference between longest and shortest duration of time from ECG onset Q/onset R-wave to maximum myocardial shortening in a 16-segment model.
EF = ejection fraction; LVEDV = left ventricular end-diastolic volume; LVESV = left ventricular end-systolic volume; other abbreviations as in Table 1.

(2 of 12 patients) (p = 0.02). Primary prevention criteria patients with the ICD indication of an EF <35% alone had fewer arrhythmic events during follow-up compared with all other patients (p = 0.04). Positive and negative predictive values for later arrhythmias were 17% and 43%, respectively, when ICD implantation was based on EF alone.

SECONDARY PREVENTION PATIENTS. In the 41 secondary prevention criteria patients, 15 had an

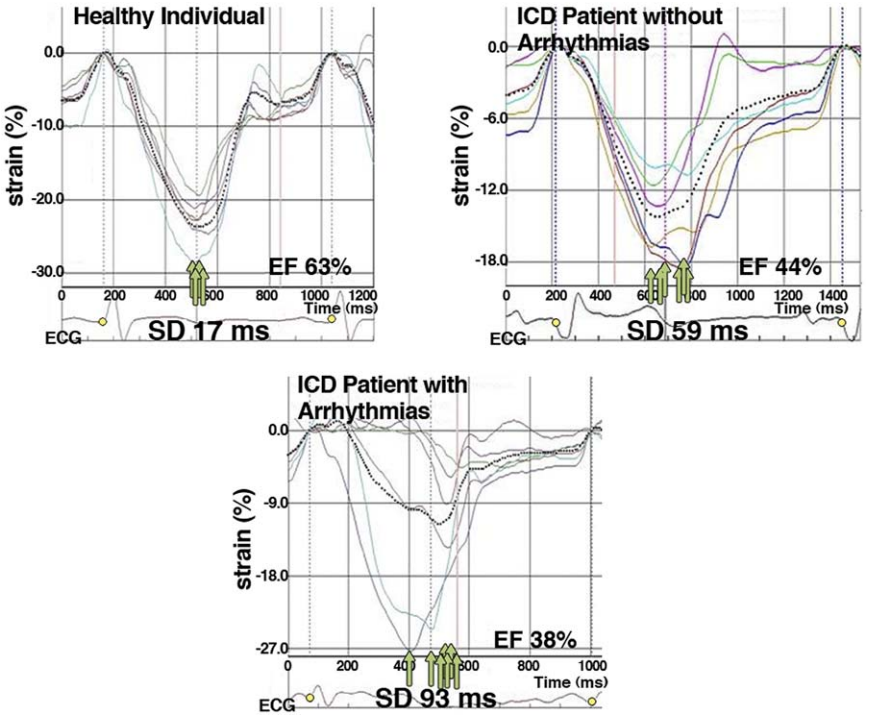

Figure 2. Mechanical Dispersion by Strain Echocardiography in a Healthy Individual and ICD Patients With and Without Arrhythmias During Follow-Up

Speckle tracking echocardiography longitudinal strain curves in a 4-chamber view from a healthy individual **(upper left panel)**, a post–myocardial infarction (MI) implantable cardioverter-defibrillator (ICD) patient without arrhythmic events **(upper right panel)**, and a post–MI ICD patient with recurrent arrhythmias **(bottom panel)**. **Green Arrows** indicate the timing of maximum myocardial shortening in each segment. Myocardial shortening is reduced in the ICD patients, and the timing of shortening is dispersed compared with the healthy individual. The **dotted line** represents the average myocardial shortening for each individual. ECG = electrocardiogram; EF = ejection fraction; SD = standard deviation of time to maximum myocardial shortening.

EF <35% and 36 had an EF >35% (Table 2). All these patients had experienced sustained VT or were cardiac arrest survivors. The index arrhythmia was VT in 24 patients and VF in 17 patients. The probability of later arrhythmias was similar regardless of whether the index arrhythmia was VT or VF ($p = 0.12$). Forty-four percent experienced arrhythmic events during follow-up.

Myocardial mechanical dispersion. Both methods of quantification of mechanical dispersion were related to the occurrence of arrhythmic events. The SD of time to maximum myocardial shortening was significantly longer in those with arrhythmias ($p < 0.001$) (Table 2 and Fig. 2). In addition, delta contraction duration (time difference between segments with the longest and shortest duration of systolic shortening) was prolonged in the ICD patients with arrhythmic events during follow-up compared to those without ($p < 0.001$) (Table 2). Univariate analyses of risk factors for ventricular arrhythmias that required appropriate ICD therapy are shown in Table 3. In the multivariate analysis, mechanical dispersion was a strong and independent predictor of arrhythmias ($p < 0.001$). Mechanical dispersion was more pronounced in patients with an EF >35% who experienced arrhythmias (n = 22) compared with those with no arrhythmias (n = 21) ($p = 0.01$) (Table 4). In patients with ICD based on an EF indication alone, 2 of 12 experienced arrhythmias during follow-up. Importantly, both of these patients had mechanical dispersion >70 ms (138 ms and 142 ms, respectively). In patients with ICD based on an EF indication alone and without further arrhythmic events (n = 10), mechanical dispersion was significantly lower compared with the rest of the patients who all had experienced arrhythmic events before or after ICD implantation (50 ± 15 ms vs. 71 ± 26 ms, $p = 0.01$). Figure 3 shows a Kaplan-Meier plot that demonstrates arrhythmic event–free survival in the ICD population. ICD patients with mechanical dispersion >70 ms experienced more frequent arrhythmic events than ICD patients with mechanical dispersion <70 ms (log-rank test, $p < 0.001$). Mechanical dispersion of 70 ms had a sensitivity of 65% (95% confidence interval [CI]: 0.55 to 0.71) and a specificity of 92% (95% CI: 0.83 to 0.96) for identifying arrhythmic events (Fig. 4).

Control patients with a previous MI without any arrhythmias had significantly lower mechanical dispersion compared with ICD patients with arrhythmias during follow-up ($p < 0.001$). Compared with

Table 3. Predictors of Arrhythmias During Follow-Up That Require Appropriate ICD Therapy in a Total of 85 Post–MI Patients With an ICD by Cox Regression Analysis

	Variable			
	Primary Prevention Criteria Patients (n = 44), HR (95% CI)	p Value	Secondary Prevention Criteria Patients (n = 41), HR (95% CI)	p Value
Univariate analyses				
Age (per 5-yr increase)	1.12 (0.90–1.40)	0.30	1.14 (0.88–1.48)	0.33
Sex (male vs. female)	1.04 (0.23–4.56)	0.95	5.42 (0.72–40.8)	0.10
Heart rate (per 5-beats/min increase)	0.96 (0.77–1.19)	0.69	0.90 (0.74–1.08)	0.25
QRS (per 10-ms increase)	0.76 (0.50–1.15)	0.20	0.97 (0.76–1.24)	0.78
QTc (per 10-ms increase)	1.02 (0.94–1.10)	0.71	0.95 (0.79–1.14)	0.56
Amiodarone therapy (yes vs. no)	1.54 (0.35–6.86)	0.57	1.06 (0.40–2.86)	0.91
Revascularization therapy (yes vs. no)	1.01 (0.39–2.62)	0.97	0.97 (0.36–2.59)	0.95
nsVT/inducible VT (yes vs. no)	2.62 (0.59–11.56)	0.21		
EF (per 5% increase)	0.80 (0.59–1.08)	0.15	1.13 (0.90–1.42)	0.30
Global strain (per 1% increase)	0.84 (0.71–0.99)	0.03	1.00 (0.89–1.12)	0.98
Mechanical dispersion (per 10-ms increase)	1.25 (1.10–1.43)	<0.01	1.30 (1.09–1.55)	<0.01
Delta contraction duration (per 10-ms increase)	1.05 (1.01–1.08)	<0.01	1.06 (1.02–1.10)	<0.01
Multivariate analyses				
Age (per 5-yr increase)	1.20 (0.93–1.55)	0.15	1.23 (0.94–1.59)	0.14
Sex (male vs. female)	0.92 (0.18–4.78)	0.92	3.80 (0.50–29.44)	0.20
EF (per 5% increase)	0.90 (0.56–1.45)	0.68	1.10 (0.83–1.46)	0.51
Global strain (per 1% increase)	0.92 (0.76–1.11)	0.37		
Mechanical dispersion (per 10-ms increase)	1.24 (1.07–1.43)	<0.01	1.31 (1.08–1.58)	<0.01

CI = confidence interval; EF = ejection fraction; HR = hazard ratio; nsVT = nonsustained ventricular tachycardia; inducible VT = inducible ventricular tachycardia in electrophysiology study; other abbreviations as in Table 1.

Table 4. Separate Results From 42 ICD Patients With an EF <35% and 43 ICD Patients With an EF >35%

	EF <35%			EF >35%		
	Without Arrhythmic Events During Follow-Up (n = 26)	With Arrhythmic Events During Follow-Up (n = 16)	p Value*	Without Arrhythmic Events During Follow-Up (n = 21)	With Arrhythmic Events During Follow-Up (n = 22)	p Value*
Age (yrs)	60 ± 9	64 ± 8	0.52	64 ± 10	67 ± 11	0.32
EF (%)	27 ± 5	27 ± 5	0.99	44 ± 8	41 ± 5	0.23
Global strain (%)	−8.9 ± 2.2	−7.2 ± 3.0	0.04	−14.0 ± 4.0	−12.0 ± 3.0	0.05
Mechanical dispersion (ms)	52 ± 13	93 ± 31	<0.001	61 ± 12	80 ± 27	0.01
Delta contraction duration (ms)	170 ± 40	340 ± 120	<0.001	225 ± 80	280 ± 110	0.06
QRS duration (ms)	104 ± 14	107 ± 26	0.88	95 ± 13	101 ± 28	0.49
ICD secondary prevention, no. (%)	12 (46)	3 (19)	0.07	11 (52)	15 (68)	0.29
ICD primary prevention, no. (%)	14 (54)	13 (81)	0.07	10 (48)	7 (32)	0.29

Values shown are mean ± SD unless otherwise indicated. *p Values for analysis of variance *F* test. Mechanical dispersion = standard deviation of time interval from onset Q/onset R-wave to maximum myocardial shortening in 16 LV segments; Delta contraction duration = difference between longest and shortest duration of time from ECG onset Q/onset R-wave to maximum myocardial shortening in a 16 segment model.
Abbreviations as in Tables 1 and 2.

ICD patients without arrhythmic events during follow-up, control patients with a previous MI had lower mechanical dispersion, although not reaching significant levels (p = 0.11) (Table 2). Healthy individuals had shorter and more homogeneous time measurements compared with all post-MI groups (Table 2).

LV volumes and function. Importantly, EF and LV volumes were equal in the ICD groups, and those with recurrent arrhythmias and those without could not be differentiated (Table 2). Global strain was not reduced in patients with arrhythmias during follow-up compared with those without in the total study population. When analyzed separately, in patients with an EF <35% and >35%, global strain was significantly reduced in patients with arrhythmias (Table 4).

Intraobserver variability and interobserver variability were 0.98 and 0.98, respectively, for strain measurements and 0.86 and 0.81, respectively, for time measurements.

DISCUSSION

This study introduces a new principle in risk assessment for life-threatening arrhythmias in patients with a previous MI. Patients with recorded arrhythmias showed greater mechanical dispersion by an SD of time to maximum myocardial shortening and delta contraction duration. Mechanical dispersion was a strong and independent predictor of arrhythmic events. Our findings support the idea that electrical abnormalities in post-MI patients are associated with mechanical dispersion. EF on echocardiography was not able to differentiate post-MI patients with respect to arrhythmic events in either primary or secondary prevention criteria patients. Global strain, however, provided added value in arrhythmia risk stratification.

Mechanical dispersion. There is ample evidence from different cardiac disease models, including heart failure (22), ischemia (13), and infarction (14,23), that increases in dispersion of conduc-

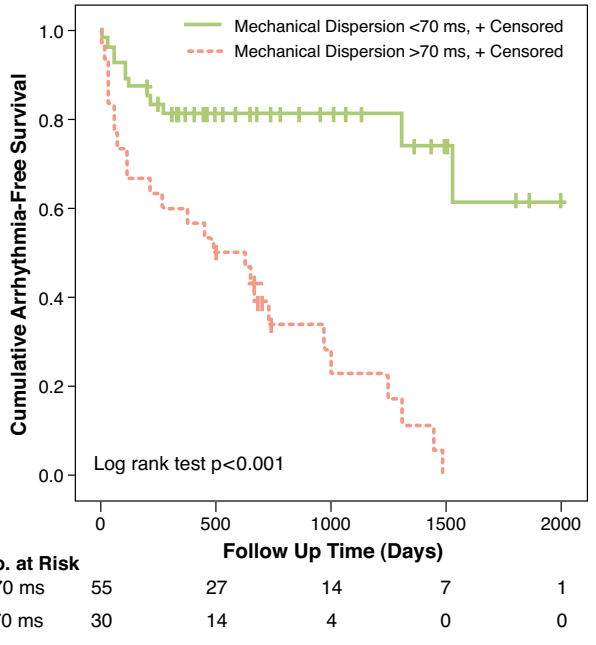

Figure 3. Kaplan-Meier Arrhythmia-Free Survival in 85 Post-MI Patients With an ICD

Kaplan-Meier plot demonstrates arrhythmia-free survival in 85 post–myocardial infarction (MI) implantable cardioverter-defibrillator (ICD) patients. Mechanical dispersion is defined as the SD of the time to maximum myocardial shortening in a 16-segment left ventricular model and reflects the heterogeneity of myocardial contraction throughout the ventricle. Patients with mechanical dispersion >70 ms show a higher arrhythmic event rate.

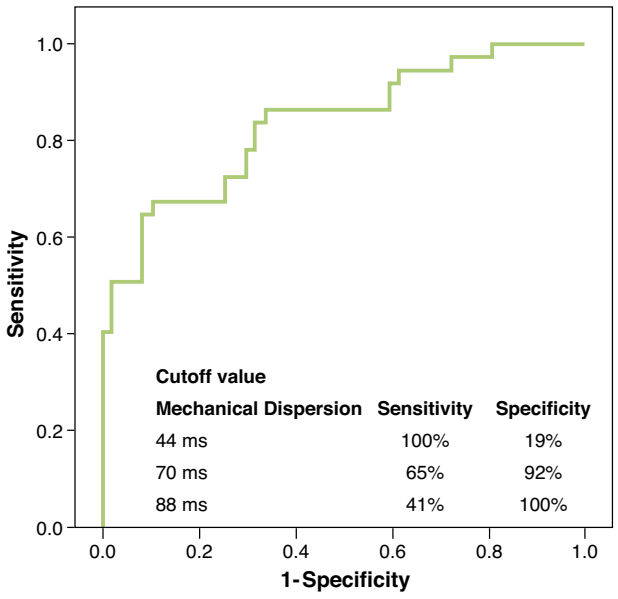

Figure 4. ROC Curve for the Ability of Mechanical Dispersion to Identify Arrhythmic Events During Follow-Up in 85 Post-MI ICD Patients

The cutoff value for mechanical dispersion of 41 ms provided 100% sensitivity and a value of 88 ms provided 100% specificity in predicting arrhythmic events. The optimal cutoff value was 70 ms for a sensitivity of 65% and a specificity of 92% in predicting arrhythmic events. Area under the curve: 0.84 (95% confidence interval: 0.75 to 0.92). ROC = receiver operator characteristic.

tion velocity result in susceptibility to arrhythmias (22,23). These electrical abnormalities will presumably lead to changes in myocardial function, as shown in our study. Assessing the extent of electrical dispersion in the individual patient has so far been difficult (22). A recent study showed that tissue heterogeneity in post-MI patients assessed by cardiac magnetic resonance correlated with increased susceptibility to ventricular arrhythmias induced by programmed ventricular stimulation (24). Our study supports the idea that tissue heterogeneity, leading to a dispersed myocardial contraction, is associated with the risk of arrhythmic events.

We recently reported mechanical dispersion to be a marker of arrhythmia in LQTS patients (16). Ion channel defects in LQTS result in dispersed electrical repolarization, and we showed that mechanical dispersion was present in these patients along with normal myocardial shortening. The mechanism for electrical dispersion in post-MI patients, however, is different from that in LQTS patients. In post-MI patients, a delayed start of ventricular activation in scarred myocardium leads to a dispersed recovery of excitability (14), resulting in dispersed electrical repolarization. The extent of mechanical dispersion appeared to be more pronounced in post-MI patients in the present study compared with LQTS patients recently reported.

In control post-MI patients with preserved EF, mechanical dispersion was significantly lower compared with ICD patients with recorded arrhythmias and tended to be lower compared with ICD patients without arrhythmic events. These findings demonstrate the presence of mechanical dispersion in all post-MI patients and support the assumption that the extent of mechanical dispersion is important for arrhythmogenesis.

Similar techniques and parameters used in this study have been used to assess dyssynchrony in patients eligible for cardiac resynchronization therapy (25). Synchronicity, the absence of mechanical dispersion, in normal individuals was reported earlier with similar techniques and values as healthy individuals in our study (26).

LV function. The relationship between LV systolic dysfunction and deaths due to progressive heart failure and ventricular arrhythmias in post-MI patients is well established (27,28). Earlier echocardiographic studies found that an EF of ≤40% serves as the threshold for identifying high-risk individuals (27,28). However, EF has reduced sensitivity in predicting sudden death; less than 50% of patients with a previous MI who die suddenly have an EF <30% (6,29).

Myocardial strain assessed by speckle tracking echocardiography represents a novel technique to quantify LV function (30). Strain measures LV contraction. Speckle tracking echocardiography–based strain has been shown to be a robust technique for the assessment of LV function. A recent study demonstrated that speckle tracking echocardiography–based strain is superior to EF for assessment of myocardial function post-MI (21). In our study, global strain was decreased in post-MI patients with an EF >35% and arrhythmic events. This finding might suggest that global strain might become a useful tool for risk stratification in post-MI patients with relatively preserved LV function. EF, however, failed to identify arrhythmic events in our post-MI patients with an EF >35%.

Clinical implications. Measurements of mechanical dispersion and global strain in post-MI patients add important information about the risk of arrhythmia beyond the EF. Importantly, in patients with a preserved or slightly reduced EF, mechanical dispersion >70 ms identified post-MI patients with an increased risk of life-threatening arrhythmias. Ac-

cording to current guidelines for primary prevention, post-MI patients with an EF <35% should be considered for ICD therapy (1,3). The novel principles presented in this study might be useful to identify the risk of arrhythmias in post-MI patients with relatively preserved EF who do not fulfill current ICD indications (EF <35%). Future trials should investigate whether mechanical dispersion and global strain can be used to select additional patients for ICD therapy among the majority of post-MI patients with a relatively preserved EF in whom current ICD indications fail. The proposed echocardiographic measurements can be easily implemented in clinical routine.

Study limitations. Our study shows that mechanical dispersion is associated with ventricular arrhythmia. Whether mechanical dispersion can be explained by electrical dispersion must be studied experimentally.

Clinical implications of these novel methods must be interpreted with respect to the fact that all patients fulfilled current guidelines for ICD therapy. The present study was not designed to find the optimal clinical cutoff value for mechanical dispersion in patients not fulfilling current ICD indications.

CONCLUSIONS

This study demonstrates that post-MI patients at risk of cardiac arrhythmias have increased myocardial mechanical dispersion. Assessment of mechanical dispersion by echocardiography might therefore help to identify post-MI patients susceptible to ventricular arrhythmias beyond the extent of reduced LV function.

Global strain may become an additional tool for risk stratification in post-MI patients with relatively preserved ventricles.

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