

Right Ventricular Strain and Dyssynchrony Assessment in Arrhythmogenic Right Ventricular Cardiomyopathy

Cardiac Magnetic Resonance Feature-Tracking Study

Giulio Prati, MD; Giancarlo Vitrella, MD; Giuseppe Allocca, MD; Daniele Muser, MD;
 Sonja Cukon Buttignoni, MD; Gianluca Piccoli, MD; Giorgio Morocutti, MD;
 Pietro Delise, MD; Bruno Pinamonti, MD; Alessandro Proclemer, MD;
 Gianfranco Sinagra, MD; Gaetano Nucifora, MD, PhD

Background—Analysis of right ventricular (RV) regional dysfunction by cardiac magnetic resonance (CMR) imaging in arrhythmogenic RV cardiomyopathy (ARVC) may be inadequate because of the complex contraction pattern of the RV. Aim of this study was to determine the use of RV strain and dyssynchrony assessment in ARVC using feature-tracking CMR analysis.

Methods and Results—Thirty-two consecutive patients with ARVC referred to CMR imaging were included. Thirty-two patients with idiopathic RV outflow tract arrhythmias and 32 control subjects, matched for age and sex to the ARVC group, were included for comparison purpose. CMR imaging was performed to assess biventricular function; feature-tracking analysis was applied to the cine CMR images to assess regional and global longitudinal, circumferential, and radial RV strains and RV dyssynchrony (defined as the SD of the time-to-peak strain of the RV segments). RV global longitudinal strain ($-17\pm 5\%$ versus $-26\pm 6\%$ versus $-29\pm 6\%$; $P<0.001$), global circumferential strain ($-9\pm 4\%$ versus $-12\pm 4\%$ versus $-13\pm 5\%$; $P=0.001$), and global radial strain ($18 [12-26]\%$ versus $22 [15-32]\%$ versus $27 [20-39]\%$; $P=0.015$) were significantly lower and SD of the time-to-peak RV strain in all 3 directions were significantly higher among patients with ARVC compared with patients with RV outflow tract arrhythmias and controls. RV global longitudinal strain $>-23.2\%$, SD of the time-to-peak RV longitudinal strain >113.1 ms, and SD of the time-to-peak RV circumferential strain >177.1 ms allowed correct identification of 88%, 75%, and 63% of ARVC patients with no or only minor CMR criteria for ARVC diagnosis.

Conclusions—Strain analysis by feature-tracking CMR helps to objectively quantify global and regional RV dysfunction and RV dyssynchrony in patients with ARVC and provides incremental value over conventional cine CMR imaging.

Key Words: arrhythmogenic right ventricular cardiomyopathy ■ magnetic resonance imaging
 ■ myocardium ■ strain

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically determined heart muscle disease, which is pathologically characterized by a progressive loss of cardiac myocytes and fibro-fatty replacement.¹ The clinical manifestations of ARVC are mainly electric disorders with potentially life-threatening ventricular arrhythmias.^{2,3} Diagnosis is established on multiple criteria, first published in 1994,⁴ then revised in the 2010 consensus,⁵ in which echocardiographic and cardiac magnetic resonance (CMR) imaging play a significant role.⁶ In particular, CMR imaging criteria for the diagnosis of ARVC are based on (1) quantification of RV volume and ejection fraction and (2) subjective assessment of RV regional wall motion abnormalities. CMR is indeed considered the gold standard

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imaging modality for the evaluation of RV dimension and function.⁷ However, analysis of regional wall motion abnormalities may still be inadequate because of the complex RV contraction pattern.⁷ Measurement of myocardial deformation by strain analysis is an emerging tool to quantitatively assess regional and global chamber systolic function and mechanical dispersion and may overcome the weakness of subjective assessment of RV regional wall motion abnormalities.⁸ Still, few is known about the value of deformation imaging in CMR in the setting of ARVC. Accordingly, aim of this study is to determine if the

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From the Cardiothoracic Department, University Hospital “Santa Maria della Misericordia,” Udine, Italy (G.P., D.M., G.M., A.P., G.N.); Cardiovascular Department, University Hospital “Ospedali Riuniti,” Trieste, Italy (G.P., G.V., B.P., G.S.); Postgraduate School of Cardiovascular Sciences, University of Trieste, Trieste, Italy (G.P., D.M.); and Divisions of Cardiology (G.A., S.C.B., P.D.) and Radiology (G.P.), “Santa Maria dei Battuti” Hospital, Conegliano, Italy.

Correspondence to Gaetano Nucifora, MD, PhD, Division of Cardiology, Cardiothoracic Department, University Hospital “Santa Maria della Misericordia”, Udine, Italy. E-mail gnucifora@outlook.com

assessment of RV strain and dyssynchrony using a novel feature-tracking CMR software system is feasible and reproducible, and whether it allows the detection of abnormalities in patients with ARVC even in the absence of RV dilatation, RV dysfunction, or RV regional wall motion abnormalities, thereby improving the diagnostic yield of conventional CMR imaging criteria.

Methods

Patient Population

A total of 32 consecutive patients with diagnosis of definite or borderline ARVC according to the 2010 revised task force criteria⁵ that were being clinically managed at the participating centers were included. These patients were referred to CMR to assess regional and global RV and left ventricular (LV) function. Furthermore, feature-tracking analysis was applied to assess regional and global RV strain and RV dyssynchrony (ie, mechanical dispersion). For comparison purpose, 32 patients with idiopathic RV outflow tract arrhythmia (ie, >1000/24 hours premature ventricular beats, nonsustained or sustained ventricular tachycardia with left bundle-branch block morphology and inferior axis; RVOT-A), a primary electric disorder that is frequently in differential diagnosis with ARVC, and 32 control subjects (ie, without evidence of structural heart disease and no history of hypertension, diabetes mellitus, or any other systemic disease), matched for age and sex to the ARVC group, were also included in the study. The study was approved by the Institutional Review Committee, and the informed consent of the subjects was obtained.

CMR Acquisition Protocol

All patients with ARVC and RVOT-A received oral antiarrhythmic therapy at least 1 week before CMR examination to optimize ECG trigger and to obtain optimal image acquisition.

CMR studies were performed using a 1.5-Tesla scanner (Siemens Avanto, Erlangen, Germany or Philips Achieva, Best, The Netherlands) with a cardiac-phased array receiver surface coil and ECG gating. Vertical and horizontal long-axis slices, a stack of contiguous cine short-axis slices from the atrioventricular ring to the apex and para-axial slices from diaphragm to the entire outflow tract were acquired using a steady-state free precession pulse sequence (slice thickness=8 mm, no interslice gap for long-axis and short-axis images; slice thickness=5 mm, no interslice gap for para-axial images; repetition time/echo time=3–4/1.2 ms for Siemens Avanto; repetition time/echo time=3.5/1.5 ms for Philips Achieva).

CMR Data Analysis

All CMR studies were analyzed offline using dedicated software (Segment 1.9, Medviso AB, Lund, Sweden) by an experienced observer blinded to clinical data. The assessment of LV and RV regional wall motion abnormalities was performed by 2 independent expert investigators; any discrepancies between the investigators were independently adjudicated by a blinded third investigator. Biventricular volumes and function and LV mass were measured using standard volumetric technique from the cine short-axis images.⁹ Volume and mass measurements were indexed to body surface area.

The absence or presence of LV wall motion abnormalities (ie, hypokinesia, akinesia, or dyskinesia) was visually assessed for each LV myocardial segment, using the 17-segment cardiac model.¹⁰ Similarly, the absence or presence of RV wall motion abnormalities (ie, hypokinesia, akinesia, or dyskinesia of the ventricular wall) was visually assessed from the short-axis, vertical long-axis, and para-axial cine views,^{11,12} using a 12-segment model (Figure 1). The absence or presence of major or minor CMR criteria for ARVC was also determined; the 2010 task force criteria were used for this purpose.⁵

Feature-Tracking Analysis

Two-dimensional Cardiac Performance Analysis Software (TomTec, Munich, Germany) was used to obtain RV strain data directly from cine images in the 4-chamber view (longitudinal strain) and in the short-axial views at the basal, mid, and apical level (circumferential and radial strain). The mathematical assumptions used and the clinical validation of the feature tracking technology have been previously described.^{13,14} After the upload of the CMR image, the brightness was optimized to ensure optimal endocardial/blood pool discrimination. The endocardial border of the RV was then manually traced on the end-diastolic frame and the software automatically propagated the contour and followed its features throughout the remainder of the cardiac cycle (Figure 2). Adjustment of contour tracking was done after visual assessment during cine loop playback to ensure that the RV segments were tracked appropriately. The software automatically generated the corresponding time-strain curves. Three measures were derived from strain analysis to measure global RV systolic function: the global longitudinal strain (GLS), the global circumferential strain, and the global radial strain. The GLS was derived from the peak systolic strain values of the 3 free wall segments in the longitudinal 4-chambers view.¹⁵ The global circumferential and the global radial strains were obtained from the peak strain values of the 11 free wall segments in the 3 short-axis sections of the RV.¹⁵ As previously suggested,¹⁶ RV

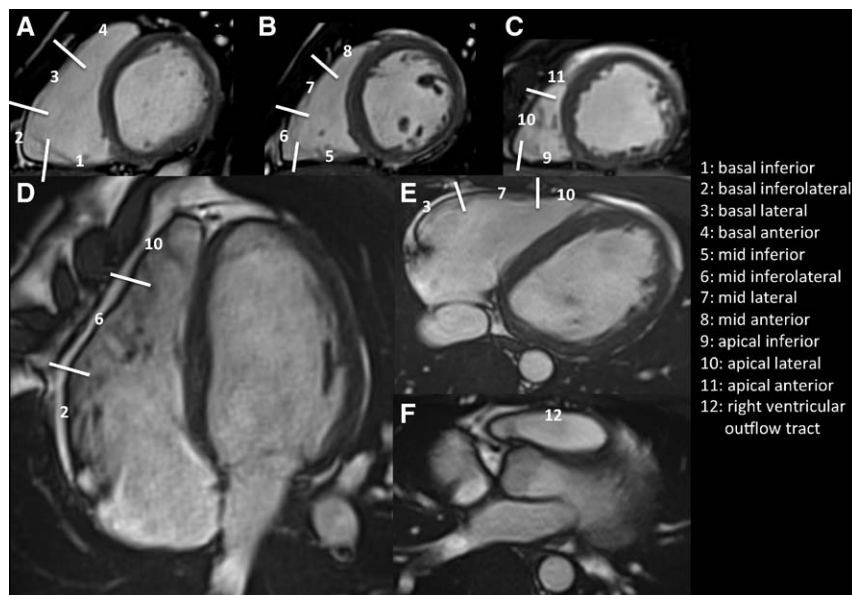


Figure 1. Segmentation of the right ventricle in the short-axis (A–C), vertical long-axis (D), and para-axial cardiac magnetic resonance cine views (E and F). The segmentation model was derived from that proposed by Sievers et al.¹²

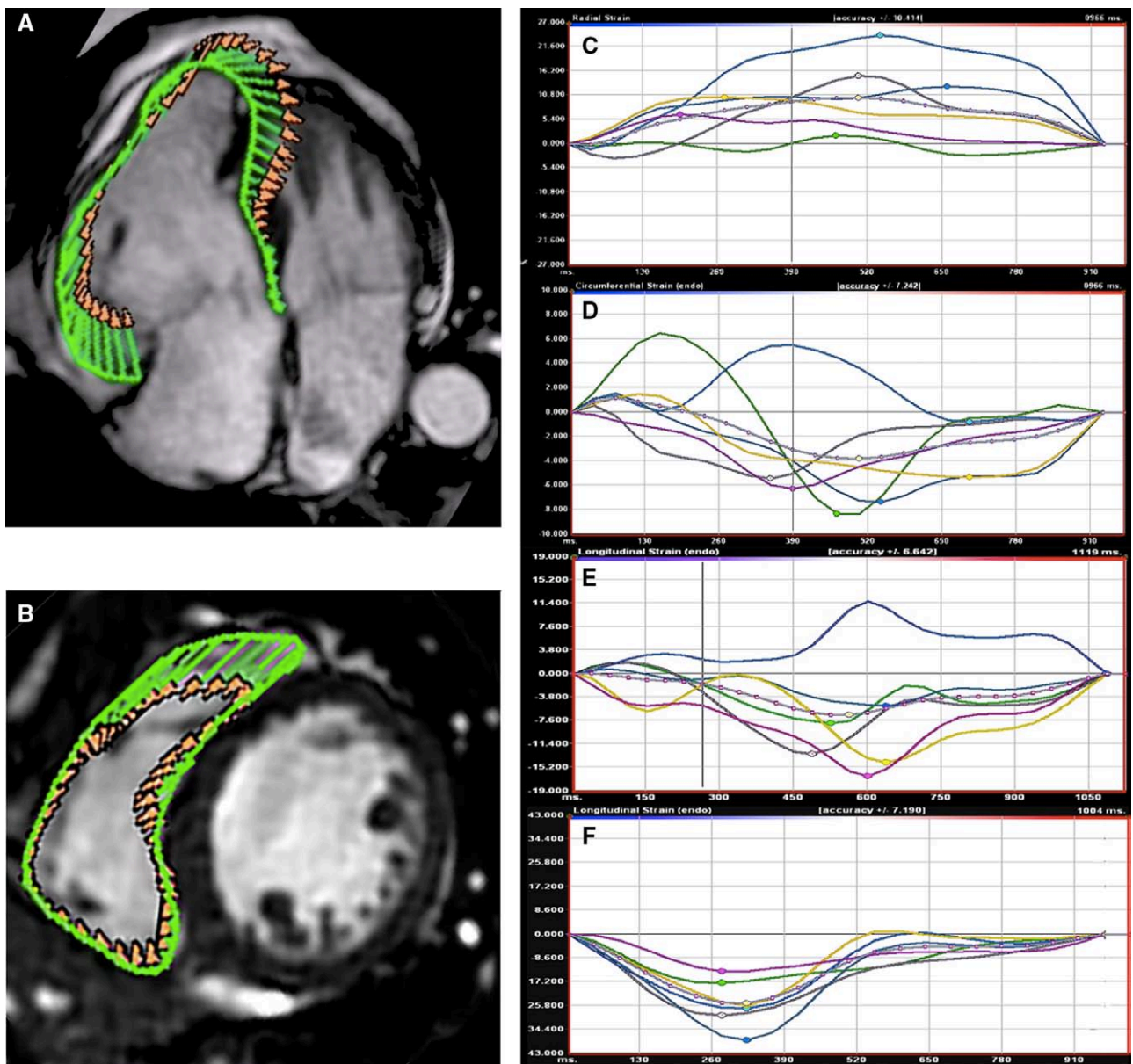


Figure 2. **A**, Tracking of the endocardial border of the right ventricle (RV) on a 4-chamber steady-state free precession image using feature-tracking software, whereas **B** shows an example of tracking on the mid section of a short-axis view. **Right**, RV radial (**C**), circumferential (**D**), and longitudinal (**E**) strain patterns of a patient with arrhythmogenic RV cardiomyopathy. For comparison purpose, **F** shows an example of the RV longitudinal strain pattern of a control subject.

dyssynchrony was assessed in the 3 directions of contraction (longitudinal, circumferential, and radial) as the SD of the time-to-peak strain (TPS) of the RV free wall segments and the interventricular septum. An investigator blinded to the clinical and all other CMR data performed the feature-tracking analysis. After an arbitrarily chosen interval of 6 weeks, both this observer and a second experienced observer blindly repeated the feature-tracking analysis on the same images of 33 randomly selected subjects to assess intra and interobserver agreement for measures.

Statistical Analysis

Continuous variables are expressed as mean and SD or as median and 25th to 75th percentiles when appropriate. Categorical data are presented as absolute numbers and percentages. Differences in continuous variables between the 3 groups were assessed with the 1-way ANOVA test or Kruskal–Wallis test, where appropriate. When the result of the analysis was significant, post hoc pairwise

comparisons using the Bonferroni correction were performed. Chi-square or Fisher exact test, where appropriate, was computed to assess differences in categorical variables; when the result of the analysis was significant, post hoc pairwise comparisons using the Bonferroni correction were performed. Receiver operator characteristic (ROC) curve analysis was performed to determine the accuracy of RV strain and dyssynchrony parameters for the detection of the patients with ARVC, with an area under the curve value of 0.50 indicating no accuracy and a value of 1.00 indicating maximal accuracy. The intra and interobserver reproducibility of RV strain and dyssynchrony parameters was assessed using the within-subject coefficient of variation, which provides a dimensionless measure of data dispersion, consequently allowing comparison between variables with different units or scales.¹⁷ Two-tailed tests were considered statistically significant at the 0.05 level. Statistical analysis was performed using the SPSS (SPSS 22; SPSS Inc, Chicago, IL) and MedCalc (MedCalc 15, Mariakerke, Belgium) software packages.

Table 1. Baseline Characteristics of the Study Population

	Controls (n=32)	RVOT-A (n=32)	ARVC (n=32)	P Value
Age	46±12	46±12	46±14	0.998
Sex (% male)	22 (68.8%)	22 (68.8%)	22 (68.8%)	1
ARVC 2010 task force criteria (definite/borderline/possible)	29/3/0	...
Imaging CMR (none/minor/major)	3/5/24	...
Tissue characterization on EMB (none/minor/major)	1/0/2	...
Repolarization abnormalities (none/minor/major)	12/3/17	...
Depolarization/conduction abnormalities (none/minor/major)	22/8/2	...
Arrhythmias (none/minor/major)	9/8/15	...
Family history (none/minor/major)	16/2/14	...

Data are expressed as mean±SD or as median with interquartile range when appropriate and as n (%). ARVC indicates arrhythmogenic right ventricular cardiomyopathy; CMR, cardiac magnetic resonance; EMB, endomyocardial biopsy; and RVOT-A, right ventricular outflow tract arrhythmias.

Results

All patients were in regular sinus rhythm during the CMR examination, which allowed optimal image acquisition. Baseline and CMR characteristics of the study population are summarized in Tables 1 and 2. According to the 2010 task force criteria, 29 patients with ARVC had a definite diagnosis, whereas 3 patients had a borderline diagnosis. Eighteen patients with ARVC complained palpitations, whereas syncope was observed in 5 patients; only 1 patient had heart failure symptoms. Major repolarization abnormalities were present in 17 patients, whereas 3 patients had minor repolarization abnormalities. Epsilon wave in the right precordial leads were observed in 2 patients, whereas late potentials by signal-averaged ECG were present in 10 patients; 2 patients had both epsilon wave in the right precordial leads (V1–V3) and late potentials by signal-averaged ECG. Fifteen patients had nonsustained (n=8) or sustained (n=7) ventricular tachycardia of left bundle-branch morphology with superior axis, whereas 8 patients had nonsustained ventricular tachycardia

of RV outflow configuration (n=1) or frequent ventricular extrasystoles (n=7). At CMR, impaired RV function, defined as RV ejection fraction ≤45%, and RV dilatation, defined as RV end-diastolic volume index ≥100 mL/m² in males and ≥90 mL/m² in females, were present in 15 and 24 patients with ARVC, respectively, whereas RV wall motion abnormalities were observed in 31 patients. Overall, 24 patients with ARVC met major CMR imaging criteria, whereas 8 patients had no or only minor CMR imaging criteria.

Feature-tracking analysis was feasible in all patients. Intra and interobserver agreement for the measurements of global RV strains and SD-TPS are shown in Table 3. Of note, among the RV strain and dyssynchrony parameters, global radial strain and radial SD-TPS had the poorest reproducibility.

Table 4 shows the differences of RV strain parameters at basal, mid, and apical level between controls, patients with RVOT-A and patients with ARVC; patients with ARVC had significantly lower systolic longitudinal strain at RV basal, mid, and apical level (ANOVA $P<0.001$) as well as lower circumferential and radial strain at RV basal and mid level

Table 2. CMR Characteristics of the Study Population

	Controls (n=32)	RVOT-A (n=32)	ARVC (n=32)	P Value
RVEDV index (mL/m ²)	71 (63–77)	74 (60–87)	108 (98–129)*,†	<0.001
RVEDV index <100 mL/m ² in males and <90 mL/m ² in females	32 (100%)	31 (97%)	8 (25%)*,†	<0.001
RVESV index (mL/m ²)	20 (14–24)	21 (16–28)	48 (39–76)*,†	<0.001
RVEF (%)	71±8	71±7	50±14*,†	<0.001
RVEF >45%	32 (100%)	32 (100%)	17 (53%)*,†	<0.001
Regional RV WMAs	0 (0%)	3 (9%)	31 (97%)*,†	<0.001
LVEDV index (mL/m ²)	77±14	77±14	89±18‡,§	0.004
LVESV index (mL/m ²)	26±10	27±10	36±15‡,§	0.002
LVEF (%)	67 (62–75)	66 (62–69)	62 (57–66)‡,§	0.011
Regional LV WMAs	0 (0%)	0 (0%)	5 (16%)*,†	0.010
LV mass index (g/m ²)	57 (50–65)	60 (49–65)	52 (47–59)	0.068

Data are expressed as mean±SD or as median with interquartile range when appropriate and as n (%). CMR indicates cardiac magnetic resonance; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; LV, left ventricular; RV, right ventricular; RVOT-A, right ventricular outflow tract arrhythmias; and WMA, wall motion abnormality.

* $P<0.001$ vs RVOT-A.

† $P<0.001$ vs control patients.

‡ $P<0.05$ vs RVOT-A.

§ $P<0.01$ vs control patients.

Table 3. Intra and Interobserver Reproducibility of Right Ventricular Strain and Dyssynchrony Parameters

	Intraobserver CV, %	Interobserver CV, %
Global longitudinal strain	8.6	9.9
Global circumferential strain	4.1	5.6
Global radial strain	13.1	16.0
Longitudinal SD-TPS	13.6	15.0
Circumferential SD-TPS	11.6	13.8
Radial SD-TPS	17.1	20.9

CV indicates within-subject coefficient of variation; and SD-TPS, SD of the time-to-peak strain.

($P<0.001$ and $P=0.003$ for comparison of circumferential strain at RV basal and mid level; $P=0.007$ and $P=0.002$ for comparison of radial strain at RV basal and mid level). Even after exclusion of RV segments with wall motion abnormalities (Table 3), patients with ARVC had significantly lower systolic longitudinal strain at RV mid and apical level ($P=0.021$ and $P=0.002$, respectively) as well as lower circumferential and radial strain at RV basal and mid level ($P=0.002$ and $P=0.016$ for comparison of circumferential strain at RV basal

and mid level; $P=0.004$ and $P=0.021$ for comparison of radial strain at RV basal and mid level).

As shown in Figure 3, RV GLS ($-17\pm5\%$ versus $-26\pm6\%$ versus $-29\pm6\%$; $P<0.001$), RV global circumferential strain ($-9\pm4\%$ versus $-12\pm4\%$ versus $-13\pm5\%$; $P=0.001$), and RV global radial strain (18 [12–26]% versus 22 [15–32]% versus 27 [20–39]%; $P=0.015$) were significantly reduced, whereas RV longitudinal SD-TPS (145 ± 90 ms versus 68 ± 47 ms versus 50 ± 23 ms; $P<0.001$), RV circumferential SD-TPS (201 ± 68 ms versus 130 ± 53 ms versus 121 ± 79 ms; $P<0.001$), and RV radial SD-TPS (181 [136–266] ms versus 149 [123–179] ms versus 105 [70–169] ms; $P<0.001$) were significantly higher among patients with ARVC compared with patients with RVOT-A and controls (Figure 4). Differences in RV GLS and RV longitudinal SD-TPS remained significant even when considering only ARVC patients with preserved RV systolic function, defined as RV ejection fraction $>45\%$ ($-19\pm6\%$ versus $-26\pm6\%$ versus $-29\pm6\%$; $P<0.001$ and 146 ± 85 ms versus 68 ± 47 ms versus 50 ± 23 ms; $P<0.001$, respectively), or only ARVC patients with non-dilated RV, defined as RV end-diastolic volume index <100 mL/m² in males and <90 mL/m² in females ($-20\pm5\%$ versus $-26\pm6\%$ versus $-29\pm6\%$; $P=0.004$ and 123 ± 89 ms versus 62 ± 35 ms versus 50 ± 23 ms; $P<0.001$). Similarly, differences

Table 4. Comparison of Right Ventricular Strain Parameters at Basal, Mid, and Apical Level Between Control Patients, Patients With RVOT-A, and Patients With ARVC

	Controls (n=32)	RVOT-A (n=32)	ARVC (n=32)	P Value
All RV segments				
Basal longitudinal strain (%)	-35 ± 15	-35 ± 14	$-22\pm11^*,\dagger$	<0.001
Mid-longitudinal strain (%)	-26 ± 11	22 ± 12	$-15\pm8\ddagger,\S$	<0.001
Apical longitudinal strain (%)	-25 ± 11	-22 ± 12	$-14\pm8\ddagger,\parallel$	<0.001
Basal circumferential strain (%)	-13 ± 4	-12 ± 4	$-8\pm4\ddagger,\dagger$	<0.001
Mid-circumferential strain (%)	-12 ± 5	-11 ± 4	$-8\pm5^*,\S$	0.003
Apical circumferential strain (%)	-15 ± 6	-14 ± 7	-14 ± 7	0.82
Basal radial strain (%)	30 (23–41)	25 (19–34)	20 (13–28) \parallel	0.007
Mid-radial strain (%)	27 (17–32)	20 (14–30)	15 (10–19) \parallel	0.002
Apical radial strain (%)	19 (13–24)	14 (9–24)	15 (9–29)	0.67
RV segments with wall motion abnormalities excluded				
Basal longitudinal strain (%)	-35 ± 15	-35 ± 14	-27 ± 10	0.18
Mid-longitudinal strain (%)	-26 ± 11	-22 ± 12	$-17\pm9\#$	0.021
Apical longitudinal strain (%)	-25 ± 11	-22 ± 12	$-14\pm8^*,\S$	0.002
Basal circumferential strain (%)	-13 ± 4	-12 ± 4	$-9\pm4^*,\S$	0.002
Mid-circumferential strain (%)	-12 ± 5	-11 ± 4	$-8\pm6\#$	0.016
Apical circumferential strain (%)	-15 ± 6	-14 ± 7	-15 ± 8	0.79
Basal radial strain (%)	30 (23–41)	25 (19–34)	19 (11–27) $\#$	0.004
Mid-radial strain (%)	27 (17–32)	20 (14–30)	16 (11–22) $\#$	0.021
Apical radial strain (%)	19 (13–24)	14 (9–24)	17 (10–27)	0.68

Data are expressed as mean \pm SD or as median with interquartile range when appropriate. ARVC indicates arrhythmogenic right ventricular cardiomyopathy; and RVOT-A, RV outflow tract arrhythmia.

* $P<0.005$ vs control patients.

† $P<0.005$ vs RVOT-A patients.

‡ $P<0.001$ vs control patients.

§ $P<0.05$ vs RVOT-A patients.

|| $P<0.01$ vs RVOT-A patients.

¶ $P<0.01$ vs control patients.

$P<0.05$ vs control patients.

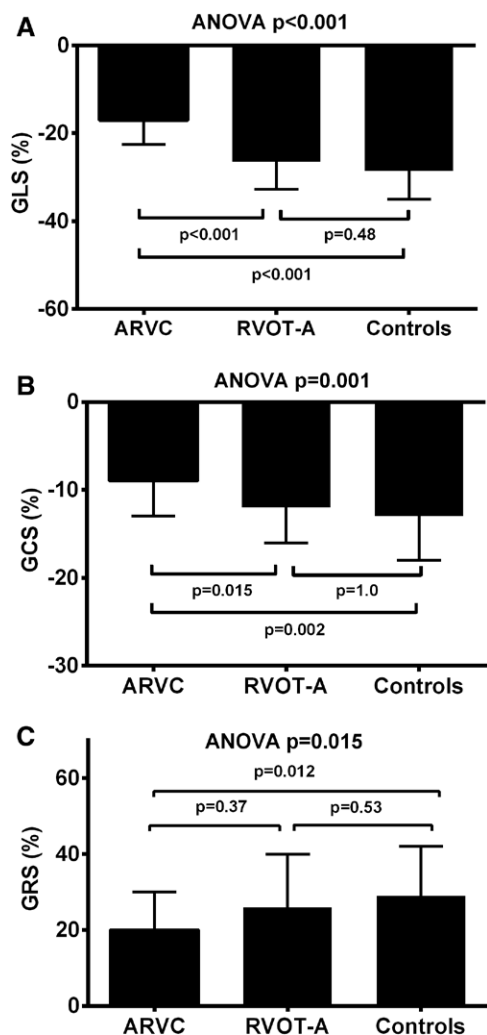


Figure 3. Differences in mean global longitudinal strain (GLS; **A**), global circumferential strain (GCS; **B**), and global radial strain (GRS; **C**) between patients with arrhythmogenic right ventricular cardiomyopathy (ARVC), patients with idiopathic RV outflow tract arrhythmias (RVOT-A) and control subjects.

in RV circumferential and radial SD-TPS remained significant when considering only ARVC patients with RV ejection fraction >45% (circumferential SD-TPS: 194±76 ms versus 130±53 ms versus 121±79 ms; $P=0.002$; radial SD-TPS: 206±78 ms versus 151±44 ms versus 126±75 ms; $P=0.001$). Examples of RV strain patterns of a patient with ARVC compared with a control subject are shown in Figure 2.

Figure 5 shows the ROC curves of RV strain and dyssynchrony parameters for the differentiation of patients with ARVC from patients with RVOT-A and control subjects. Among the strain parameters, RV GLS had the largest area under the ROC curves; RV GLS $\geq -23.2\%$ provided the highest sensitivity (91%) and specificity (75%) for identification of patients with ARVC. Among the dyssynchrony parameters, longitudinal and circumferential SD-TPS had the largest area under the ROC curves; longitudinal SD-TPS >113.1 ms and circumferential SD-TPS >177.1 ms provided the highest sensitivity (59% and 66%, respectively) and specificity (95% and 83%, respectively) for identification of patients with ARVC. Applying these cut-off values, RV GLS, longitudinal SD-TPS,

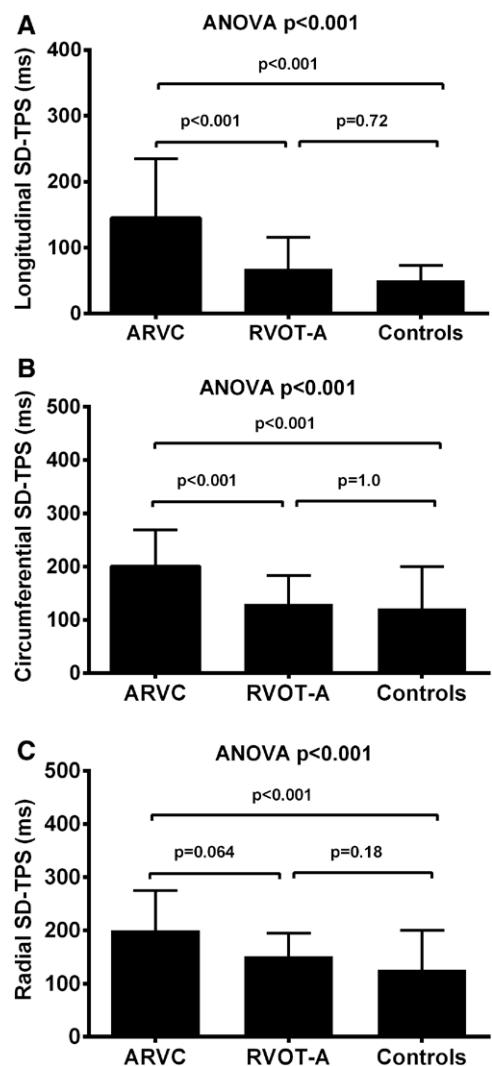


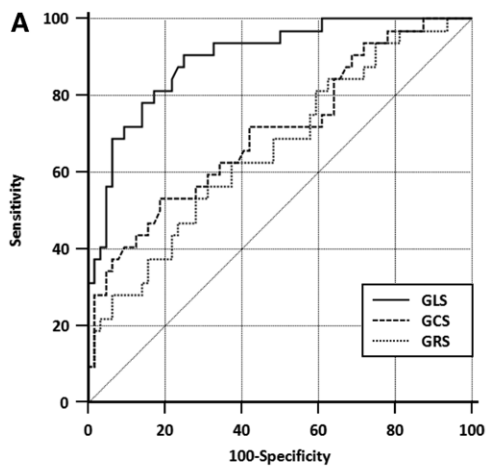
Figure 4. Differences in SD of the time-to-peak strain (SD-TPS) in longitudinal (**A**), circumferential (**B**), and radial (**C**) direction between patients with arrhythmogenic right ventricular cardiomyopathy (ARVC), patients with idiopathic RV outflow tract arrhythmias (RVOT-A) and control subjects.

and circumferential SD-TPS allowed the detection of the disease, respectively in 7 of 8 (88%), 6 of 8 (75%), and 5 of 8 (63%) ARVC patients with no or minor CMR criteria for ARVC diagnosis according to the 2010 task force criteria.

Discussion

The results of this study can be summarized as follows: (1) patients with ARVC have impaired RV regional and global strain and significant RV mechanical dispersion, compared with patients with RVOT-A and controls; (2) impaired RV strain and RV mechanical dispersion are present even when regional and global RV function are preserved or RV dilatation is absent; and (3) analysis of RV strain and dyssynchrony by feature-tracking CMR allows correct identification of most ARVC patients with no or only minor CMR criteria for ARVC diagnosis according to the 2010 task force criteria.

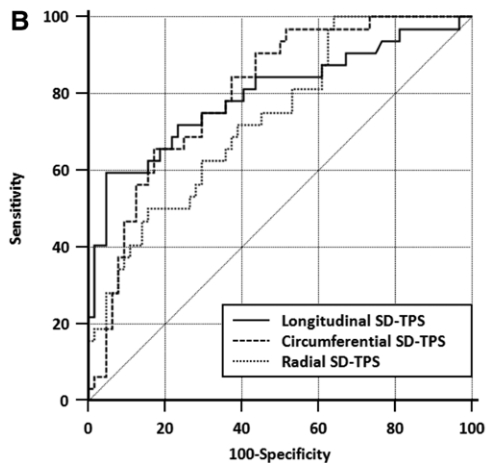
The diagnosis of ARVC is a clinical challenge because of the low prevalence of the disease and the lack of a single



GLS
AUC = 0.90 (95% CI 0.82-0.95); $p < 0.001$

GCS
AUC = 0.71 (95% CI 0.60-0.79); $p < 0.001$

GRS
AUC = 0.66 (95% CI 0.56-0.75); $p = 0.007$



Longitudinal SD-TPS
AUC = 0.80 (95% CI 0.70-0.87); $p < 0.001$

Circumferential SD-TPS
AUC = 0.80 (95% CI 0.71-0.88); $p < 0.001$

Radial SD-TPS
AUC = 0.74 (95% CI 0.64-0.82); $p < 0.001$

Figure 5. Receiver-operating characteristic curves of right ventricular strain (A) and dyssynchrony (B) parameters for the differentiation of patients with arrhythmogenic right ventricular cardiomyopathy from patients with idiopathic right ventricular outflow tract arrhythmias and control subjects. AUC indicates area under the curve; GCS, global circumferential strain; GLS, global longitudinal strain; GRS, global radial strain; and SD-TPS, SD of the time-to-peak strain.

conclusive diagnostic test.¹⁸ According to the 2010 task force criteria, definition by imaging modalities relies on the presence of RV dilatation and dysfunction, regional RV wall motion abnormalities and dyssynchronous RV contraction.⁵ CMR is currently considered the gold standard imaging modality for the assessment of the RV because of its high spatial resolution, allowing a more accurate and reproducible evaluation of RV morphology and function than echocardiography.⁶ However, analysis of regional wall motion abnormalities may still be cumbersome because of the complex contraction pattern of the RV.^{7,12} Moreover, Vermes et al¹⁹ recently observed that the 2010 task force CMR imaging criteria for ARVC are highly specific but lack in sensitivity, especially in the early stages of the disease. These observations underscore the need for novel tools able to improve the diagnosis of ARVC.

RV Strain and Dyssynchrony in ARVC

The usefulness of myocardial strain imaging to objectively quantify global and regional RV function and mechanical dispersion in ARVC has been previously demonstrated in tissue-Doppler and speckle-tracking echocardiography studies;^{16,20-23} these studies consistently showed reduced regional and global RV myocardial strain and increased RV mechanical dispersion in patients with ARVC compared with control subjects. The clinical use of the assessment of RV contraction pattern in ARVC has been recently demonstrated also in a nuclear imaging study.²⁴

Conversely to echocardiographic and nuclear imaging data, little information is available about the value of deformation and dyssynchrony imaging in CMR in the setting of ARVC.¹⁵ Myocardial tagging (in which virtual markers in the myocardium are obtained with magnetization saturation bands) is considered as the standard of reference CMR technique for the assessment of regional LV deformation²⁵; however, main limitations of this technique are the application of tagging lines to the thin wall of RV myocardium and the complex and time-consuming procedure of data acquisition and postprocessing.^{26,27} The new feature-tracking CMR software system applied in this study overcomes these challenges; as recently demonstrated, it compares favorably with CMR tagging and relies on the basic cine CMR sequences without any need for a specific encoding pulse.²⁸⁻³⁰ In this study, the entire feature-tracking CMR analytic process of the RV was feasible in all patients; even though not specifically evaluated, it was short, requiring few minutes, similarly to what previously reported for the LV by Augustine et al²⁸ and Onishi et al.³¹ In addition, the learning curve was steep, and an inexperienced user could be able to accurately perform the analysis after a brief training. Consequently, feature-tracking analysis may be added as a routine procedure in the CMR laboratory, especially if the reproducibility of the measurements, particularly in the radial direction, would be improved in future versions of the feature-tracking software system.

In this study, impaired RV regional and global strain and significant RV mechanical dispersion was observed among patients with ARVC when compared with controls and among patients with RVOT-A. Of note, the ability of RV strain and dyssynchrony parameters to differentiate ARVC from RVOT-A seems to be clinically relevant, considering that RVOT-A is a primary electric disorder that is frequently in differential diagnosis with ARVC but is rarely associated to functional and structural RV abnormalities and has a good prognosis.^{32,33} Interestingly, the abnormalities observed in patients with ARVC seemed to precede overt RV functional changes because they were recognized even among patients without RV wall motion abnormalities, impaired RV ejection fraction or RV dilatation.

At ROC curve analysis, RV GLS $>-23.2\%$, longitudinal SD-TPS >113.1 ms, and circumferential SD-TPS >177.1 ms had the highest sensitivity and specificity for identification of patients with ARVC; of note, applying these cut-off values, most ARVC patients with no or only minor CMR criteria for ARVC diagnosis according to the 2010 task force criteria were correctly recognized, fulfilling the need for more sensitive CMR parameters for early diagnosis of this pathology. This finding suggests a potential incremental diagnostic value of these parameters over conventional cine CMR imaging criteria.

Study Limitations

This study has some limitations that should be acknowledged. First, the study population was relatively small, with a high prevalence of patients fulfilling major CMR imaging criteria; consequently, our results need to be confirmed by further prospective studies with larger sample size, including a higher proportion of patients with subtler or earlier disease. Second, reproducibility of strain and dyssynchrony parameters was good in the longitudinal and particularly circumferential directions, whereas it was suboptimal in the radial direction; improvement to the feature-tracking software system is, therefore, needed to further enhance the reproducibility of the analyses. Third, T1-weighted sequences and late gadolinium enhancement imaging, which may allow detection of intramyocardial fat and replacement fibrosis, respectively, were not part of the CMR protocol because they are not considered by the 2010 revised task force criteria.⁵ For the same reason, T1 mapping, which may allow detection of extracellular volume expansion because of interstitial fibrosis, was not performed. Further studies are therefore needed to determine the incremental diagnostic value of these CMR techniques over conventional cine CMR imaging. Fourth, clinical follow-up data were not available; consequently, no information can be provided about the incremental prognostic role of strain and dyssynchrony parameters in ARVC. To this end, larger studies with long-term follow-up are necessary.

Conclusions

Feature-tracking CMR helps to quantify global and regional RV strain and RV dyssynchrony in patients with ARVC; in addition, it provides incremental value over conventional cine CMR imaging, allowing the identification of abnormalities even when overt RV functional changes (ie, wall motion

abnormalities, impaired RV ejection fraction, and RV dilatation) are absent.

Disclosures

None.

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CLINICAL PERSPECTIVE

Analysis of right ventricular (RV) regional dysfunction by cardiac magnetic resonance (CMR) imaging in arrhythmogenic RV cardiomyopathy (ARVC) may be inadequate because of the complex contraction pattern of the RV. Measurement of myocardial deformation by strain analysis is an emerging tool to quantitatively assess regional and global chamber systolic function and mechanical dispersion and may overcome the weakness of subjective assessment of RV regional wall motion abnormalities. In this study, the use of RV strain and dyssynchrony assessment in ARVC using feature-tracking CMR analysis was evaluated. Patients with ARVC were found to have impaired RV regional and global strain and significant RV mechanical dispersion, compared with patients with idiopathic RV outflow tract arrhythmias and controls, even when regional and global RV function were preserved or RV dilatation was absent. Of note, analysis of RV strain and dyssynchrony by feature-tracking CMR allowed correct identification of most ARVC patients with no or only minor CMR criteria for ARVC diagnosis according to the 2010 task force criteria. Accordingly to these observations, strain analysis by feature-tracking CMR may provide incremental value over conventional cine CMR imaging, helping the physician to objectively quantify global and regional RV dysfunction and RV dyssynchrony in patients with ARVC. However, some improvement to the feature-tracking software system is still needed to enhance the reproducibility of the analyses.