Diagnostic Concordance of Echocardiography and CMR-Based Tissue Tracking for Differentiating Constrictive Pericarditis from Restrictive Cardiomyopathy

Amaki et al: LV Mechanics in Constriction and Restriction

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Abstract

**Background**—Variations in longitudinal deformation of the left ventricle (LV) have been suggested to be useful for differentiating chronic constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM). We assessed LV mechanics derived from cardiac magnetic resonance (CMR) cine–based and two-dimensional (2D) echocardiography-based tissue-tracking to determine inter-modality consistency of diagnostic information for differentiating CP from RCM.

**Methods and Results**—We retrospectively identified 92 patients who underwent both CMR and 2D echocardiography and who had a final diagnosis of CP (n=28), RCM (n=30), or no structural heart disease (n=34). Global longitudinal strain (GLS) from long-axis views and circumferential strain from short-axis views were measured on 2D echocardiographic and CMR cine images using the same off-line software. Logistic regression models with receiver operating characteristics curves, continuous net reclassification improvement (NRI), and the integrated discrimination improvement (IDI) were used for assessing the incremental predictive performance. GLS was higher in patients with CP than in those with RCM (P<0.001), and both techniques were found to have similar diagnostic value (area under the curve, 0.84 vs. 0.88 for CMR and echocardiography, respectively). For echocardiography, the addition of GLS to respiratory septal shift and early diastolic mitral annular velocity resulted in improved continuous NRI (P< 0.001 for both) and IDI (P=0.005 and 0.024) for both models. Similarly, for CMR, the addition of GLS to septal shift and pericardial thickness resulted in improved continuous NRI (P<0.001 for both) and IDI (P=0.003 and <0.001).

**Conclusions**—CMR and echocardiography tissue-tracking-derived LV mechanics provide comparable diagnostic information for differentiating CP from RCM.

**Key Words:** pericarditis, cardiomyopathy, echocardiography, magnetic resonance imaging
Differentiating constrictive pericarditis (CP) from restrictive cardiomyopathy (RCM) in patients with right heart failure can be a challenge. Cardiac catheterization, while often performed for hemodynamic confirmation, may not always be conclusive.\textsuperscript{1,2} This has led to continued interest in other diagnostic modalities. Several echocardiographic measurements have been proposed to differentiate myocardial diseases from pericardial constriction.\textsuperscript{3,4} Cardiac magnetic resonance (CMR) imaging has superior contrast-to-noise and signal-to-noise ratios, permitting accurate quantification of pericardial thickening and providing assessment of the entire thorax.\textsuperscript{5} As noninvasive imaging techniques continue to advance, the clinical differentiation of CP from RCM is based on the recognition of a cluster of structural, mechanical and hemodynamic aberrations rather than a single structural or functional variable used in isolation. Specifically the recent growth in tissue-tracking software allows myocardial functional data to be extracted from both echocardiography and CMR images with equal ease and accuracy.\textsuperscript{6-8} An emphasis on inter-modality comparison may permit consistent data collection for serial comparisons. We therefore sought to compare the diagnostic value of strain measurements derived from two-dimensional (2D) echocardiography-based and CMR cine–based tissue-tracking methods for differentiating CP from RCM.

\textbf{Methods}

\textbf{Patient Population}

The institutional review board at the Mount Sinai Medical Center approved the protocol. We retrospectively identified 92 patients who underwent both transthoracic echocardiography and CMR imaging between May 2006 and May 2013. This included 28 patients with CP, 30 patients with RCM, and 34 control patients who had no structural or functional abnormality on
echocardiography or CMR. The control subjects were age- and gender-balanced to the mean values obtained for both CP and RCM. Among these subjects, 80 (87%) had both imaging tests with a median interval between the tests of 2.0 days and interquartile range of 12 to 21 days, while twelve subjects (13%) had both examinations on the same day.

**Cardiac Magnetic Resonance Imaging**

CMR was performed using either a 1.5-T magnet (Magnetom Sonata, Siemens Medical Solutions, Erlangen, Germany; Optima MR450w, General Electric, Milwaukee, USA) or a 3.0-T magnet (Ingenuity TF scanner, Philips, Best, The Netherlands) and a dedicated surface coil with retrospective electrocardiographic gating, as previously described.9-11 Contiguous cine short-axis views were acquired using steady-state free precession imaging at end-expiratory breath-holds. Left ventricle (LV) end-diastolic (EDV) and end-systolic volumes (ESV), ejection fraction (EF), and mass were obtained according to the Simpson’s method using specialized software and indexed to body surface area. The presence of increased pericardial thickness (>4mm)12, and septal shifts during respiration13 were reported. Constrictive physiology on CMR was defined by increased LV- right ventricle (RV) coupling as defined by visual determination of septal shifts during respiration.14

Findings consistent with RCM in CMR included normal or thickened right- and left-ventricular walls, normal or small LV cavity size, and enlarged atria. Gadolinium-enhanced CMR was also performed and the presence of circumferential delayed enhancement involving the entire subendocardium and extending into the surrounding myocardium was considered typical for amyloidosis15, the most common underlying etiology for RCM. Other patterns—including
localized enhancement with a vascular distribution, and focal or subepicardial delayed enhancement, were excluded. Three experienced, blinded readers (J. Sanz and two colleagues) reviewed the CMRs.

**Echocardiographic-Doppler Studies**

All patients had comprehensive 2D echocardiogram and Doppler studies, performed and interpreted according to American Society of Echocardiography standards. Three different commercially-available ultrasound machines were used (Philips IE33 system, Philips Medical Systems, Andover, Massachusetts; Acuson 512, Siemens Medical Solutions USA, Inc., Mountain View, CA; Vivid 7; GE Vingmed Ultrasound AS, Horten, Norway). From the apical four and two-chamber views LVEDV, LVESV, and LVEF were calculated using the biplane modified Simpson’s method, and left atrial (LA) volume index was calculated using the biplane area length method. LV mass index (LVMI) was derived from the parasternal long axis view using M-mode measurements. Findings consistent with CP on echocardiography included plethora of the inferior vena cava, abnormal motion of the interventricular septum, respiratory variation of LV inflow velocities, and increased expiratory hepatic vein flow reversal, as has been previously described. The echocardiographic findings of RCM were similar to those described for CMR (with the exception of delayed enhancement imaging), as well as restrictive filling pattern of transmural flow and reduced tissue-Doppler peak early-diastolic mitral-annular velocities.
Diagnosis of CP and RCM

The identification of subjects with CP for inclusion was based on a previously described diagnostic paradigm. We included patients presenting with heart failure with preserved EF (>50%) in whom the initial echocardiographic assessment suggested CP and who fulfilled at least one of four additional criteria: (1) surgically confirmation during pericardiectomy; (2) cardiac catheterization findings consistent with CP; (3) evidence of thickened pericardium (thickness >4 mm by CMR); or, (4) evidence of increased LV-RV coupling (septal shift with respiration) by both echo and CMR.4,23,24 The catheterization criteria included two or more of the following criteria: (1) a difference between left ventricular end-diastolic pressure and right ventricular end-diastolic pressure of ≤5 mm Hg; (2) pulmonary arterial systolic pressure <55 mm Hg; (3) a ratio of right ventricular end-diastolic pressure to right ventricular systolic pressure of >1/3; (4) inspiratory decrease in pulmonary capillary wedge pressure/left ventricular end-diastolic pressure difference of >5 mm Hg; and, (5) systolic area index >1.1.24 A total of 24 patients (86%) were referred for pericardiectomy, with preoperative cardiac catheterization in 22 patients (79%). Four patients without surgical referral were managed with medical therapy because of end-stage malignancy. Of the patients who were referred for pericardiectomy, 16 (57%) underwent partial or complete removal of the pericardium, 3 (11%) refused the operation, 2 (7%) were deemed too high risk for the procedure and three (11%) were lost to follow up. Of the 12 patients who did not undergo pericardiectomy, the criteria for diagnosing CP were fulfilled using cardiac catheterization in 6 (21%) patients, by demonstration of echocardiographic feature of CP and thickened pericardium in 4 (14%) and by demonstration of increased LV-RV coupling on echocardiography and CMR in 2 (7%) patients.
The diagnosis of RCM was made by presence of all of the following echocardiographic features: 1) an interventricular septum greater than 12 mm, 2) preserved EF (>50%), 3) bialtrial enlargement, and 4) restrictive filling pattern, as well as delayed gadolinium-enhanced CMR evidence of myocardial involvement.

**Strain Analysis by Tissue Tracking in CMR and in Echocardiography**

Gray-scale echocardiographic images were saved with a frame rate of 25-40 frames/second and CMR cine images were obtained with a temporal resolution <50 msec and reconstructed into 20-25 phases per cardiac cycle. The images were digitally stored in the Digital Imaging and Communications in Medicine platform (The National Electrical Manufacturers Association). Strain measurements were performed using the vendor-customized offline 2D Cardiac Performance Analysis software for the echocardiography (2D-CPA version 1.1.3) and for CMR (2D-CPA MR version 1.1.2.36) (TomTec Imaging Systems GmbH, Unterschleissheim, Germany). The software enabled measurement of the angle-independent, 2D strain previously validated with sonomicrometry and tagging CMR both in echocardiography\textsuperscript{25,26} and CMR.\textsuperscript{27} 2D-CPA determines myocardial motion based on the user-defined myocardial border; endocardial borders are traced throughout one cardiac cycle. From this motion, myocardial velocity and strain components are calculated for endocardial regions along the trace.\textsuperscript{28} Measurements of LV longitudinal strain by CMR were derived from the two-, three-, and four-chamber views, and circumferential strain from short-axis views at the level of the papillary muscles.\textsuperscript{29} Global longitudinal strain for both techniques was expressed as the average endocardial strain value from apical four-chamber and two-chamber views as previously described because the apical three-chamber view in patients with CP was frequently suboptimal.\textsuperscript{4} To obtain differences in
septal versus lateral wall deformation, LV septal-wall strains and lateral-wall strains were measured by averaging strains from three segments in each wall. The peak values for all strain parameters were recorded and analyzed. Figure 1 shows examples of longitudinal strains in CP, RCM and controls in both modalities. The offline analysis was performed independently by one observer (M.A.) who was not involved in image acquisition. The retrospective review of electronic medical records and offline analysis of stored echocardiography and CMR images for the present study was approved by institutional review board of Mount Siani Hospital.

Statistical Analysis

Continuous data were reported as the median and interquartile range within each group, and categorical data as numbers and percentages. For continuous variables the differences between the groups were evaluated with Kruskal-Wallis test because the majority of the variables showed skewed distribution in one or more groups. For categorical variables, the chi-square test was used. Mann-Whitney tests for pairwise comparisons with Bonferroni-adjusted levels were used to assess differences among groups. We performed a logistic regression analysis to determine univariate echocardiographic predictors for differentiating RCM from CP. The univariate predictors were subsequently entered into stepwise multivariable logistic regression analysis. The comparison of ROC curves was performed according to the method described by DeLong et al.\textsuperscript{30} using Medcalc Software (version 12.7.1.0; Mariakerke, Belgium), with p-value reported for a two-sided test. We also determined the incremental value of GLS by comparing logistic regression models with and without GLS in addition to the known echocardiographic and CMR discriminators between CP and RCM. For this, we used four characteristics that capture conceptually differing domains of incremental value: (1) information content (quantified as
Akaike information criterion, AIC); (2) diagnostic accuracy (measured as area under receiver operating characteristics curve (ROC curve); (3) improved discrimination (measured as improvement discrimination index, IDI); and, (4) reclassification (measured as net reclassification index, NRI). We used the R package PredictABEL\(^31\) to estimate continuous NRI and IDI\(^32,33\) and MedCalc to determine AIC and AUC. All significance values for improvement were one-sided. Interobserver agreement and intraobserver consistency were presented using interclass correlation coefficients and a 95% confidence interval (95% CI). A \(P\) value <0.05 was considered significant.

### Results

**Clinical Characteristics, echocardiographic and CMR measurements**

The etiology of CP was previous cardiac surgery in 7 (25%), post pericarditis in 6 (21%), malignancy in 2 (7%) and post radiation in 1 patient (4%). The remaining 12 patients (43%) had idiopathic CP. Of the patients with RCM, 11 (37%) had cardiac biopsy proven amyloidosis and 11 (37%) had extracardiac biopsy suggesting cardiac amyloidosis. The etiology of myocardial restriction could not be determined in the remaining 8 patients (27%).

Table 1 summarizes the clinical characteristics, conventional echocardiographic measurements, and CMR measurements of the three groups. CP patients had higher heart rates than (\(P=0.02\)) RCM patients. Other parameters, including sex, body surface area, blood pressure and the percentage of atrial fibrillation and coronary artery disease risk factors were comparable between the CP and RCM groups.
With respect to the echocardiographic findings, in comparison with CP patients, those with RCM had significantly higher LV wall thickness and LV mass index, lower septal early diastolic mitral annular velocity (e’), and higher E/e’ (P<0.001 for all). Other echocardiographic parameters including LV dimensions, and transmitral flow characteristics, and LA volume index demonstrated no significant difference between the two disease groups. Both CP and RCM had preserved LVEF (EF>50%), although the absolute values for LVEF was marginally lower for RCM patients. Septal shifts and > 25% respiratory variation in LV inflow velocities were seen in 25 (89%) and 11 (39%) patients with CP, respectively. Mild-to-moderate mitral regurgitation was found in three CP patients and six RCM patients. Six patients with CP and two patients with RCM had mild to moderate tricuspid regurgitation.

CMR measurements also revealed higher LVMI in RCM but LVEF was comparable between the two groups. Respiratory septal shifts were seen in 22 patients (79%) with CP. Delayed contrast CMR was performed in 19 patients (68%) with CP and revealed pericardial enhancements in 10 patients and focal subsegmental myocardial enhancements in two. In comparison, multi-segmental diffuse enhancement was seen in all RCM patients.

**Strain Analysis by Echocardiogram and CMR**

Echocardiography-derived GLS was significantly reduced in the RCM group compared with the CP (P<0.001) and control (P<0.001) groups (Table 2, Figure 2). The ratio between lateral and septal longitudinal strain was not significantly different among the three groups (P=0.78). Similarly, patients with RCM had marginally lower circumferential strains when compared with CP (P=0.07).
Similar to echocardiography, CMR-derived GLS was reduced in the RCM group compared with the CP (P<0.001) and control groups (P<0.001). The ratio between lateral to septal longitudinal strain showed no difference among three groups, as with echocardiography (P=0.20). Circumferential strain was also comparable between the CP and RCM (P=0.07).

Echocardiography and CMR derived GLS were correlated and did not significantly differ (mean difference 0.7, limits of agreement -6.3 to 7.7%) (Figure 3).

Multivariable analysis

Using logistic regression analysis we identified LV EF (OR= 0.93; 95% CI, 0.87-0.99; P=0.036); LV MI (OR=1.075; 95% CI, 1.039-1.112; P<0.001); e’ (OR=0.45; 95% CI, 0.29-0.68; P<0.001); respiratory septal shift (OR= 0.004; 95% CI, 0.000-0.043; P<0.001) and GLS (OR= 1.72; CI, 1.29-2.30; P<0.001) as echocardiographic predictors for differentiating RCM from CP. On stepwise multivariable logistic regression, GLS (OR=2.44; CI, 1.06-5.60, P=0.034) and septal shift (OR=0.002; CI, 0-0.195, p=0.009) were independent predictors for differentiating CP from RCM.

Diagnostic Value of Global Longitudinal Strain

The receiver-operating curve for GLS derived by echocardiography and CMR for differentiating RCM from CP is shown in Figure 4. The area under the curve was comparable for both CMR and echocardiographic-derived GLS. Table 3 shows summary measures of different aspects of logistic regression models exploring the incremental value of GLS over known echocardiographic and CMR discriminators. The overall model fit (Akaike information criterion, AIC) was significantly improved when echocardiographically-derived GLS was added
individually to septal shift and e’ (P=0.001 and 0.0020 respectively). Addition of GLS to septal shift and e’ also resulted in significant improvement in continuous NRI (P< 0.001 for both models) and IDI (P=0.0057 and 0.024 respectively).

Similarly, for CMR, the addition of GLS to respiratory septal shift and pericardial thickness resulted in significant improvement in AIC (P= 0.0022 and 0.0014 respectively), continuous NRI (P<0.001 for both models) and IDI (P=0.003 and <0.001 respectively).

**Reproducibility**

Interclass correlation coefficients are shown in Table 4. All significant parameters demonstrated good reproducibility when tested for inter-observer and intra-observer variability.

**Discussion**

The diagnosis of CP\textsuperscript{34} and RCM\textsuperscript{35, 36} by CMR has previously been described. Aside from pericardial thickening, exaggerated respiratory-related LV-RV coupling, defined as the difference in the maximal septal excursion between inspiration and expiration, has been demonstrated to discriminate CP from RCM and from normal hearts.\textsuperscript{13} However, the use of CMR tissue-tracking strain for differentiating LV mechanics in CP and RCM has not been previously reported. In this study CMR-measured GLS had similar diagnostic value as echocardiography-derived GLS for distinguishing CP from RCM. The results of our work underscore the value of extracting more diagnostic variables from a single modality, particularly for conditions in which a constellation of diagnostic parameters (structural, mechanics or hemodynamic) are needed to recognize a specific pattern of disease such as CP and RCM.\textsuperscript{37} Such
assessment increases the cost efficacy and conviction in following a patient or identifying an interval change in disease severity using a single technique.

**Myocardial deformation in CP and RCM**

Several previous investigations have shown that LV longitudinal motion and diastolic-lengthening velocities are impaired to a greater degree in RCM compared with CP.21, 38-40 We have also previously demonstrated that longitudinal shortening strain is significantly reduced in RCM compared with CP, reflecting marked impairment of endocardial function3. Similar observations were reported by Kusunose et al4, who additionally illustrated the incremental value of the lateral-to-septal strain ratio over regional velocities in discriminating CP from RCM. Since the free wall of the LV is tethered in CP, LV lateral wall shortening strains are seen to be lower than septal shortening strains. However, the prior studies have analyzed LV deformation using techniques that are not resolved for the layers of the LV wall. In the present investigation we derived strain selectively from the subendocardial region of the LV (average 4 pixel spatial resolution). The addition of GLS using such a uniform strategy for both echocardiography and CMR showed incremental value. In particular, the use of GLS using cine CMR images showed incremental value over pericardial thickness and assessment of LV-RV coupling by septal shift during respiration. Such assessments may have value for situations where gadolinium contrast enhancement is not used or are relatively contraindicated.41

Both echocardiography and CMR data showed concordant diagnostic information and incremental value for differentiating CP from RCM. However, in contrast to previously reported findings, we found that among CP patients the septal shortening strains were similar to those in
the lateral wall, and the endocardial shortening strains in the circumferential direction were similar for all three groups. These differences from prior studies may be related to the selective sampling from the subendocardial region which is spared from myocardial tethering. Indeed in a previous experimental model of pericardial adhesion we demonstrated that myocardial motion is reduced due to pericardial adhesions over the epicardial surface, however, the epi-to-endocardial gradient of myocardial function remained unaltered, suggesting that endocardial shortening proceeds relatively normally despite the process of epicardial adhesions.\textsuperscript{42}

Our results suggest that the pericardial-myocardial functional relationships are more complex, and that a constrictive pericardium may alter myocardial function differentially in the myocardial layers. Perhaps with improved spatial resolution, in the near future investigations could be undertaken to resolve the transmural gradient of strains in patients with CP and RCM.

\textbf{Study Limitations}

The present study has limitations. First, our patients were evaluated in a tertiary referral center and were referred for CMR; therefore, a selection bias may be present. While patients with structural heart disease were excluded from the control population; these patients still had risk factors for heart disease, such as hypertension and diabetes mellitus. This may partly explain the lower GLS values in the control subjects.

Only two patients with CP had minimal myocardial involvement on delayed gadolinium enhanced CMR. This may not be representative of all subgroups of CP, such as radiation related CP where concomitant myocardial involvement may also affect myocardial deformation.\textsuperscript{43}
Further studies that provide more in-depth assessment of role of LGE, a powerful technique to identify the pattern and the extent of myocardial abnormalities for differentiating CP from RCM, are needed.

The RCM group was predominantly comprised of amyloid cardiomyopathy. Consequently, ventricular wall thickness was statistically different between the two groups with different values by CMR and echocardiography. The over estimation of LVMI by echocardiography may be related to geometric assumptions. Cardiac magnetic resonance does not require cardiac geometry assumptions, as opposed to linear measurements and formulae used in echocardiography. Despite these differences, the CP and RCM patients in our study had classic diagnostic features and are comparable to those in recent studies. Moreover, the use of both CMR and echocardiography helped to clearly define these patient populations and enabled the exploration of differences in LV mechanics.

A final limitation concerns the quantitative estimates of strain obtained from echocardiography and CMR. There were differences in the type of imaging data, differences in views (less foreshortening on CMR), and the frame rates obtained by both techniques. The feature tracking software used for computing strains has been shown to work at lower frame rates due to the combination of speckle-tracking, endocardial tissue-blood border (edge detection) and the periodicity of the cardiac cycle used in this feature tracking algorithm (also used in the current study). Despite these limitations, the correlation between tissue tracking strain values from both techniques are similar to previously published data for both modalities. Moreover, the substantial concordance in patient characterization suggests potential diagnostic value.
Conclusions

CMR and echocardiography tissue-tracking-derived LV mechanics provide concordant information that is useful for differentiating CP from RCM.

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Disclosures

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References


<table>
<thead>
<tr>
<th>Clinical characteristic</th>
<th>CP (n=28)</th>
<th>RCM (n=30)</th>
<th>Control (n=34)</th>
<th>P value</th>
</tr>
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<tr>
<td>Age, y</td>
<td>60 (48, 69)</td>
<td>64 (59, 76)</td>
<td>61 (55, 66)</td>
<td>0.182</td>
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<tr>
<td>Men, n (%)</td>
<td>19 (68)</td>
<td>20 (67)</td>
<td>19 (56)</td>
<td>0.550</td>
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<td>Body surface area, cm²</td>
<td>1.88 (1.70, 2.06)</td>
<td>1.93 (1.78, 2.05)</td>
<td>1.92 (1.78, 2.07)</td>
<td>0.687</td>
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<td>Systolic BP, mmHg</td>
<td>117 (110.0, 124.0)</td>
<td>109.5 (102.0, 130.0)</td>
<td>123.0 (110.0, 136.0)</td>
<td>0.045</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>70.0 (65.0, 73.0)</td>
<td>67.0 (60.0, 74.0)</td>
<td>72.0 (67.0, 83.0)</td>
<td>0.016</td>
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<td>Heart rate, bpm</td>
<td>83.5 (72.0, 94.5)</td>
<td>73.0 (68.0, 81.0)</td>
<td>70.0 (65.0, 80.0)</td>
<td>0.009</td>
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<td>Atrial fibrillation, n (%)</td>
<td>4 (14)</td>
<td>3 (10)</td>
<td>0 (0)</td>
<td>0.090</td>
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<td>Hypertension, n (%)</td>
<td>11 (39)</td>
<td>14 (47)</td>
<td>18 (53)</td>
<td>0.474</td>
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<td>Hyperlipidemia, n (%)</td>
<td>10 (36)</td>
<td>14 (47)</td>
<td>17 (50)</td>
<td>0.510</td>
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<td>Diabetes, n (%)</td>
<td>8 (29)</td>
<td>5 (17)</td>
<td>8 (24)</td>
<td>0.354</td>
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<td>Smoking, n (%)</td>
<td>8 (29)</td>
<td>7 (23)</td>
<td>8 (24)</td>
<td>0.872</td>
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<tr>
<td>Familial history of CAD, n (%)</td>
<td>3 (11)</td>
<td>3 (10)</td>
<td>5 (15)</td>
<td>0.610</td>
</tr>
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**Echocardiogram**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>CP</th>
<th>RCM</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV septum, mm</td>
<td>8.0 (7.0, 9.5)</td>
<td>13.5 (12.0, 15.0)</td>
<td>10.0 (8.2, 10.8)</td>
<td>&lt;0.001</td>
</tr>
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<td>LV Dd, mm</td>
<td>42.0 (37.0, 46.0)</td>
<td>41.0 (38.0, 45.0)</td>
<td>46.6 (42.0, 50.2)</td>
<td>0.002</td>
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<tr>
<td>LV Ds, mm</td>
<td>26.0 (23.0, 28.0)</td>
<td>28.0 (25.0, 29.0)</td>
<td>27.6 (25.6, 32.2)</td>
<td>0.103</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>60.5 (50.5, 72.5)</td>
<td>124.5 (107.0, 147.0)</td>
<td>81.0 (75.0, 119.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E wave, m/sec</td>
<td>79.5 (70.0, 97.5)</td>
<td>99.0 (79.5, 116.3)</td>
<td>69.0 (57.6, 83.3)</td>
<td>&lt;0.001</td>
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<tr>
<td>A wave, m/sec</td>
<td>49.0 (39.0, 66.5)</td>
<td>38.0 (28.0, 49.0)</td>
<td>67.5 (56.5, 76.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E / A wave</td>
<td>1.55 (1.30, 2.00)</td>
<td>2.50 (2.10, 2.90)</td>
<td>0.95 (0.80, 1.30)</td>
<td>&lt;0.001</td>
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<td>DT, msec</td>
<td>184.5 (136.5, 202.0)</td>
<td>138.5 (127.0, 159.5)</td>
<td>230.0 (188.3, 270.3)</td>
<td>&lt;0.001</td>
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<td>e', cm/sec</td>
<td>9.9 (9.0, 13.3)</td>
<td>5.2 (4.1, 6.4)</td>
<td>7.4 (6.1, 9.8)</td>
<td>&lt;0.001</td>
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<td>E / e'</td>
<td>8.0 (5.7, 11.3)</td>
<td>18.4 (14.8, 23.6)</td>
<td>8.5 (7.1, 12.5)</td>
<td>&lt;0.001</td>
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<td>LAV index, mL/m²</td>
<td>41.0 (30.0, 53.0)</td>
<td>45.0 (31.0, 52.0)</td>
<td>28.0 (23.8, 36.0)</td>
<td>&lt;0.001</td>
</tr>
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**CMR**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>CP</th>
<th>RCM</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EDV, mL</td>
<td>114.5 (95.5, 147.0)</td>
<td>146.5 (124.0, 166.0)</td>
<td>125.5 (113.0, 147.5)</td>
<td>0.011</td>
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<tr>
<td>LV ESV, mL</td>
<td>41.5 (34.0, 68.5)</td>
<td>63.5 (53.0, 75.0)</td>
<td>49.0 (40.0, 57.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>60.5 (56.5, 67.0)</td>
<td>54.5 (50.0, 61.0)</td>
<td>63.0 (56.8, 66.0)</td>
<td>0.066</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>44.3 (40.4, 62.9)</td>
<td>87.3 (63.0, 113.6)</td>
<td>53.8 (44.2, 63.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CP=constrictive pericarditis; RCM= restrictive cardiomyopathy; BP=blood pressure; CAD=coronary artery disease; LV=left ventricle; Dd=diastolic dimension; Ds=systolic dimension; EF=ejection fraction; LVMI=left ventricular mass index; E=early transmital diastolic flow; A=late transmital diastolic flow; DT=deceleration time; e’ = septal early diastolic mitral annular velocity; LAV=left atrial volume; IVC=inferior vena cava; EDV=end diastolic volume; ESV=end systolic volume
Values are median (interquartile range); P value across three groups by Kruskal-Wallis test and chi square test for categorical value
*, p<0.05; †, p<0.01 vs. CP;‡, p<0.05; §, p<0.01 vs. RCM by Mann-Whitney tests
∥, Focal enhancement in CP patients and diffuse enhancement in RCM patients
Table 2. Echocardiography and CMR Derived Strain Characteristics

<table>
<thead>
<tr>
<th></th>
<th>CP (n=28)</th>
<th>RCM (n=30)</th>
<th>Control (n=34)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Echocardiogram</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LS (4ch), %</td>
<td>-17.2 (-20.3, -15.0)</td>
<td>-13.0 (-14.7, -9.0)†</td>
<td>-17.2 (-21.7, -12.9)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LS (2ch), %</td>
<td>-17.0 (-21.6, -15.5)</td>
<td>-11.0 (-14.3, -9.4)†</td>
<td>-18.0 (-23.4, -16.8)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLS[1], %</td>
<td>-18.5 (-20.1, -15.2)</td>
<td>-11.6 (-14.6, -9.3)†</td>
<td>-18.2 (-20.4, -16.2)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal LS (4ch), %</td>
<td>-17.6 (-21.7, -13.8)</td>
<td>-12.3 (-14.6, -8.5)†</td>
<td>-16.8 (-20.9, -12.4)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lateral LS (4ch), %</td>
<td>-17.5 (-22.1, -15.7)</td>
<td>-12.9 (-15.2, -7.5)†</td>
<td>-17.4 (-23.2, -14.2)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lat/Sep LS ratio (4ch)</td>
<td>0.90 (0.85, 1.25)</td>
<td>1.00 (0.90, 1.15)</td>
<td>1.10 (0.90, 1.30)</td>
<td>0.781</td>
</tr>
<tr>
<td>Mid CS, %</td>
<td>-23.9 (-28.3, -20.2)</td>
<td>-19.3 (-23.3, -16.0)</td>
<td>-26.2 (-30.3, -18.8)</td>
<td>0.070</td>
</tr>
<tr>
<td><strong>Cardiac MR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LS (4ch), %</td>
<td>-17.6 (-21.7, -15.0)</td>
<td>-12.2 (-14.2, -10.0)†</td>
<td>-17.2 (-20.4, -15.0)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LS (2ch), %</td>
<td>-20.0 (-23.6, -15.0)</td>
<td>-13.9 (-17.0, -11.6)†</td>
<td>-19.6 (-22.6, -14.6)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LS (3ch), %</td>
<td>-18.6 (-21.3, -14.6)</td>
<td>-13.9 (16.7, -10.0)†</td>
<td>-19.6 (-22.6, -14.6)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLS[1], %</td>
<td>-18.8 (-22.3, -15.4)</td>
<td>-13.3 (-14.7, -11.8)†</td>
<td>-18.3 (-20.4, -16.5)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal LS (4ch), %</td>
<td>-19.3 (-22.0, -14.8)</td>
<td>-12.6 (-15.4, -8.8)†</td>
<td>-17.0 (-19.4, -11.6)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lateral LS (4ch), %</td>
<td>-16.5 (-20.9, -14.3)</td>
<td>-11.5 (-14.9, -9.6)†</td>
<td>-18.8 (-22.4, -14.9)§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lat/Sep LS ratio (4ch)</td>
<td>0.99 (0.76, 1.14)</td>
<td>0.93 (0.77, 1.50)</td>
<td>1.19 (0.79, 1.73)</td>
<td>0.204</td>
</tr>
<tr>
<td>Mid CS, %</td>
<td>-26.5 (-30.3, -21.7)</td>
<td>-23.2 (-26.1, -18.5)</td>
<td>-26.8 (-31.2, -20.9)§</td>
<td>0.024</td>
</tr>
</tbody>
</table>

CP=Constrictive pericarditis; RCM= restrictive cardiomyopathy; LS=longitudinal strain; GLS=global longitudinal strain; Mid=LV short axis at mid level; CS=circumferential strain

Values are median (interquartile range), P value across three groups by Kruskal-Wallis test and chi square test for categorical value.

* p<0.05; † p<0.01 vs. CP; ‡ p<0.05; § p<0.01 vs. RCM by Mann-Whitney tests

[1] Global strain was derived by the average of 4ch and 2ch.
Table 3. Incremental value of global longitudinal strain over echocardiographic and CMR variables for differentiating CP from RCM

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Echo</th>
<th>CMR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LV-RV vs. LV-RV + GLS</td>
<td>e’ vs. e’ + GLS</td>
</tr>
<tr>
<td>Difference</td>
<td>P</td>
<td>Difference</td>
</tr>
<tr>
<td>AIC</td>
<td>8.49</td>
<td>0.0018</td>
</tr>
<tr>
<td>ΔAUC</td>
<td>0.053</td>
<td>0.0282</td>
</tr>
<tr>
<td>NRI (95% CI)</td>
<td>1.40 (1.03 – 1.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IDI (95% CI)</td>
<td>0.09 (0.02 – 0.16)</td>
<td>0.0057</td>
</tr>
</tbody>
</table>

AIC, Akaike information criterion; ΔAUC, difference in the area under the ROC curve; NRI, net reclassification index (continuous); IDI, incremental discrimination index (continuous); CI, 95% confidence interval; LV-RV, LV-RV coupling assessed by septal shifts; PT, pericardial thickening; CMR, cardiac magnetic resonance.
### Table 4. Interobserver and Intraobserver Variability

<table>
<thead>
<tr>
<th></th>
<th>Interobserver Variability</th>
<th>Intraobserver Variability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICC</td>
<td>95% CI</td>
</tr>
<tr>
<td>Echo GLS</td>
<td>0.93</td>
<td>0.75-0.98</td>
</tr>
<tr>
<td>Echo mid CS</td>
<td>0.89</td>
<td>0.61-0.97</td>
</tr>
<tr>
<td>CMR GLS</td>
<td>0.93</td>
<td>0.76-0.98</td>
</tr>
<tr>
<td>CMR mid CS</td>
<td>0.94</td>
<td>0.79-0.98</td>
</tr>
</tbody>
</table>

Intraobserver and interobserver variability were assessed in 12 randomly selected from each group of patients. Interobserver agreement and intraobserver consistency were presented by using interclass correlation coefficients (ICCs) and a 95% confidence interval (95% CI).

Echo=Echocardiography, GLS=global longitudinal strain, CS=circumferential strain, CMR=cardiac magnetic resonance
Figure Legends

**Figure 1.** Longitudinal strain (LS) measured from both echocardiogram and CMR images using apical four-chamber view in a patient with constrictive pericarditis (A and B), restrictive cardiomyopathy (C and D) and control (E and F).

**Figure 2.** Box plot showing median global longitudinal strain (GLS) derived by echocardiogram (Echo) and CMR (A and B) in patients with constrictive pericarditis (CP), restrictive cardiomyopathy (RCM), and controls.

**Figure 3.** Correlation plot showing Global longitudinal strain (GLS) from echocardiogram (Echo) and CMR in patients with constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM) (A). Brand-Altman plot of Echo and CMR derived GLS (B).

**Figure 4.** Area under the curve (AUC) to discriminate constrictive pericarditis (CP) from restrictive cardiomyopathy (RCM) using global longitudinal strain (GLS) derived by echocardiography (Echo) and CMR images.
A

Y = -5.3383 + 0.6939 X
r = 0.68, p < 0.001

B

Echo and CMR GLS, %

Echo - CMR GLS, %

CP
RCM

+1.96 SD
7.7
Mean
0.7
-1.96 SD
-6.3
Sensitivity

100
80
60
40
20
0

100-Specificity

0
20
40
60
80
100

Echo GLS; AUC 0.883
CMR GLS; AUC 0.836
Diagnostic Concordance of Echocardiography and CMR-Based Tissue Tracking for Differentiating Constrictive Pericarditis from Restrictive Cardiomyopathy

Makoto Amaki, John Savino, David L. Ain, Javier Sanz, Gianni Pedrizzetti, Hemant Kulkarni, Jagat Narula and Partho P. Sengupta

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