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Clinical Utility of Longitudinal Strain to Predict Functional Recovery in Patients With Tachyarrhythmia and Reduced LVEF

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ABSTRACT

OBJECTIVES This study sought to assess the time course of presumptive tachycardia-induced cardiomyopathy and the predictors of left ventricular (LV) functional recovery in such patients.

BACKGROUND Tachycardia-induced cardiomyopathy is a potentially reversible cardiomyopathy with effective treatment of the tachyarrhythmia. However, cases without improvement of LV systolic function were found occasionally. The diagnosis of tachycardia-induced cardiomyopathy can be challenging, and the role of echocardiographic imaging in the prediction of LV functional recovery is limited.

METHODS LV segmental longitudinal strains (LS) were evaluated by 2-dimensional speckle tracking in 71 consecutive patients (65 ± 16 years; 61% men) with tachyarrhythmia and reduced left ventricular ejection fraction (LVEF) without any other known cardiovascular disease, and 30 age and sex-matched control subjects. Relative apical LS ratio (RALSR) was defined using the equation: average apical LS / (average basal LS + average mid LS) as a marker of strain distribution.

RESULTS Compared with control subjects, patients with tachyarrhythmia had significantly lower global LS. Improvement in LVEF within 6 months after treatment of index arrhythmia was observed in 41 patients, and LVEF did not improve in 30 patients. In univariate analysis, lower LVEF at baseline (hazard ratio: 0.59 per 1 SD; $p = 0.04$) and higher RALSR (hazard ratio: 11.2 per 1 SD; $p < 0.001$) were associated with no recovery in LVEF during follow-up. In a multivariate logistic regression model, the significant predictor of LV systolic functional recovery was RALSR (hazard ratio: 22.9 per 1 SD; $p = 0.001$). A RALSR of 0.61 was sensitive (71%) and specific (90%) in differentiating LV systolic functional recovery (area under the curve: 0.88).

CONCLUSIONS The RALSR was associated with LV systolic functional recovery. This information might be useful for clinical evaluation and follow-up in patients with reduced LVEF. (J Am Coll Cardiol Img 2017;10:118–26)

Long-standing tachycardia is a well-known cause of left ventricular (LV) dysfunction and heart failure. This type of LV dysfunction is called tachycardia-induced cardiomyopathy (TIC) (1). TIC is an acquired, potentially reversible form of cardiomyopathy characterized by atrial and/or ventricular myocardial dysfunction resulting from increased atrial and/or ventricular rate (2–5). The diagnosis is

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usually made after demonstrating recovery of LV function with treatment of arrhythmia in the absence of other identifiable etiologies (6). However, cases without improvement of LV systolic function were found occasionally in the clinical setting. The incidence of TIC is not well characterized, but it is estimated that approximately 50% of patients in tachyarrhythmia have impairment of LV systolic function (7). Some previous studies showed that risk factors for the development of TIC were older age and higher premature ventricular contraction (PVC) burden compared with control subjects (8). A better understanding of the mechanism and improved recognition of its presence can be clinically relevant to the prognosis of patients with tachyarrhythmia.

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Quantitation of myocardial deformation is an emerging field of clinical cardiac imaging. In addition, recent clinical work using speckle tracking imaging shows that there are significant differences in regional strain in several cardiomyopathies, even in the absence of ischemia. Knowledge of the characteristic LV strain distribution pattern facilitates diagnosis for constrictive pericarditis, cardiac amyloidosis, hypertrophic cardiomyopathy, and hypertensive heart disease (9–13). Characteristic of strain distribution may help in the differential diagnosis of individual patients. In our previous study, longitudinal strain (LS) slightly increased from base to apex in control subjects. In contrast, decreased LS was more profound in the apex in animal models of rapid pacing-induced cardiomyopathy (14). Thus, this "reverse" distribution of LV strain may help to understand LV dysfunction in the presence of tachyarrhythmia.

The aim of this study was to investigate incidence, time course, and echocardiographic predictors of functional recovery in LV systolic function in a prospective and consecutive group of patients with reduced left ventricular ejection fraction (LVEF) and tachyarrhythmia.

METHODS

STUDY POPULATION. We designed a prospective study to assess the LV functional recovery in patients with tachyarrhythmia. A total of 304 consecutive patients having supraventricular/ventricular tachyarrhythmia were referred to our echocardiographic examination center between January 2013 and February 2016. Reasons for referral included tachyarrhythmia (heart rate >100 beats/min) noted on resting 12-lead electrocardiogram, telemetry monitoring, or 24-h Holter monitor. Patients were excluded because of the following criteria: preserved LVEF (>50%; n = 160), incomplete echocardiographic follow-up (n = 55), coronary artery disease (≥70% stenosis of any major epicardial vessel; n = 18), hypertension (n = 12), diabetes mellitus (n = 4), hypertrophic cardiomyopathy (n = 3), moderate or severe valvular disease (n = 2), end-stage renal disease (n = 4), and stress-induced cardiomyopathy (n = 5). There were no patients with New York Heart Association functional class III or IV symptoms. After exclusions, 71 patients remained for final analysis who had LVEF ≤50% and who were diagnosed as presumptive TIC (Figure 1). Thirty age- and sex-matched control patients were selected from our healthy volunteer database based on a comprehensive history and physical examination. The Institutional Review Board of the Tokushima University Hospital approved the study protocol and written informed consent was obtained from all subjects.

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

EF = ejection fraction

GLS = global longitudinal strain

LGE = late gadolinium enhancement

LS = longitudinal strain

LV = left ventricular

PVC = premature ventricular contraction

RALSR = relative apical longitudinal strain ratio

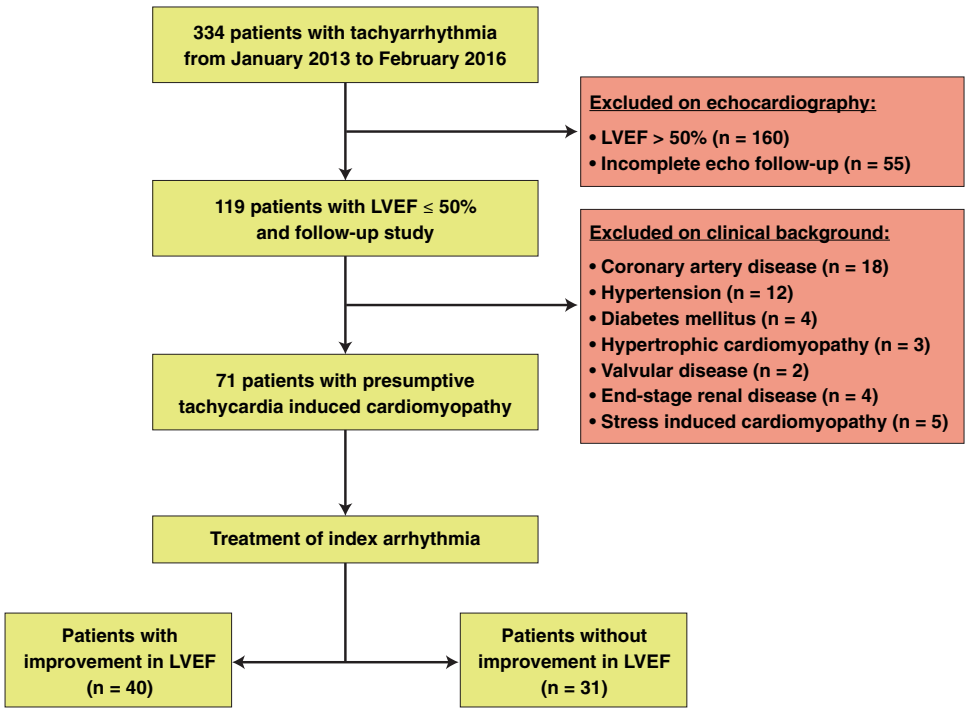
TIC = tachycardia-induced cardiomyopathy

TR-PG = tricuspid regurgitant pressure gradient

DATA ACQUISITION. A detailed medical history was obtained in all patients. Every patient had 12-lead electrocardiogram during his or her index clinical arrhythmia. Twenty-four-hour Holter monitoring was performed to evaluate the frequency of arrhythmia (arrhythmia burden: the ratio of total number of premature atrial/ventricular contractions to total heartbeat). Patients were classified into 3 groups according to the index arrhythmia: 1) atrial fibrillation; 2) paroxysmal supraventricular tachycardia including atrioventricular re-entry tachycardia and AV nodal re-entry tachycardia; and 3) monomorphic PVCs or nonsustained ventricular tachycardia. In patients undergoing initiation of medical antiarrhythmic therapy or cardiac catheter ablation, echocardiographic measurements were repeated within 6 months of index clinical arrhythmia. The primary endpoint was LV functional recovery during follow-up, defined as improvement of LVEF ≥15% or improvement of LVEF ≥10% to more than 50% after effective treatment of index clinical arrhythmia (6).

STANDARD ECHOCARDIOGRAPHIC ASSESSMENT. Transthoracic echocardiography was performed by experienced sonographers/doctors using a commercially available ultrasound machine (iE33, Philips Healthcare, Amsterdam, the Netherlands; Vivid E9, GE Healthcare, Waukesha, Wisconsin; and SSA-770A, Toshiba Medical, Otawara, Japan). Measurements and recordings were obtained according to the American Society of Echocardiography recommendations (15). LV end-diastolic volume, LV end-systolic volume, left atrial volume, and LVEF were

FIGURE 1 Patient Selection



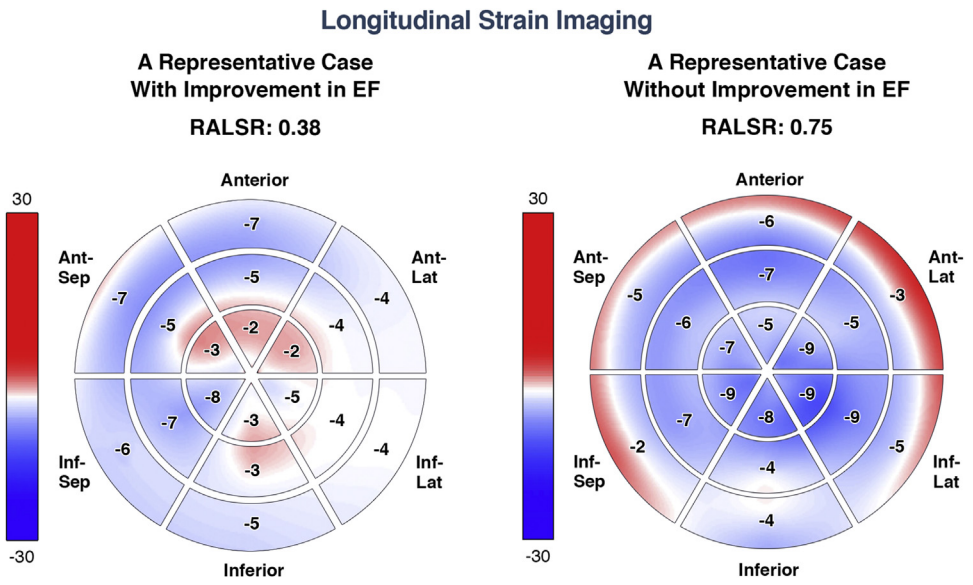
LVEF = left ventricular ejection fraction.

calculated by the biplane method of disks using 2-dimensional images and indexed to body surface area. The early diastolic (e′) mitral annular tissue velocity was also measured in the apical 4-chamber view with the sample volume positioned at the lateral mitral annulus. The systolic transtricuspid pressure gradient (PG) was calculated by the modified Bernoulli equation using maximal continuous-wave Doppler velocity of the tricuspid regurgitant (TR) jet. Tricuspid annular plane systolic excursion was measured as the distance of systolic movement of the junction between the tricuspid valve and the RV free wall using M-mode in accordance with current guidelines (16).

2-DIMENSIONAL STRAIN ECHOCARDIOGRAPHY. Peak systolic LS measurements were obtained from gray-scale images recorded in the apical 4-chamber, 2-chamber, and long-axis views. The frame rate was maintained at a level >50 frame/s. LV strain was analyzed offline using speckle tracking software (EchoInsight, Epsilon Imaging, Ann Arbor, Michigan). Good image quality was defined as clear detection of the endocardial border throughout the cardiac cycle, and regions of interest at the apex and annulus were ensured. After manual definition of the LV endocardial border, the endocardium was automatically tracked throughout the cardiac cycle. The software algorithm automatically divided the LV apical view into 6 segments for speckle tracking throughout the cardiac cycle. Global longitudinal strain (GLS) was obtained by averaging all segmental strain values from the apical 4-chamber, 2-chamber, and long-axis views. Strain values for the 6 basal, 6 mid, and 6 apical segments of the LV were averaged to obtain regional LS values (basal, mid, and apical, respectively) (14,17). Relative apical longitudinal strain ratio (RALSR) was calculated by dividing the apical LS by the sum of the basal and mid-LS values (**Figure 2**) (11). These offline analyses were independently performed in a blinded manner by 2 observers who were not involved in the image acquisition and had no knowledge of examination dates and other echocardiographic or clinical data.

STATISTICAL ANALYSIS. Data are presented as mean ± SD. Normality was assessed using the Kolmogorov-Smirnov test. One-way general linear model analysis of variance, followed by Dunnett T3 post hoc test analysis, was used to assess the

FIGURE 2 **Representative Recordings of Longitudinal Strain Imaging in Patients With and Without Improvement in LVEF During Follow-Up**



RALSR = relative apical longitudinal strain ratio; other abbreviation as in Figure 1.

difference between parameters in patients with improvement versus without improvement in EF. Logistic regression analysis was used to evaluate the associations between several potential variables and improvement in EF. Identified variables ($p < 0.20$ in the univariate model) were considered to enter in a stepwise manner into a multivariate logistic regression model. We checked for collinearity among predictors by using Pearson correlation coefficients, and no evidence had been found for collinearity problems in our model (variance inflation factor values <2). Receiver-operating characteristic curve analysis was used to identify parameters that were best to diagnose improvement in EF. The best cutoff value was based on the maximum Youden index. The method of DeLong was used to compare the C statistic (18). To assess the changes of LVEF before and after treatment of index arrhythmia, we applied a linear mixed effects model with unstructured covariance for random effects using standard statistical software (SPSS software 20.0; SPSS Inc., Chicago, Illinois). We used patient groups as factors, time after initial echocardiographic assessment as a covariate, and their first-degree interactions (time × groups) with the significance of the corresponding parameter estimates reported in the results. Reproducibility was expressed as the mean percentage error (absolute difference divided by the average of the 2 observations). Measurement was performed in 20 randomly selected subjects by 1 observer and then repeated on 2 separate days by 2 observers who were unaware of the measurements of the others and of the study time point. The intraobserver and interobserver variability of the LS was 7.4 ± 4.2% and 9.1 ± 5.3%.

RESULTS

PATIENT CHARACTERISTICS AND TREATMENT OF TACHYARRHYTHMIA. Baseline characteristics of the study group are presented in Table 1. The study population consisted of 71 patients (65 ± 16 years; 61% men) with LVEF of 50% or less and diagnosed as presumptive TIC and 30 control subjects. Compared with control subjects, patients with tachyarrhythmia had significantly lower GLS. Presenting symptoms were palpitation in 30 patients (42%), syncope in 4 patients (6%), shortness of breath in 12 patients (17%), and no symptoms in 25 patients (35%). Atrial fibrillation was the most common underlying the index arrhythmia (n = 43; 61%), followed by paroxysmal supraventricular tachycardia (n = 15; 20%) and PVCs/ventricular tachycardia (n = 13; 10%). There was no association of symptoms/type of tachyarrhythmia with the primary endpoint in this cohort.

Effective treatment of index tachyarrhythmia was achieved in all patients with presumptive TIC with

TABLE 1 Clinical Characteristics

	Control Subjects (n = 30)	Patients With Improvement in EF (n = 40)	Patients Without Improvement in EF (n = 31)	p Value
Age, yrs	62 ± 5	64 ± 16	67 ± 14	0.53
Male	17 (57)	23 (58)	20 (64)	0.55
Body surface area, m^2	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	0.70
Heart rate, beats/min	62 ± 7	101 ± 20*	103 ± 21*	0.39
Systolic blood pressure, mm Hg	121 ± 12	122 ± 19	119 ± 26	0.57
Diastolic blood pressure, mm Hg	72 ± 10	75 ± 13	78 ± 15	0.31
Holter monitoring				
Total heartbeat/day	–	122,909 ± 13,999	129,256 ± 22,119	0.14
Total number of arrhythmia	–	16,532 ± 8,134	22,174 ± 14,212	0.04
Arrhythmia burden	–	14 ± 7	17 ± 12	0.09
Atrial fibrillation	–	23 (58)	20 (65)	0.55
Echocardiographic variables				
LVEDVi, ml	49 ± 15	66 ± 19*	81 ± 27*	0.008
LVESVi, ml	19 ± 7	40 ± 15*	53 ± 21*	0.004
LVEF, %	61 ± 6	40 ± 8*	35 ± 10*	0.04
LAVi, ml/m^2	20 ± 5	38 ± 25*	40 ± 22*	0.82
LVMi, g/m^2	92 ± 19	93 ± 28	112 ± 36*	0.02
TMF-E, cm/s	64 ± 11	71 ± 24	84 ± 19*	0.02
TMF-DT, ms	228 ± 23	172 ± 58*	142 ± 42*	0.03
e', cm/s	8.5 ± 1.4	8.9 ± 3.1	8.7 ± 4.2	0.83
E/e'	7.7 ± 1.7	8.5 ± 2.9	11.1 ± 5.2*	0.008
TR-PG, mm Hg	–	21 ± 6	29 ± 9	<0.001
TAPSE, mm	22 ± 2	17 ± 4	17 ± 4	0.77
LS, %				
Basal	-20 ± 1	-11 ± 3*	-9 ± 3*	0.005
Mid	-20 ± 1	-10 ± 3*	-8 ± 3*	0.001
Apical	-21 ± 1	-9 ± 3*	-11 ± 4*	0.06
Global	-21 ± 1	-10 ± 3*	-9 ± 3*	0.15
RALSR	0.51 ± 0.04	0.45 ± 0.11*	0.69 ± 0.16*	<0.001

Values are mean ± SD or n (%). *Versus control, p < 0.05.

DT = deceleration time; E = early diastolic transmitral flow velocity; e' = early diastolic mitral annular motion; EF = ejection fraction; LAVi = left atrial volume index; LS = longitudinal strain; LVEDV = left ventricular end-diastolic volume; LVEDVi = left ventricular end-diastolic volume index; LVEF = left ventricular ejection fraction; LVESVi = left ventricular end-systolic volume index; LVMi = left ventricular mass index; LVSDV = left ventricular end-systolic volume; RALSR = relative apical longitudinal strain ratio; TAPSE = tricuspid annular plane systolic excursion; TMF = transmitral flow; TR-PG = tricuspid regurgitant pressure gradient.

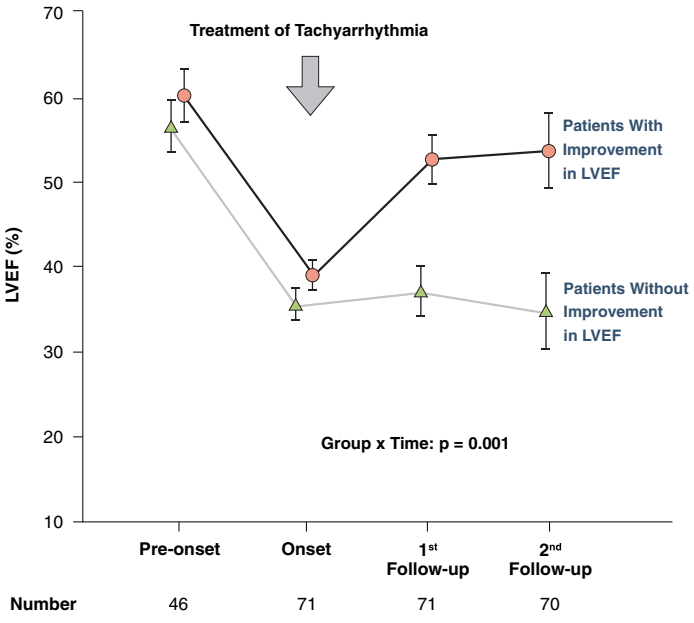
either antiarrhythmic drugs or catheter ablation. Twenty-seven patients underwent electrophysiological study and catheter ablation. Effective treatment of index tachyarrhythmia was achieved with drugs in 44 patients: bisoprolol in 16 patients, carvedilol in 10, amiodarone in 8, and verapamil in 10. Elimination of index tachyarrhythmia was achieved in 23 of 27 (85%) patients treated with radiofrequency ablation and 30 of 44 (68%) patients treated with antiarrhythmic drugs. Followed Holter recordings were available in 59 patients (83%). After the treatment of index tachyarrhythmia, averaged total heartbeats were decreased in both groups with and without improvement in LVEF (from 122,909 ± 13,999 to 102,418 ± 15,068 and from 129,256 ± 22,119 to 109,767 ± 14,012; both p < 0.001). Averaged arrhythmia burdens were also decreased in both groups (from 13.6 ± 6.9 to 1.5 ± 1.9 and from 17.5 ± 11.8 to 2.5 ± 2.9; both p < 0.001). There were no statistical differences of total heartbeats and arrhythmia burdens between groups with and without improvement in LVEF.

PREDICTION OF IMPROVEMENT IN EF. Improvement in LVEF within 6 months of treatment of index tachyarrhythmia was observed in 40 of 71 patients (64 ± 16 years; 58% men). LVEF did not improve in 31 of 71 patients (67 ± 14 years; 64% men). They remained unchanged at 6-month follow-up and were considered to be suffering from another cause of cardiomyopathy. Pre-onset echocardiographic data showed that LV function was preserved before the onset of LV dysfunction in both groups (n = 46). In patients with improved LVEF, the average LVEF improved from 39 ± 8% to 53 ± 12% after treatment of the index tachyarrhythmia. In patients without improvement in LVEF, average LVEF remained unchanged from 35 ± 10% to 36 ± 9% after treatment of the index ventricular arrhythmia (Figure 3). In patients with improvement in LVEF, GLS and RALSR increased from −10 ± 3% to −14 ± 3% and from 0.45 ± 0.10 to 0.59 ± 0.07 after treatment of the index tachyarrhythmia (both p < 0.001). In contrast, GLS and RALSR remained unchanged from −9 ± 3% to −10 ± 3% (p = 0.46) and from 0.69 ± 0.16 to 0.67 ± 0.12 (p = 0.68) in patients without improvement in LVEF (Figure 4). Patients without improvement in LVEF had significantly enlarged LV size, reduced LVEF, increased E/e', and elevated TR-PG at baseline (all p < 0.05) (Table 1). In 2-dimensional speckle tracking echocardiography, patients without improvement in LVEF had significantly lower basal LS, lower mid-LS, and higher RALSR than the remainder (all p < 0.01).

To determine the predictors of recovery in LVEF, we performed univariate and multivariate analysis of association between baseline clinical and echocardiographic variables and recovery in LVEF during follow-up. In the univariate model, recovery in LVEF was correlated with LV size, LVEF, E/e', TR-PG, basal LS, mid LS, and RALSR (Table 2). In the stepwise multivariate logistic regression model, recovery in LVEF was correlated with TR-PG (hazard ratio: 5.3; 95% confidence interval: 1.67 to 16.6; p = 0.005) and RALSR (hazard ratio: 22.9; 95% confidence interval: 3.40 to 153.76; p = 0.001) (Table 2). Results of the receiver operating characteristic curve

analysis used to identify the optimal cutoff point for predicting the improvement in LVEF during follow-up are shown in **Figure 5**. A RALSR of 0.61 was sensitive (71%) and specific (90%) in predicting LV systolic functional recovery. This RALSR had the highest area under the curve (0.88; $p < 0.001$) among echocardiographic variables. In a subgroup with successful catheter ablation ($n = 23$), a RALSR of 0.58 was also sensitive (93%) and specific (75%) in predicting LV systolic functional recovery with the high area under the curve (0.89; $p < 0.001$) (Online Table 1).

FIGURE 3 Follow-Up Data for LVEF



Error bars show 1 standard error of the mean. Abbreviation as in **Figure 1**.

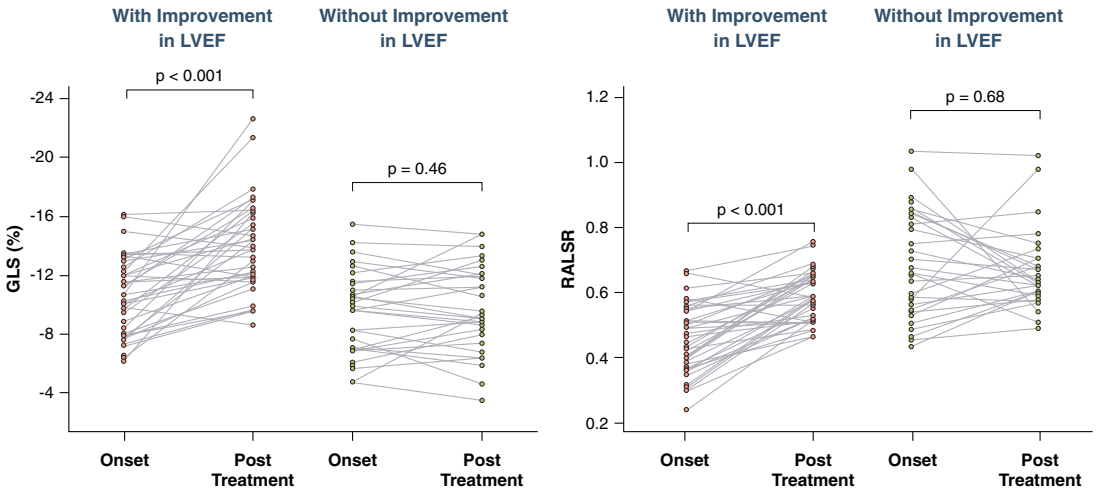
DISCUSSION

Our study sought to determine the prevalence and predictors of improvement in LVEF in patients with tachyarrhythmia and reduced LVEF using echocardiography including speckle tracking imaging. Our study brings several new insights into the understanding of improvement in LVEF in patients with tachyarrhythmia: 1) no recovery in LVEF occurred in about 42% of patients with presumptive TIC; 2) LV size, LVEF, E/e′, and TR-PG at baseline predicted improvement of LVEF; and 3) strain distribution (e.g., RALSR) was the most powerful independent predictor of improvement of LVEF during follow-up. The decrease of strain was more profound in the apex in patients with improvement in LVEF. Interestingly, the relatively preserved apical strain was shown in patients without improvement in LVEF. This information might be useful for clinical evaluation and follow-up in patients with reduced LVEF before the treatment of index arrhythmia (e.g., catheter ablation).

PREDICTORS OF RECOVERY IN LVEF. The incidence of TIC has been described as ranging from 10% to 50% in patients with atrial/ventricular tachyarrhythmia (4,19,20). In PVCs, risk factors for the development of TIC were reported to be older age and higher PVC burden compared with control subjects (8). In atrial tachycardia, younger patients, males, those with slower heart rate, and incessant tachyarrhythmia are more likely to have reduced LVEF in tachyarrhythmia (4). In our cohort, there was no association of arrhythmia type with incidence of LV functional recovery. There are some controversial findings in the literature in regards to the recovery of LVEF. Classically, the diagnosis of TIC is made after demonstrating recovery of LV function with treatment of arrhythmia. Despite strict exclusion criteria of other cardiomyopathy causes, LVEF recovery occurred in only 55% of patients with presumptive TIC in our cohort. This finding emphasized the importance of follow-up echocardiography, because some cases do not recover LVEF in patients with presumptive TIC.

Our study also demonstrated the prognostic power of LV size, LVEF, E/e′, and TR-PG at baseline. The results of this study are consistent with the previous basic work demonstrating the mechanism of TIC. In animal models of pacing-induced HF, sustained atrial or ventricular pacing produced severe biventricular systolic dysfunction (21-23). This is characterized by increased ventricular filling pressures, decreased cardiac output, and increased systemic vascular resistance. In the no functional recovery group, LV systolic dysfunction (e.g., LV size and LVEF) and diastolic function (e.g., E/e′ and TR-PG) frequently occurred compared with the recovery group. There were several pathophysiological mechanisms in TIC, such as diastolic interval change, myocardial blood flow, neurohormonal changes, and oxidative stress (6). Traditionally, it has been believed that functional recovery usually occurred in TIC. Thus, our data suggest that there is some occult LV dysfunction in tachyarrhythmia in the clinical setting.

FIGURE 4 Comparison of GLS and RALSR in Patients With and Without Improvement in LVEF



GLS = global longitudinal strain; other abbreviations as in Figures 1 and 2.

MECHANICS OF TIC. The clinical utility of advanced echocardiographic imaging, such as 2-dimensional speckle tracking, has been supported by numerous studies. In recent years, a number of literature citations showed that the assessment of strain distribution has emerged as an aid in the diagnosis of several causes of cardiomyopathy with nonischemic etiology (9–13). In an animal study, the decrease of LS was more profound in the apex in rapid pacing animal models (14). In our cohort, the patients with recovery in LVEF had a "reverse" distribution similar to the previous works. A possible explanation could be that basal and mid-ventricular levels were protected from stress increases and subsequent remodeling by the mitral annulus and papillary muscles in patients with tachyarrhythmia.

Interestingly, apical strain was relatively preserved in patients without recovery in LVEF. Previous papers described that LS in the basal and mid-segments of the LV is more severely impaired compared with the strain values in the apical segments in patient with infiltrative cardiomyopathies and with a systemic disease (e.g., amyloidosis) (11,24). A potential pathophysiological mechanism of apical sparing may be heterogeneous myocardial deposition. In addition, 1 previous study showed that the myocardial scar burden was associated with impaired recovery in LVEF in patients with PVCs or ventricular tachycardia (25). Apical sparing may be a marker of occult myocardial impairment in patients with tachyarrhythmia.

CLINICAL IMPLICATIONS. To the best of our knowledge, this is the first report of strain distribution and may help differentiate that type of cardiomyopathy from other possible causes of decreased

TABLE 2 Associations of Improvement in EF

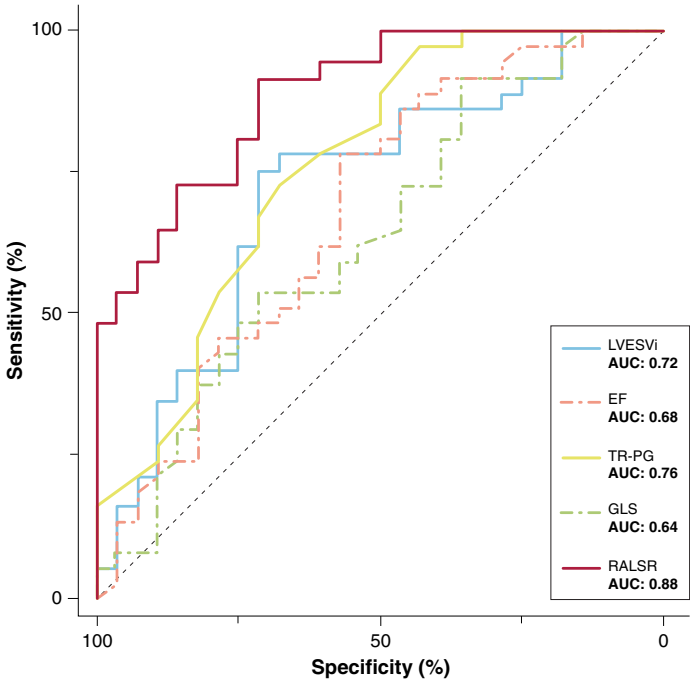
	Univariate Logistic Regression Analysis			Stepwise Multivariate Logistic Regression Analysis		
	Hazard Ratio	95% CI	p Value	Hazard Ratio	95% CI	p Value
Age, yrs	1.01	0.98–1.04	0.52			
Male	1.34	0.51–3.53	0.55			
Total heartbeat (per 1 SD)	1.43	0.88–2.33	0.15			
Arrhythmia burden (per 1 SD)	1.53	0.93–2.50	0.09			
Atrial fibrillation	1.34	0.51–3.53	0.55			
Heart rate (per 1 SD)	1.25	0.77–2.02	0.36			
Systolic blood pressure (per 1 SD)	0.87	0.54–1.41	0.57			
Diastolic blood pressure (per 1 SD)	1.25	0.77–2.01	0.36			
Echocardiographic variables						
LVEDVi (per 1 SD)	2.03	1.15–3.57	0.01			
LVESVi (per 1 SD)	2.13	1.20–3.80	0.01			
LVEF (per 1 SD)	0.59	0.36–0.98	0.04			
E/e' (per 1 SD)	2.25	1.16–4.37	0.02			
TR-PG (per 1 SD)	3.50	1.71–7.14	0.001	5.3	1.67–16.6	0.005
LS						
Basal (per 1 SD)	0.31	0.16–0.61	0.001			
Mid (per 1 SD)	0.47	0.27–0.82	0.008			
Apical (per 1 SD)	1.60	0.97–2.62	0.065			
Global (per 1 SD)	0.68	0.42–1.12	0.131			
RALSR (per 1 SD)	11.2	3.51–35.9	<0.001	22.9	3.40–153.76	0.001

CI = confidence interval; other abbreviations as in Table 1.

systolic function. RALSR is a simple and reproducible assessment for strain distribution. Subjects at higher risk, such as those with higher RALSR, are known to have an abnormal response in LVEF during follow-up. RALSR may prove to be a noninvasive surrogate to predict LV recovery in patients with tachyarrhythmia. Although this study suggests an association between strain distribution and LV functional recovery, the results should be tested on a large cohort of patients with tachyarrhythmia using other cardiovascular imaging modalities (e.g., cardiac magnetic resonance [CMR]) to detect the occult cardiomyopathy.

STUDY LIMITATIONS. Because of the strict exclusion criteria including complete follow-up and a small single-center study, the sample size was small with relatively few endpoints. We could not enter some clinical variables (e.g., age, sex, heart rate) into the model because of the relatively small number of outcomes (31 events), which poses a potential risk of model overfit. Therefore, we were unable to completely adjust our model. The present study should be considered as a proof of concept, and we believe larger multicenter studies are warranted. It was hard to determine the duration of tachyarrhythmia in most patients. We could not determine the temporal relationship between duration of tachyarrhythmia and improvement in LVEF. We did not have myocardial damage data on other cardiovascular imaging modalities (e.g., delayed enhanced imaging of CMR) and were unable to determine detailed characteristics in patients without functional recovery. Despite the exclusion of known cardiovascular diseases, we may not have been able to avoid the potential effect on myocardial mechanics by the other unknown etiologies. Some investigators showed that patients without functional recovery had myocardial scar by late gadolinium enhancement. Although this study suggests an association between strain distribution and LV functional recovery, this hypothesis should be tested on a large cohort of patients with tachyarrhythmia (late gadolinium enhancement [LGE]-CMR imaging) (26). In our cohort, LGE-CMR imaging was performed in 4 of 30 patients with recovery in LVEF and 10 of 41 patients without recovery in LVEF. One of 4 patients (25%) had LGE in patients with recovery in LVEF and 7 of 10 patients (70%) had LGE in patients without recovery in LVEF. Our results suggested that if patients with presumptive TIC had high RALSR, we may recommend LGE-CMR to check the occult cardiomyopathy.

FIGURE 5 Receiver Operating Characteristic Curve Analysis of Echocardiographic Variables for Prediction of Left Ventricular Functional Recovery



AUC = area under the curve; EF = ejection fraction; LVESVi = left ventricular end-systolic volume index; TR-PG = tricuspid regurgitant pressure gradient; other abbreviations as in Figures 2 and 4.

CONCLUSIONS

Assessment of RALSR can be considered a useful tool in patients with tachyarrhythmia and reduced LVEF. This study highlights the use of strain distribution in patients with a nonischemic etiology. This knowledge may be useful for clinical evaluation and follow-up of patients with reduced LVEF and tachyarrhythmia (presumptive TIC). We might consider that patients without functional recovery had occult myocardial damage caused by a nonischemic etiology. Further studies are needed to assess whether strain can be used to assess the prognostic value in tachyarrhythmia in long-term follow-up.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The relative apical longitudinal strain ratio obtained by 2-dimensional speckle tracking echocardiography was a predictor of left ventricular systolic functional recovery in patients with reduced LVEF and tachyarrhythmia. This information might be useful for clinical evaluation and follow-up in patients with reduced LVEF before the treatment of index arrhythmia.

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Strain distribution should be carefully assessed in patients with reduced LVEF and tachyarrhythmia. Our results suggest the importance of follow-up echocardiography, because some patients with presumptive tachycardia-induced cardiomyopathy do not recover LVEF.

TRANSLATIONAL OUTLOOK: Although this study suggests an association between strain distribution and left ventricular functional recovery, this hypothesis should be tested on a large cohort of patients with tachyarrhythmia.

REFERENCES

1. Fenelon G, Wijns W, Andries E, Brugada P. Tachycardiomyopathy: mechanisms and clinical implications. Pacing Clin Electrophysiol 1996;19:95–106.

2. Bikkina M, Larson MG, Levy D. Prognostic implications of asymptomatic ventricular arrhythmias: the Framingham Heart Study. Ann Intern Med 1992;117:990–6.

3. Yarlagadda RK, Iwai S, Stein KM, et al. Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract. Circulation 2005;112:1092–7.

4. Medi C, Kalman JM, Haqqani H, et al. Tachycardia-mediated cardiomyopathy secondary to focal atrial tachycardia. J Am Coll Cardiol 2009;53:1791–7.

5. Shinbane JS, Wood MA, Jensen DN, Ellenbogen KA, Fitzpatrick AP, Scheinman MM. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies. J Am Coll Cardiol 1997;29:709–15.

6. Gupta S, Figueredo VM. Tachycardia mediated cardiomyopathy: pathophysiology, mechanisms, clinical features and management. Int J Cardiol 2014;172:40–6.

7. Zimmermann AJ, Bossard M, Aeschbacher S, et al. Effects of sinus rhythm maintenance on left heart function after electrical cardioversion of atrial fibrillation: implications for tachycardia-induced cardiomyopathy. Can J Cardiol 2015;31:36–43.

8. Hasdemir CAN, Ulucan CEM, Yavuzgil O, et al. Tachycardia-induced cardiomyopathy in patients with idiopathic ventricular arrhythmias: the incidence, clinical and electrophysiologic characteristics, and the predictors. J Cardiovasc Electrophysiol 2011;22:663–8.

9. Phelan D, Thavendiranathan P, Popovic Z, et al. Application of a parametric display of two-dimensional speckle-tracking longitudinal strain to improve the etiologic diagnosis of mild to moderate left ventricular hypertrophy. J Am Soc Echocardiog 2014;27:888–95.

10. Kusunose K, Dahiya A, Popovic ZB, et al. Biventricular mechanics in constrictive pericarditis comparison with restrictive cardiomyopathy and impact of pericardiectomy. Circ Cardiovasc Imaging 2013;6:399–406.

11. Phelan D, Collier P, Thavendiranathan P, et al. Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis. Heart 2012;98:1442–8.

12. Foell D, Jung B, Germann E, Staehle F, Bode C, Markl M. Hypertensive heart disease: MR tissue phase mapping reveals altered left ventricular rotation and regional myocardial long-axis velocities. Eur Radiol 2013;23:339–47.

13. Chang SA, Kim HK, Kim DH, et al. Left ventricular twist mechanics in patients with apical hypertrophic cardiomyopathy: assessment with 2D speckle tracking echocardiography. Heart 2010;96:49–55.

14. Kusunose K, Zhang Y, Mazgalev TN, Thomas JD, Popovic ZB. Left ventricular strain distribution in healthy dogs and in dogs with tachycardia-induced dilated cardiomyopathy. Cardiovasc Ultrasound 2013;11:43.

15. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39.e14.

16. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685–713; quiz 786–8.

17. Voigt JU, Pedrizzetti G, Lysyansky P, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. J Am Soc Echocardiogr 2015;28:183–93.

18. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837–45.

19. Donghua Z, Jian P, Zhongbo X, et al. Reversal of cardiomyopathy in patients with congestive heart failure secondary to tachycardia. J Interv Card Electrophysiol 2013;36:27–32; discussion 32.

20. Nia AM, Gassanov N, Dahlem KM, et al. Diagnostic accuracy of NT-proBNP ratio (BNP-R) for early diagnosis of tachycardia-mediated cardiomyopathy: a pilot study. Clin Res Cardiol 2011;100:887–96.

21. Moe GW, Armstrong P. Pacing-induced heart failure: a model to study the mechanism of disease progression and novel therapy in heart failure. Cardiovasc Res 1999;42:591–9.

22. Dandamudi G, Rampurwala AY, Mahenthiran J, Miller JM, Das MK. Persistent left ventricular dilatation in tachycardia-induced cardiomyopathy patients after appropriate treatment and normalization of ejection fraction. Heart Rhythm 2008;5:1111–4.

23. McMahon WS, Mukherjee R, Gillette PC, Crawford FA, Spinale FG. Right and left ventricular geometry and myocyte contractile processes with dilated cardiomyopathy: myocyte growth and beta-adrenergic responsiveness. Cardiovasc Res 1996;31:314–23.

24. Lagies R, Beck BB, Hoppe B, Sreeram N, ten Cate FEAU. Apical sparing of longitudinal strain, left ventricular rotational abnormalities, and short-axis dysfunction in primary hyperoxaluria type 1. Circ Heart Fail 2013;6:e45–7.

25. Moore JP, Patel PA, Shannon KM, et al. Predictors of myocardial recovery in pediatric tachycardia-induced cardiomyopathy. Heart Rhythm 2014;11:1163–9.

26. Hasdemir CAN, Yuksel A, Camli D, et al. Late gadolinium enhancement CMR in patients with tachycardia-induced cardiomyopathy caused by idiopathic ventricular arrhythmias. Pacing Clin Electrophysiol 2012;35:465–70.

KEY WORDS functional recovery, strain imaging, tachycardia-induced cardiomyopathy

APPENDIX For a supplemental table, please see the online version of this article.