Right Ventricular Strain and Dyssynchrony Assessment in Arrhythmogenic Right Ventricular Cardiomyopathy
Cardiac Magnetic Resonance Feature-Tracking Study

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Background—Analysis of right ventricular (RV) regional dysfunction by cardiac magnetic resonance (CMR) imaging in arrhythmogenic right ventricular 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±5% versus −26±6% versus −29±6%; P<0.001), global circumferential strain (−9±4% versus −12±4% versus −13±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

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See Editorial by Bluemke
See Clinical Perspective

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. The clinical manifestations of ARVC are mainly electric disorders with potentially life-threatening ventricular arrhythmias. Diagnosis is established on multiple criteria, first published in 1994, then revised in the 2010 consensus, in which echocardiographic and cardiac magnetic resonance (CMR) imaging play a significant role. 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 imaging modality for the evaluation of RV dimension and function. However, analysis of regional wall motion abnormalities may still be inadequate because of the complex RV contraction pattern. 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. 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
assessment of RV strain and dysynchrony 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 criteria\(^5\) 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 dysynchrony (ie, mechanical dispersion). For comparison purpose, 32 patients with idiopathic RV outflow tract arrhythmia (ie, RVOT-A), a primary electric disorder that is frequently 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. 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 trigger and to obtain optimal image acquisition.

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.\(^2\) 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-axis 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
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.

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.

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.
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 1. Baseline Characteristics of the Study Population

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

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.

Table 2. CMR Characteristics of the Study Population

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=32)</th>
<th>RVOT-A (n=32)</th>
<th>ARVC (n=32)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVEDV index (mL/m²)</td>
<td>71 (63–77)</td>
<td>74 (60–87)</td>
<td>108 (98–129)*,†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVEDV index &lt;100 mL/m² in males and &lt;90 mL/m² in females</td>
<td>32 (100%)</td>
<td>31 (97%)</td>
<td>8 (25%)*,†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVESV index (mL/m²)</td>
<td>20 (14–24)</td>
<td>21 (16–28)</td>
<td>48 (39–76)*,†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>71±8</td>
<td>71±7</td>
<td>50±14*,†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVEF &gt;45%</td>
<td>32 (100%)</td>
<td>32 (100%)</td>
<td>17 (53%)*,†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regional RV WMAs</td>
<td>0 (0%)</td>
<td>3 (9%)</td>
<td>31 (97%)*,†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDV index (mL/m²)</td>
<td>77±14</td>
<td>77±14</td>
<td>89±18‡,§</td>
<td>0.004</td>
</tr>
<tr>
<td>LVESV index (mL/m²)</td>
<td>26±10</td>
<td>27±10</td>
<td>36±15‡,§</td>
<td>0.002</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>67 (62–75)</td>
<td>66 (62–69)</td>
<td>62 (57–66‡,§</td>
<td>0.011</td>
</tr>
<tr>
<td>Regional LV WMAs</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (16%)*,†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>57 (50–65)</td>
<td>60 (49–65)</td>
<td>52 (47–59)</td>
<td>0.068</td>
</tr>
</tbody>
</table>

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.
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(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±5% versus −26±6% versus −29±6%; P<0.001), RV global circumferential strain (−9±4% versus −12±4% versus −13±4%; 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 [115–32] 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±6% versus −26±6% versus −29±6%; P<0.001 and 146±85 ms versus 68±47 ms versus 50±23 ms; P<0.001, respectively), or only ARVC patients with nondilated RV, defined as RV end-diastolic volume index <100 mL/m² in males and <90 mL/m² in females (−20±5% versus −26±6% versus −29±6%; P=0.004 and 123±89 ms versus 62±35 ms versus 50±23 ms; P<0.001). Similarly, differences

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

<table>
<thead>
<tr>
<th></th>
<th>Intraobserver CV, %</th>
<th>Interobserver CV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global longitudinal strain</td>
<td>8.6</td>
<td>9.9</td>
</tr>
<tr>
<td>Global circumferential strain</td>
<td>4.1</td>
<td>5.6</td>
</tr>
<tr>
<td>Global radial strain</td>
<td>13.1</td>
<td>16.0</td>
</tr>
<tr>
<td>Longitudinal SD-TPS</td>
<td>13.6</td>
<td>15.0</td>
</tr>
<tr>
<td>Circumferential SD-TPS</td>
<td>11.6</td>
<td>13.8</td>
</tr>
<tr>
<td>Radial SD-TPS</td>
<td>17.1</td>
<td>20.9</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=32)</th>
<th>RVOT-A (n=32)</th>
<th>ARVC (n=32)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All RV segments</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal longitudinal strain (%)</td>
<td>−35±15</td>
<td>−35±14</td>
<td>−22±11†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid-longitudinal strain (%)</td>
<td>−26±11</td>
<td>22±12</td>
<td>−15±8‡,§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apical longitudinal strain (%)</td>
<td>−25±11</td>
<td>−22±12</td>
<td>−14±8‡,</td>
<td></td>
</tr>
<tr>
<td>Basal circumferential strain (%)</td>
<td>−13±4</td>
<td>−12±4</td>
<td>−8±4†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid-circumferential strain (%)</td>
<td>−12±5</td>
<td>−11±4</td>
<td>−8±5‡</td>
<td>0.003</td>
</tr>
<tr>
<td>Apical circumferential strain (%)</td>
<td>−15±6</td>
<td>−14±7</td>
<td>−14±7</td>
<td>0.82</td>
</tr>
<tr>
<td>Basal radial strain (%)</td>
<td>30 (23–41)</td>
<td>25 (19–34)</td>
<td>20 (13–28¶)</td>
<td>0.007</td>
</tr>
<tr>
<td>Mid-radial strain (%)</td>
<td>27 (17–32)</td>
<td>20 (14–30)</td>
<td>15 (10–19¶)</td>
<td>0.002</td>
</tr>
<tr>
<td>Apical radial strain (%)</td>
<td>19 (13–24)</td>
<td>14 (9–24)</td>
<td>15 (9–29)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

RV segments with wall motion abnormalities excluded

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=32)</th>
<th>RVOT-A (n=32)</th>
<th>ARVC (n=32)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal longitudinal strain (%)</td>
<td>−35±15</td>
<td>−35±14</td>
<td>−27±10</td>
<td>0.18</td>
</tr>
<tr>
<td>Mid-longitudinal strain (%)</td>
<td>−26±11</td>
<td>−22±12</td>
<td>−17±9#</td>
<td>0.021</td>
</tr>
<tr>
<td>Apical longitudinal strain (%)</td>
<td>−25±11</td>
<td>−22±12</td>
<td>−14±8‡,§</td>
<td>0.002</td>
</tr>
<tr>
<td>Basal circumferential strain (%)</td>
<td>−13±4</td>
<td>−12±4</td>
<td>−9±4‡</td>
<td>0.002</td>
</tr>
<tr>
<td>Mid-circumferential strain (%)</td>
<td>−12±5</td>
<td>−11±4</td>
<td>−8±6#</td>
<td>0.016</td>
</tr>
<tr>
<td>Apical circumferential strain (%)</td>
<td>−15±6</td>
<td>−14±7</td>
<td>−15±8</td>
<td>0.79</td>
</tr>
<tr>
<td>Basal radial strain (%)</td>
<td>30 (23–41)</td>
<td>25 (19–34)</td>
<td>19 (11–27¶)</td>
<td>0.004</td>
</tr>
<tr>
<td>Mid-radial strain (%)</td>
<td>27 (17–32)</td>
<td>20 (14–30)</td>
<td>16 (11–22¶)</td>
<td>0.021</td>
</tr>
<tr>
<td>Apical radial strain (%)</td>
<td>19 (13–24)</td>
<td>14 (9–24)</td>
<td>17 (10–27)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Data are expressed as mean±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.
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 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.

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.

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 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
conclusive diagnostic test. 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 dysynchronous RV contraction. 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. However, analysis of regional wall motion abnormalities may still be cumbersome because of the complex contraction pattern of the RV. Moreover, 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; 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.

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. 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 deformation; 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. 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. 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 al and Onishi et al. 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.

**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.
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.12,23 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.2 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.

**References**


**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 dyssynchrony in patients with ARVC. However, some improvement to the feature-tracking software system is still needed to enhance the reproducibility of the analyses.
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