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Title: Deformation imaging and three-dimensional echocardiography : implications on clinical management of patients with ischemic heart disease

Issue Date: 2016-01-26

CHAPTER 8

The Relationship between Time from Myocardial Infarction, Left Ventricular Dyssynchrony, and the Risk for Ventricular Arrhythmia: Speckle-Tracking Echocardiographic Analysis

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J Am Soc Echocardiogr 2015;28:470–7



ABSTRACT

Background: Differences in arrhythmogenic substrate may explain the variable efficacy of implantable cardioverter-defibrillators (ICDs) in primary sudden cardiac death prevention over time after myocardial infarction (MI). Speckle-tracking echocardiography allows the assessment left ventricular (LV) dyssynchrony, which may reflect the electromechanical heterogeneity of myocardial tissue. The aim of the present study was to evaluate the relationship among LV dyssynchrony, age of MI, and their association with the risk for ventricular tachycardia (VT) after MI.

Methods: A total of 206 patients (median age 67 years; 87% men) with prior MIs (median MI age 6.2 years; interquartile range 0.66–15 years) who underwent programmed electrical stimulation, speckle-tracking echocardiography, and ICD implantation were retrospectively evaluated. LV dyssynchrony was defined as the standard deviation of time to peak longitudinal systolic strain values using speckle-tracking strain echocardiography. LV scar burden was evaluated by the percentage of segments exhibiting scar (defined as an absolute longitudinal strain of magnitude $<4.5\%$). Patients were followed up for the occurrence of first monomorphic VT requiring ICD therapy (antitachycardia pacing or shock) for a median of 24 months.

Results: In total, 75 individuals experienced the primary end point of monomorphic VT. LV dyssynchrony was independently associated with the occurrence of VT at follow-up (hazard ratio per 10-msec increase 1.12, 95% confidence interval 1.07–1.18, $p<0.001$), together with nonrevascularization of the infarct-related artery and VT inducibility. Patients with older (>180 months) MIs had a higher likelihood of VT inducibility (88% vs 63%, $p=0.003$) and greater scar burden ($14.7 \pm 15.8\%$ vs. $10.7 \pm 11.4\%$, $p=0.03$) compared with patients with recent (<8 months) MIs.

Conclusions: LV dyssynchrony is independently associated with the occurrence of VT after MI.

INTRODUCTION

Sudden cardiac death (SCD), which is attributed mostly to ventricular tachycardia (VT), accounts for approximately 50% of all deaths in patients with coronary heart disease.¹ The interaction between the arrhythmogenic substrate and several factors that influence electrical stability (e.g., autonomic tone, myocardial ischemia) is crucial in the genesis of VT. The use of an implantable cardioverter-defibrillator (ICD) in patients with left ventricular (LV) ejection fractions (LVEFs) $\leq 35\%$ within 40 days after myocardial infarction (MI) has not demonstrated a survival advantage,² despite the known survival benefit of ICD use in other patients with LVEFs $\leq 35\%$.³ Moreover, a progressive increase in mortality risk late after MI has been described among ICD recipients.⁴ Differences in arrhythmogenic substrate early and late after MI may explain those findings and underscore the importance of substrate characterization to determine the mechanisms of SCD. A key feature of the myocardial substrate after MI is slow conduction through inhomogeneous scar tissue.^{5,6} Collagen deposition in particular within the infarct border zone may occur over years after the index MI, resulting in progressive separation of viable myocardial fibers and thus more dispersed electrical impulse propagation through the left ventricle.⁷

The emergence of speckle-tracking echocardiography has permitted more refined evaluation of LV myocardial function and tissue characteristics after MI.⁸ This technique allows the assessment of the temporal heterogeneity of segmental myocardial deformation, which may reflect the electromechanical heterogeneity of myocardial tissue.⁹ With the use of speckle-tracking echocardiography, in the present evaluation we investigated (1) the relationship between MI age and LV mechanical and electrophysiologic characteristics and (2) the association between LV dyssynchrony and risk for VT in ICD recipients after MI.

METHODS

Patient Population

The population comprised patients with prior MIs who underwent programmed electrical stimulation (PES) followed by ICD implantation at the Leiden University Medical Center. All patients underwent transthoracic echocardiography before or < 6 months after ICD implantation. For patients undergoing biventricular ICD (CRT-D) implantation, echocardiography was performed after CRT-D placement, with the pacemaker on to ensure representation of current physiology. Exclusion criteria were an uncertain date of MI, the presence of reversible ischemia, pacemaker dependence before ICD implantation, and the occurrence of VT between ICD insertion and echocardiography.

All clinical, electrophysiologic, and echocardiographic data were collected in the departmental cardiology information system (EPD-Vision; Leiden University Medical Center, Leiden, The Netherlands) and retrospectively analyzed.

Echocardiography

Patients were imaged in the left lateral decubitus position using a commercially available system equipped with 3.5-MHz and 5S transducers (Vivid 7 and E9; GE Vingmed Ultrasound AS, Horten, Norway). Two-dimensional grayscale, color, pulsed-wave, and continuous-wave Doppler data were acquired in the parasternal and apical views. Images were recorded digitally in cine-loop format and analyzed offline with EchoPAC version 11.0.0 (GE Vingmed Ultrasound AS). Left atrial volume and LV end-systolic and end-diastolic volumes were measured from the apical two- and four-chamber views and indexed to body surface area. LVEF was calculated using the biplane Simpson's technique.⁹ Mitral regurgitation severity was graded as none/mild or moderate/severe by incorporating a number of echocardiographic indicators, including regurgitant jet vena contracta width, proximal flow convergence, effective regurgitant orifice area measured with the proximal isovelocity surface area method, color jet area, continuous-wave Doppler spectral profile intensity, E-wave velocity, and pulmonary venous flow reversal.¹⁰

Strain Analysis

Evaluation of LV myocardial deformation was performed with speckle-tracking echocardiography.¹¹ These measurements were performed by two investigators blinded to patient outcomes using the Q-analysis application on an EchoPAC version 11.0.0 workstation. In each of the three apical views, the LV myocardium was manually contoured, and the contours were adjusted to achieve optimal tracking of all myocardial segments over the cardiac cycle. The software automatically generated curves of strain as a function of time (Figure 1). Using an 18-segment model derived from the three apical views, segmental peak systolic longitudinal myocardial strain and time to peak longitudinal strain were recorded. Longitudinal strain in normally contracting myocardium is by convention negative, but for simplicity, we report absolute strain values, denoted as *lstrainl*. Thus, poorer myocardial contraction is reflected by a lower *lstrainl* value. Myocardial segments were classified as having transmural scar if the longitudinal *lstrainl* value was <4.5%. This threshold has been previously validated against late gadolinium enhancement cardiac magnetic resonance imaging.¹²

LV scar burden was evaluated by the percentage of LV segments exhibiting transmural scar. LV dyssynchrony was defined as the standard deviation of values of time to peak longitudinal systolic strain in this 18-segment model (Figure 1).¹¹ Global longitudinal strain (GLS) was measured as the mean of peak *lstrainl* values from each myocardial segment.¹¹

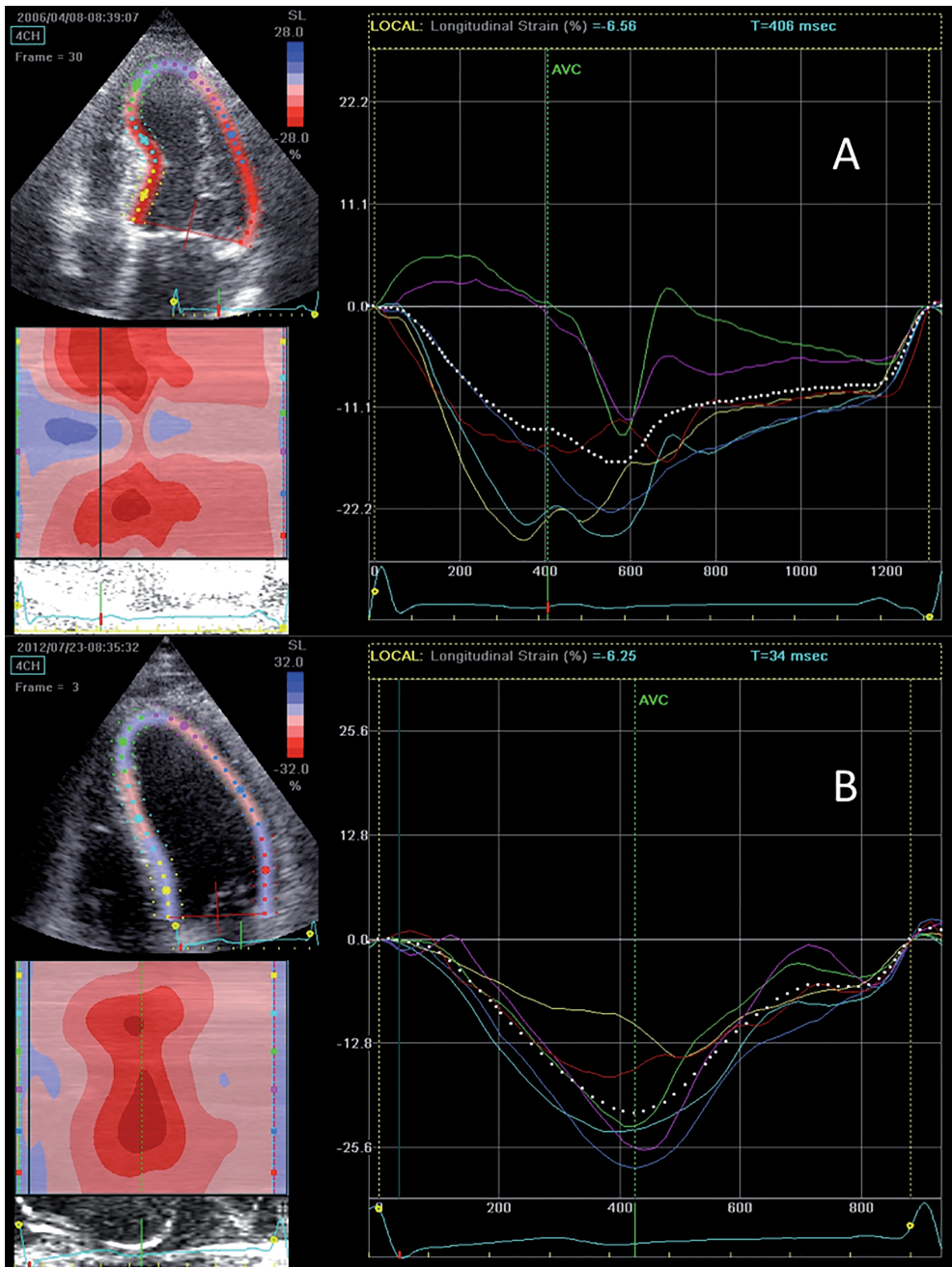


Figure 1. Speckle-tracking echocardiographic strain. Representative examples of speckle-tracking strain curves from two patients with LVEFs of 55%. Patient A demonstrated greater heterogeneity in time to peak segmental strain compared with patient B. LVEF = left ventricular ejection fraction.

PES

PES was performed according to current guidelines.¹³ In brief, patients were studied in a fasting, nonsedated state and after the discontinuation of antiarrhythmic medications (except for amiodarone) for five half-lives.¹⁴ PES included up to three drive-cycle lengths (600, 500, and 400 msec) with up to three ventricular extrastimuli and burst pacing from the right ventricular apex and right ventricular outflow tract. Positive response to PES was defined as the reproducible induction of sustained monomorphic VT lasting >30 sec or requiring termination because of hemodynamic compromise.

Outcomes

VT was identified from examination of ICD electrograms stored after device therapy administration. The appropriateness of this therapy and the nature of the ventricular arrhythmia (to distinguish monomorphic VT from polymorphic VT or ventricular fibrillation) were adjudicated by an electrophysiologist who was blinded to patients' clinical characteristics. The primary end point was the occurrence of first monomorphic VT requiring device therapy (antitachycardia pacing or shock) after ICD implantation. Patients were censored at the date of most recent outpatient appointment unless the primary end point occurred earlier. In addition, the occurrence and date of occurrence of the following significant competing risks were recorded if they took place after ICD implantation and before VT occurrence: polymorphic VT, ventricular fibrillation, upgrade to CRT-D, VT ablation, revascularization for acute coronary syndrome, or LV reconstructive surgery.

Statistical Analysis

Patients were divided into quartiles according to age of MI (i.e., time from index MI to ICD insertion). Nominally, these groups were described as very old for the quartile with the oldest MI age and recent for the quartile with the youngest MI age. Categorical data are summarized as frequencies and percentages and were compared using χ^2 or Fisher exact tests as appropriate. Continuous variables are presented as mean $\pm$ SD or median (interquartile range [IQR]) and were compared between groups using analysis of variance or Kruskal-Wallis tests for normally and non-normally distributed data, respectively. Post hoc testing for pairwise comparisons was performed with Bonferroni adjustment. The relationship between scar percentage and MI age was evaluated by generalized linear modeling. Because of the highly skewed distribution and wide variance relative to the mean of scar percentage, a negative binomial probability distribution was assumed.

For time-to-event (monomorphic VT) analysis, a competing-risks strategy was adopted. A competing risk is an event whose occurrence alters or precludes the occurrence of an event of interest (monomorphic VT). When competing risks are present, competing-risks regression is regarded as an appropriate approach to time-to-event analysis.^{15,16} In the present analysis, the following events occurring before the occurrence of the primary end point of monomorphic VT were treated as competing risks: ventricular fibrillation,

polymorphic VT, ICD upgrade, coronary revascularization, and LV reconstructive surgery.¹⁷⁻¹⁹ The covariates that were examined as potential predictors of monomorphic VT were chosen on the basis of clinical relevance or demonstrated prognostic value after MI. These covariates included.

- Clinical factors (age, gender, hypertension, diabetes mellitus, infarct territory, New York Heart Association functional class III or IV, creatinine clearance, ICD indication [secondary vs primary], revascularization of the infarct-related artery, and age of MI),
- QRS duration on electrocardiography,
- Conventional echocardiographic parameters (LV end-systolic volume index, left atrial volume index, and LVEF),
- Speckle-tracking echocardiographic parameters that formed the focus of the present study (GLS, LV scar burden, and LV dyssynchrony), and
- VT inducibility on PES.

Those covariates achieving p-values <0.20 at the univariate level were evaluated in a multivariate competing-risks analysis that was performed with backward elimination. Differences in the cumulative incidence of monomorphic VT between groups were assessed.²⁰

The incremental benefit of novel predictors of monomorphic VT was evaluated first by the Wald test comparing the model with the novel predictor and the model without the novel predictor. Second, the incremental value of novel risk predictors was evaluated using the integrated discrimination improvement index; a value significantly greater than zero is indicative of additive discriminatory value of the new risk predictor of interest.²¹

In 10 randomly selected individuals, echocardiographic strain measurements were repeated by a second investigator to determine interobserver variability. The interrater agreement for classification of scar was evaluated by the κ statistic and the interobserver variability for LV dyssynchrony and GLS by the intraclass correlation coefficient for a two-way random-effects model for consistency of agreement and by the absolute difference between observers divided by the mean of the repeated observations expressed as a percentage.

For all tests, a two-sided α value of 0.05 was adopted to determine statistical significance. Analysis was performed using Stata version 13.1 (StataCorp LP, College Station, TX).

RESULTS

Patient Characteristics

A total of 206 patients (median age 67 years; IQR 57–73 years; 180 [87%] men) meeting the inclusion criteria were studied. These comprised 171 ICD recipients (83%) and 35 CRT-D recipients (17%). The median MI age was 6.2 years (IQR 0.66–15 years). Patient characteristics are displayed as a function of age of MI in Table 1. Individuals with very old MIs (MI age in the highest quartile, >180 months prior) were of more advanced age ($p<0.001$), had worse renal function ($p=0.007$), and had longer QRS durations ($p<0.001$). They also had less frequent revascularization of the infarct-related artery ($p<0.001$), and the infarct-related artery more often subtended the inferoposterior LV segments ($p=0.03$) compared with those with more recent MIs. These patients more often received ICDs as secondary prevention ($p=0.002$).

Echocardiographic and Electrophysiologic Characteristics

Table 2 summarizes the echocardiographic and electrophysiologic characteristics of the patient population. Patients with very old MIs exhibited greater scar burden ($14.7 \pm 15.8\%$ vs. $10.7 \pm 11.4\%$, $p=0.03$) and more left atrial dilatation (36 mL/m^2 [IQR 27–50 mL/m^2] vs. 28 mL/m^2 [IQR 23–35 mL/m^2], $p=0.005$) compared with patients with recent MIs (MI age in the lowest quartile, <8 months). Patients with very old MIs showed a higher likelihood of VT inducibility compared with those with recent MIs (88% vs. 63%, $p=0.003$). To examine the possibility that the increase in scar burden with infarct age was related to the confounding effects of changing practice over time with regard to revascularization of the culprit artery, we also adjusted for revascularization status in the generalized linear model of infarct age. This adjusted analysis did not significantly affect the positive relationship between scar burden and infarct age (coefficient 0.15, 95% confidence interval [CI] 0.013–0.28, $p=0.03$). We undertook two post hoc sensitivity analyses in which a scarred segment was defined as one with $|\text{strain}| <4\%$ and $<5\%$, respectively. The adjusted coefficients for the relationship between scar burden and infarct age were 0.18 (95% CI 0.043 to 0.32, $p=0.01$) and 0.11 (95% CI –0.022 to 0.25, $p=0.10$), respectively.

Outcomes

The median follow-up time after ICD implantation was 24 months (IQR 7.8–47 months). In total, 75 individuals experienced the primary end point of monomorphic VT, and 18 patients had competing events. VT ablation was performed in six patients (3%) after ICD implantation: in four individuals, this occurred after a primary end point event, whereas in the remaining two, the date of ablation was treated as the study exit date. In a further eight patients, subsequent ICD upgrade to CRT-D resulted in study exit at the time of the upgrade. LV reconstructive surgery was performed in four individuals (2%) after ICD

Table 1. Patient characteristics

	Quartile 1 (<8 mo) (n=52)	Quartile 2 (8–75 mo) (n=52)	Quartile 3 (75–180 mo) (n=51)	Quartile 4 (>180 mo) (n=51)	p
Age (y)	63 (51–71)	62 (53–67)	68 (58–73)	74 (67–76)*,†,‡	<0.001
Men	47 (90%)	42 (81%)	43 (84%)	48 (94%)	0.20
Hypertension	25 (48%)	16 (31%)	17 (33%)	19 (37%)	0.30
Diabetes mellitus	13 (25%)	6 (12%)	8 (16%)	8 (16%)	0.30
Smoking					0.20
Never	20 (38%)	24 (46%)	19 (37%)	27 (53%)	
Previous	11 (21%)	18 (35%)	20 (39%)	15 (29%)	
Current	21 (41%)	10 (19%)	12 (24%)	9 (18%)	
Infarct territory					0.03
Inferior/posterior	17 (33%)	15 (29%)	16 (31%)	28 (55%)	
Anterior	35 (67%)	37 (71%)	35 (69%)	23 (45%)	
NYHA class					0.04
I or II	48 (92%)	37 (71%)	38 (75%)	40 (78%)	
III or IV	4 (8%)	15 (29%)	13 (25%)	11 (22%)	
Secondary prevention ICD	34 (65%)	21 (40%)	29 (57%)	39 (76%)	0.002
Revascularized infarct-related artery	21 (40%)	24 (46%)	14 (27%)	1 (2%)	<0.001
AF/atrial flutter	5 (10%)	13 (25%)	13 (25%)	11 (22%)	0.10
Creatinine clearance (mL/min)	78 (56–103)	74 (58–98)	75 (59–94)	62 (48–77)*,†,‡	0.007
QRS duration (msec)	107 ± 26	109 ± 23	130 ± 26	138 ± 35*,†	<0.001

AF = atrial fibrillation; ICD = implantable cardioverter-defibrillator; NYHA = New York Heart Association.

Data are expressed as median (IQR), number (percentage), or mean ± SD. The threshold p-value for pairwise comparisons between groups was $p < 0.004$, by Bonferroni adjustment.

* $p < 0.004$ compared with quartile 1.

† $p < 0.004$ compared with quartile 2.

‡ $p < 0.004$ compared with quartile 3.

Table 2. Echocardiographic and electrophysiologic characteristics

	Quartile 1 (<8 mo) (n=52)	Quartile 2 (8–75 mo) (n=52)	Quartile 3 (75–180 mo) (n=51)	Quartile 4 (>180 mo) (n=51)	p
LVESVI (mL/m ²)	41 (33 to 52)	49 (34 to 66)	49 (33 to 64)	47 (35 to 65)	0.20
LVEDVI (mL/m ²)	69 (57 to 85)	80 (65 to 97)	79 (59 to 100)	77 (56 to 97)	0.30
LAVI (mL/m ²)	28 (23 to 35)	27 (21 to 37)	32 (22 to 40)	36 (27 to 50)*, †	0.005
Moderate/severe MR	1 (2%)	5 (10%)	4 (9%)	6 (12%)	0.20
LVEF (%)	41 ± 9.9	40 ± 13	38 ± 11	36 ± 8.2	0.10
GLS (%)	10.9 (9.81 to 14.3)	12.8 (10.4 to 14.9)	–10.1 (8.25 to 13.6)	–11.7 (8.58 to 13.4)	0.10
LV percentage scar (%)	10.7 ± 11.4	12.1 ± 15.1	13.1 ± 12.9	14.7 ± 15.8*	0.03
Patients with ≥1 dyskinetic myocardial segment	7 (13%)	12 (23%)	11 (25%)	10 (20%)	0.60
LV dyssynchrony (msec)	82 ± 29	81 ± 34	97 ± 40	91 ± 43	0.09
VT inducible	33 (63%)	30 (58%)	36 (71%)	45 (88%)	0.003
VF/PVT inducible	8 (15%)	18 (35%)	8 (16%)	4 (8%)	0.006

GLS = global longitudinal strain; LAVI = left atrial volume index; LV = left ventricular; LVEDVI = left ventricular end-diastolic volume index; LVEF = left ventricular ejection fraction; LVESVI = left ventricular end-systolic volume index; MR = mitral regurgitation; PVT = polymorphic ventricular tachycardia; VF = ventricular fibrillation; VT = ventricular tachycardia.

Data are expressed as median (IQR), number (percentage), or mean ± SD.

* p<0.004 compared with quartile 1.

† p<0.004 compared with quartile 2.

implantation: in two cases, this occurred after a primary end point event, whereas in the other two, the date of surgery was used as the study exit date.

Time-to-Monomorphic VT Analysis

Table 3 contains the competing-risks regression for predictors of time to monomorphic VT. Those factors achieving univariate p-values <0.20 included age, creatinine clearance, QRS duration, revascularization of the infarct-related artery, age of MI, LV end-systolic volume index, LVEF, GLS, LV scar burden, LV dyssynchrony, and VT inducibility on PES. On multivariate analysis, nonrevascularization of the infarct-related artery (p=0.02), longer QRS duration (p=0.001), greater LV dyssynchrony (p<0.001), and lower GLS (p=0.02) were independently associated with later development of VT. Each 10-msec increment in LV dyssynchrony was associated with a 12% increase in the risk for monomorphic VT. In addition, the evaluation of LV dyssynchrony conferred incremental predictive value to an infarct-related artery nonrevascularization, QRS duration, and GLS, as demonstrated by the Wald test ($\chi^2 = 17$, p=0.001) and an integrated discrimination improvement index of 0.027

($p=0.001$). These indicate that the measurement of LV dyssynchrony in addition to PES provided superior prediction of subsequent VT.

The cohort was dichotomized on the basis of the median value of LV dyssynchrony into those exhibiting LV dyssynchrony ≤ 90 and >90 msec. Those with LV dyssynchrony >90 msec had a significantly greater incidence of monomorphic VT compared with those with less LV dyssynchrony ($p<0.001$) (Figure 2).

Table 3. Multiple competing-risks regression for the occurrence of VT

	Univariate		Multivariate	
	SHR (95% CI)	p	SHR (95% CI)	p
Age	1.02 (1.00–1.05)	0.03	0.995 (0.963–1.03)	0.90
Female gender	0.83 (0.43–1.6)	0.60		
Hypertension	0.81 (0.50–1.3)	0.40		
Diabetes mellitus	1.0 (0.58–1.9)	0.90		
NYHA class III or IV	1.1 (0.63–1.9)	0.70		
Creatinine clearance	0.988 (0.981–0.996)	0.002	0.998 (0.989–1.00)	0.70
QRS duration	1.012 (1.006–1.019)	<0.001	1.011 (1.004–1.019)	0.001
Anterior infarct-related territory	0.94 (0.59–1.5)	0.80		
Secondary prevention ICD	1.4 (0.86–2.4)	0.20		
Revascularized infarct-related artery	0.42 (0.23–0.79)	0.007	0.49 (0.26–0.91)	0.02
Time from index MI	1.002 (1.001–1.004)	0.005	0.9999 (0.9971–1.003)	1.00
LVESVI	1.007 (1.000–1.013)	0.05	0.9920 (0.9843–0.9998)	0.05
LAVI	1.00 (0.989–1.02)	0.70		
LVEF	0.97 (0.95–0.99)	0.008	0.99 (0.96–1.0)	0.60
GLS, % reduction in magnitude	1.08 (1.02–1.15)	0.01	1.08 (1.02–1.16)	0.02
LV percentage scar	1.03 (1.01–1.04)	0.001	0.997 (0.969–1.03)	0.80
LV dyssynchrony, 10-msec increase	1.14 (1.09–1.19)	<0.001	1.12 (1.06–1.18)	<0.001
VT inducible	2.9 (1.6–5.5)	0.001	1.8 (0.90–3.5)	0.10

GLS = global longitudinal strain; ICD = implantable cardioverter-defibrillator; LAVI = left atrial volume index; LV = left ventricular; LVEF = left ventricular ejection fraction; LVESVI = left ventricular end-systolic volume index; MI = myocardial infarction; NYHA = New York Heart Association; SHR = subdistribution hazard ratio; VT = ventricular tachycardia.

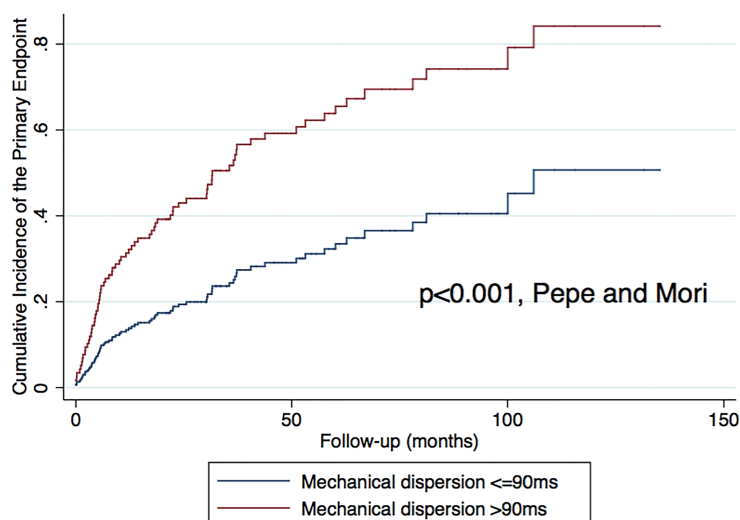


Figure 2. LV dyssynchrony and VT risk. Cumulative incidence of the primary end point of monomorphic VT that required ICD therapy, as a function of LV dyssynchrony. The p-value was obtained by the approach of Pepe and Mori.²⁰ ICD = implantable cardioverter-defibrillator; LV = left ventricular; VT = ventricular tachycardia.

Interobserver Variability

For segmental scar classification, the κ statistic for interrater agreement was 0.72, indicating substantial concordance between observers. For GLS measurement, the average intraclass correlation coefficient was 0.94 (95% CI 0.74–0.98), while for LV dyssynchrony, it was 0.96 (95% CI 0.84–0.99). The difference between observers expressed as a percentage of the mean of their measurements was 0.022% for GLS and 4.5% for LV dyssynchrony.

DISCUSSION

The main findings of this study are that (1) greater LV dyssynchrony is associated with an increased risk for monomorphic VT, independent of MI age and revascularization of the infarct-related vessel, and (2) older MI is associated with greater LV scar burden than more recent infarction, independent of whether the culprit artery was revascularized.

Myocardial Infarction Age, Myocardial Scar, and VT

LV remodeling after MI is a complex time-related process involving ultrastructural and histologic myocardial changes that may be reflected in macroscopic alterations in LV geometry and function.^{22–24} Specifically, edema and inflammation early after MI are superseded by collagen deposition and myocardial scar formation late after MI.²³ This process of scar formation in the infarct zone, as well as myocardial collagen deposition in remote areas, continues months to years after the index MI.²³ This evolution is manifest by LV dilatation and dysfunction.^{25–27} However, there is scant evidence on very late scar

progression after MI. In the present study, a trend toward worse LV systolic function was indeed observed in advancing quartiles of MI age. In fact, a more marked and significant increase in LV scar burden was demonstrated in advancing quartiles of MI age. This was accompanied by increasing left atrial volume with increasing MI age, a finding that provides some face validity to our observation of increasing LV scar with MI age. These findings add to the existing research by characterization of myocardial substrate very late after MI.

VT, an important cause of SCD after MI, has been associated with an increased scar burden on electroanatomic mapping⁶ and using late gadolinium enhanced cardiac magnetic resonance imaging.²⁸ Data from the Multicenter Automatic Defibrillator Implantation Trial II study showed a direct association between mortality risk and increasing time from MI; the presence of extensive scar after MI (as reflected by an LVEF $\leq 30\%$) was an independent determinant of lethal ventricular arrhythmias.⁴ The present study has delivered consistent findings by demonstrating that at the univariate level, scar burden by speckle-tracking echocardiography is associated with the risk for monomorphic VT. However, myocardial scar burden is only one of the characteristics of the arrhythmogenic substrate. Other factors, such as how scar influences electrical impulse propagation and electromechanical coupling, may be important in the development of reentrant VT.

LV Dyssynchrony and VT

Collagen deposition and remodeling occur after MI principally in the infarcted zone but also in the peri-infarct and remote regions. The slowed and heterogeneous electrical impulse propagation associated with scar tissue favors the development of clinical VT by permitting reentry. In the present evaluation, we hypothesized that the mechanical consequences of MI might be related to the subsequent risk for VT. LV dyssynchrony was measured using speckle-tracking strain echocardiography as an index of the heterogeneity of timing of segmental myocardial contraction. The potential slowing of global LV electromechanical coupling, which could result from both scar in the infarct zone and collagen deposition in the peri-infarct and remote zones, would result in less coordinated LV contraction and a higher LV dyssynchrony index. We found that greater LV dyssynchrony was associated with an elevated risk for subsequent VT. There are several possible explanations for this finding. First, LV dyssynchrony may promote ongoing ventricular remodeling, particularly in the infarct or peri-infarct zones that form the LV substrate for VT. Second, LV dyssynchrony may also be an indicator of scar and the functional consequences of scar that promote VT.

There is growing recognition of the importance of myocardial substrate characteristics in the pathogenesis of VT after MI.²⁹ This may be particularly true for monomorphic VT, which, in contrast to polymorphic VT and ventricular fibrillation, is mediated by fixed scar and heterogeneous scar conduction.⁶ In the present study, although LV scar burden was associated with the occurrence of VT during follow-up, LV dyssynchrony was independently associated with VT. Thus, LV dyssynchrony as a marker of

the heterogeneity of LV activation seems able to characterize the substrate that predisposes to VT.

The results of the present evaluation are consistent with those of a previous study showing that LV dyssynchrony was greater in post-MI patients with recurrent VT.⁹ The present study also demonstrates that LV dyssynchrony provides complementary information to QRS duration in the identification of patients who will experience recurrent VT. Both QRS duration and wider LV dyssynchrony, in addition to nonrevascularization of the infarct-related artery and GLS, were shown in the present study to be independently associated with the risk for subsequent VT.

Limitations

Echocardiography was performed at a single time point, so the temporal evolution of LV remodeling is inferred rather than proved by serial measurements in each individual. This research was undertaken at a tertiary center among patients referred for electrophysiologic assessment and consideration for ICD placement. Referral bias is therefore likely, which may have implications for the generalizability of the study findings. Our findings must be externally validated to confirm their clinical importance.

CONCLUSIONS

LV dyssynchrony, which results from myocardial scar tissue interspersed with viable myocytes, is independently associated with the subsequent occurrence of VT. Older MI exhibits greater scar burden, and more LV dyssynchrony independently of whether the culprit artery was revascularized or not. These observations may help understanding of the survival benefit seen with ICD implantation later after MI, compared with earlier.

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