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Myocardial oedema in acute myocarditis detected by echocardiographic 2D myocardial deformation analysis

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Aims The clinical diagnosis of acute myocarditis is based on symptoms, electrocardiography, elevated myocardial necrosis biomarkers, and echocardiography. Often, conventional echocardiography reveals no obvious changes in global cardiac function and therefore has limited diagnostic value. Myocardial deformation imaging by echocardiography is an evolving method used to characterize quantitatively longitudinal systolic function, which may be affected in acute myocarditis. The aim of our study was to assess the utility of echocardiographic deformation imaging of the left ventricle in patients with diagnosed acute myocarditis in whom cardiovascular magnetic resonance (CMR) evaluation was performed.

Methods and results We included 28 consecutive patients (mean age 32 $\pm$ 13 years) with CMR-verified diagnosis of acute myocarditis according to the Lake Louise criteria. Cardiac function was evaluated by a comprehensive assessment of left ventricular (LV) function, including 2D speckle-tracking echocardiography. We found no significant correlation between the peak values of cardiac enzymes and the amount of myocardial oedema assessed by CMR (troponin: $r = 0.3$; $P = 0.05$ and CK-MB: $r = 0.1$; $P = 0.3$). We found a larger amount of myocardial oedema in the basal part of the left ventricle [American Heart Association (AHA) segments 1–6] in inferolateral and inferior segments, compared with the anterior, anterolateral, anteroseptal, and inferoseptal segments. In the mid LV segments (AHA segments 7–12), this was more pronounced in the anterior, anterolateral, and inferolateral segments. Among conventional echocardiographic parameters, LV function was not found to correlate with the amount of myocardial oedema of the left ventricle. In contrast, we found the wall motion score index to be significantly correlated with the amount of myocardial oedema, but this correlation was only present in patients with an extensive amount of oedema (>11% of the total left ventricle). Global longitudinal systolic myocardial strain correlated significantly with the amount of oedema ($r = 0.65$; $P < 0.001$). We found that both the epicardial longitudinal and the endocardial longitudinal systolic strains were significantly correlated with oedema ($r = 0.55$; $P = 0.003$ and $r = 0.54$; $P < 0.001$).

Conclusion In patients with acute myocarditis, 2D speckle-tracking echocardiography was a useful tool in the diagnostic process of acute myocarditis. Global longitudinal strain adds important information that can support clinical and conventional echocardiographic evaluation, especially in patients with preserved LV ejection fraction in relation to the diagnosis and degree of myocardial dysfunction.

Keywords myocarditis • cardiovascular magnetic resonance • speckle tracking • left ventricular function • myocardial oedema

Introduction

Establishing a clinical diagnosis of acute myocarditis is often hampered by a diffuse spectrum of symptoms ranging from sudden death and the new onset of arrhythmias and complete heart block to acute chest pain and flu-like symptoms.[1] The reported burden of myocarditis as a percentage of prevalent heart failure varies from ~0.5 to 4%.[2] This spectrum is probably due to an underestimation of myocarditis in the community. In clinical presentations matching acute myocarditis, the diagnosis is often established only after other medical conditions have been excluded by means of objective measures such as conventional echocardiography, electrocardiography,

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serological testing, and coronary angiography. To improve the quality of the diagnosis, endomyocardial biopsy (EMB), using the Dallas criteria, was established.[3] However, in cases with normal left ventricular (LV) ejection fraction (EF) and transient symptoms, EMBs are infrequently performed, among others, due to the inherent procedural risk of this invasive procedure.[4] More recently, cardiovascular magnetic resonance (CMR) has been used as a non-invasive diagnostic tool, offering a 79% accuracy rate, to underpin the diagnosis of acute myocarditis.[5] However, so far CMR as a stand-alone diagnostic tool neither adequately confirms the diagnosis of acute myocarditis nor provides sufficient prognostic value.[6,7] In addition, the accessibility of CMR is often limited, and evaluating using CMR requires substantial experience. Consequently, diagnosis of acute myocarditis by an objective measure remains problematic despite the need for a tailored therapeutic strategy (immunosuppressive, immunomodulatory, and/or antiviral) to reduce the risk of progression or manage recurrent symptoms.[8]

Conventional 2D echocardiography is often the initial imaging test, but its diagnostic accuracy is often limited.[9] In many patients with CMR-proven acute myocarditis, conventional echocardiographic measurements of LV function are normal. Promising algorithms to evaluate LV deformation have been introduced by 2D speckle-tracking echocardiography, which is an evolving method used to characterize myocardial function quantitatively. The measurement of myocardial deformation may offer better sensitivity than conventional echocardiography for the detection of subclinical LV dysfunction.[10] It may therefore improve the diagnostic accuracy in acute myocarditis patients, which is relevant especially when conventional echocardiographic parameters of the left ventricle are normal.

The aim of our study was to assess the utility of echocardiographic deformation imaging of the left ventricle in patients with diagnosed acute myocarditis in whom CMR evaluation was performed. We report the results of global, regional, and layer-specific myocardial deformation analysis using 2D speckle-tracking echocardiography. We compare and correlate these results with the amount of myocardial oedema and conventional echocardiographic parameters in order to evaluate the usefulness of deformation analysis in patients with acute myocarditis.

Methods

Patient population

We prospectively identified patients in our institution who were diagnosed with acute myocarditis when discharged from hospital. We analysed the medical history, CMR, and echocardiographic data of 28 patients admitted to our institution between 2009 and 2015. After admission, all participants underwent a comprehensive echocardiography and a detailed CMR examination. Only patients with CMR-confirmed acute myocarditis were enrolled. Coronary angiography was performed on all patients to rule out significant coronary artery disease.

CMR acquisition protocol

Patients were scanned on an Ingenia 1.5T whole body scanner (Philips Healthcare, Best, the Netherlands). The diagnosis of myocarditis was based on the Lake Louise criteria.[11] First, a survey scan was performed to localize the heart and the diaphragm. To ensure a strong T2-weighting, a T2-STIR fast spin echo sequence with a long echo time was obtained in the short-axis orientation to assess myocardial oedema. The sequence was navigator-gated and cardiac-triggered. The following imaging parameters were used: repetition time (TR) 2400 ms, echo time (TE) 100 ms, echo train length 20, fat inversion time 180 ms, flip angle 90°, spatial resolution 0.54 × 0.54 mm in-plane, number of averages 2, slice thickness 8 mm, field of view (FOV) 320 × 320 mm, and 14 slices. Subsequently, an intravenous bolus dose of 0.1 mmol/kg Gd-DTPA (Gadobutrol, Gadovist, Bayer Schering Pharma, Berlin) was administered manually for the purpose of early enhanced cine imaging as a marker of hyperaemia, and late gadolinium enhancement (LGE) was used to identify myocardial fibrosis. LV function was assessed using a retrospective, electrocardiogram (ECG)-triggered Balanced-Steady-State-Free-Precession (B-SSFP) breath-hold cine sequence in the cardiac short-axis, vertical long-axis, and horizontal long-axis planes. In the cardiac short-axis plane, the left ventricular volume was completely encompassed by contiguous 8-mm slices with a spatial resolution of 1.22 × 1.22 mm and a FOV of 288 × 288 mm. The following imaging parameters were used: TR 3.0 ms, TE 1.5 ms, flip angle 60°, and 30 heart phases. LGE was acquired 15 min after the gadolinium injection using a 3D phase-sensitive, inversion recovery-prepared, T1-weighted gradient echo sequence with the following parameters: TR 5.78 ms, TE 2.78 ms, echo train length 20, inversion time ~320 ms, flip angle 25°, spatial resolution 1.5 × 1.5 mm, slice thickness 8 mm, FOV 350 × 350 mm, and 14 slices acquired in the LV short-axis plane with no interslice gap.

CMR analysis

All CMR studies were analysed blinded to clinical and echocardiographic data. The total volume and localization of tissue with oedema were evaluated offline using dedicated software for cardiac image analysis (Segment, Medviso AB, version 1.9 R3364). The 17-segment tomographic standard model [American Heart Association (AHA) definition] was applied to analyse segments 1–6 using the three corresponding basal short-axis images, and segments 7–12 using the three corresponding medial short-axis images. Apical segments (AHA segments 13–17) were excluded from the CMR oedema analysis since slow-flowing blood in the apex of the LV may mimic oedema. The LV area was manually traced in all slices, and the area corresponding to oedema was identified by an automated thresholding protocol (*K*-means mode). Planimetry was used to calculate the percentage of myocardium with oedema in the total myocardium in each segment (*Figure 1*). The diagnostic criteria defined by Caforio *et al.* were used.[12]

Transthoracic echocardiography

Comprehensive transthoracic echocardiography (TTE) was performed and interpreted in a blinded fashion. LV dimensions, volumes, EF, global longitudinal strain (GLS), and regional longitudinal systolic strain (RLS) were measured offline using standard methods. The LV EF was calculated by a modified biplane Simpson's method from apical four- and two-chamber views. GLS was measured by speckle-tracking echocardiography. This was obtained from 2D greyscale images of the apical four-chamber, two-chamber, and long-axis view with optimized focus on the LV and frame rate ≥ 60 frames/s. Duration of systole was defined in the five-chamber apical view by marking the aorta valve opening and closure from the continuous wave Doppler curve. Strain analyses were done in EchoPAC version 1.13.0 (GE, Vingmed). The LV borderline was manually traced in each apical plane, and motion tracking was performed automatically by the software. Peak systolic strain was determined both for epicardial, mid-wall and endocardial values in every segment of the ventricle. Global strain for the LV was provided by the software as the average value of the peak systolic longitudinal strain of the three

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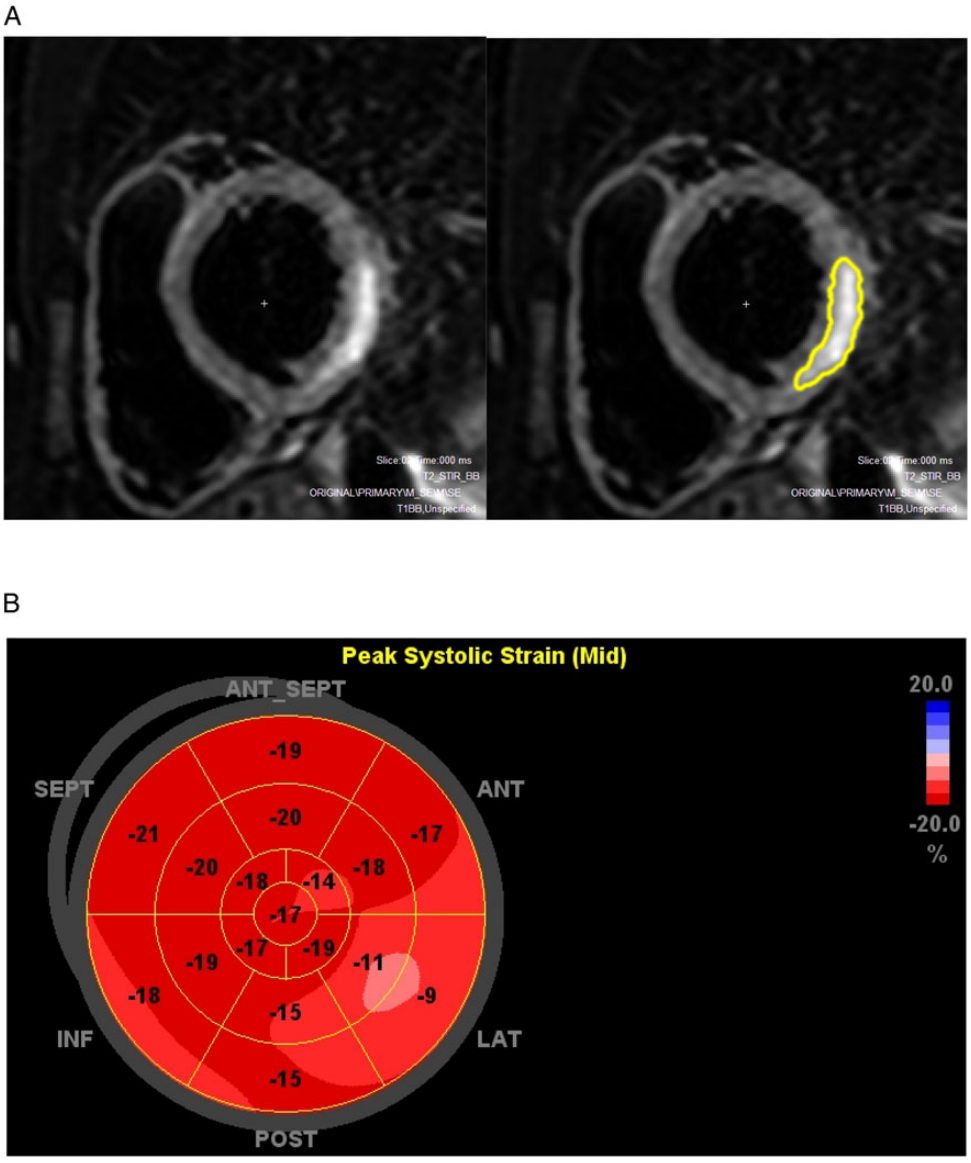

Figure 1 CMR image showing oedema in the LV and the oedema tracing (*A*). The corresponding deformation analysis according to myocardial layer by echocardiography is shown in *B*, *C*, and *D*. (*B*) Global systolic strain values showing the exact localization as visualized by CMR. (*C*) Epicardial strain values showing more decreased values compared with endocardial strain (see *D*). (*D*) Endocardial strain values.

apical views. *Figure 1* shows an example of deformation analysis in a patient with acute myocarditis showing non-multilayer and multilayer analyses.

Statistics

Normally distributed data are presented as mean ± standard deviation (SD). Categorical data are presented as absolute values with percentages. Histograms and Q–Q plots were used to check continuous values for normality. Between-group differences were assessed by *t*-test for normally distributed data and the Mann–Whitney *U* test for non-normally distributed data. Linear regression was used comparing continuous variables and predicted value, and the residual was used to check the regression models. Logistic regression was used in the univariate analysis. Furthermore, we decided in advance the maximum number of covariates ($n = 5$) according to sample size ($n = 28$). Covariate was selected by clinical perspective and applied in the multivariate linear regression model. All tests were two sided, and $P < 0.05$ was considered statistically significant. Analyses were performed using STATA (STATA/IC 12, StataCorp LP, College Station, TX, USA).

Reproducibility

Inter- and intra-observer agreement for longitudinal strain was assessed in all the subjects by two independent observers. The

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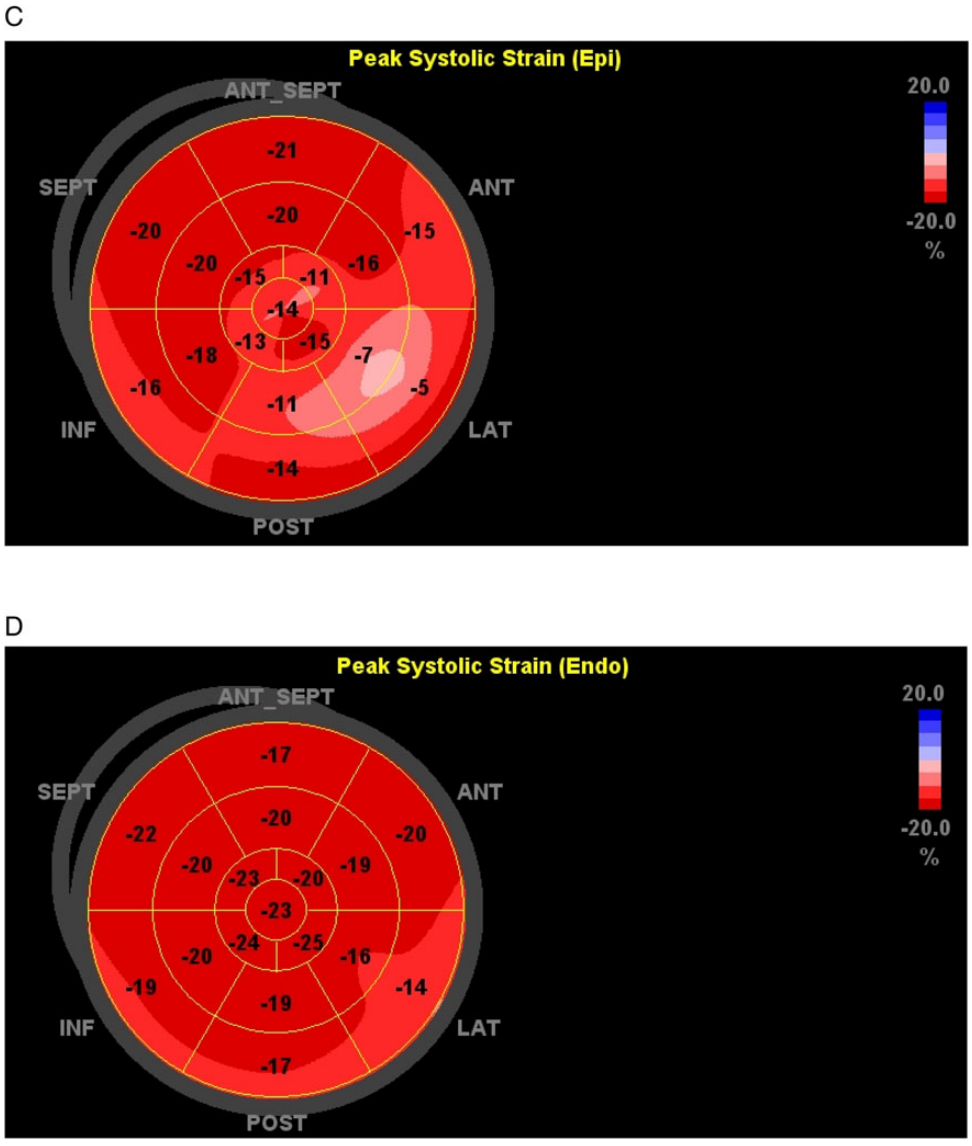

Figure 1 (Continued).

intra-observer agreement was measured 10 days later by a single independent observer. Reproducibility was analysed by interclass correlation coefficients (ICCs); the point estimates and the 95% confidence intervals (CIs) of the agreement rate were reported.

Results

All participants underwent a comprehensive echocardiographic examination and a detailed CMR scanning a mean of 2 days apart (range −10 to 14 days) after admission.

Baseline characteristics and echocardiographic parameters are shown in *Tables 1* and *2*. Mean age was 32 ± 13 years, 4 patients were female, and all patients presented with chest pain. Classic, diffuse ST-segment elevation on ECG was observed in 21 patients. Cardiac enzymes were elevated in all patients. The inflammatory parameters, i.e. C-reactive protein and/or leucocytes, were elevated in 21 of the 28 patients. Pericardial effusion was present in four patients; one patient had a large pericardial perfusion. All patients were free of any other concomitant disorders (hypertension, diabetes, dyslipidemia, and prior ischaemic heart disease), except one patient who suffered from colitis ulcerosa.

The amount of oedema by CMR is visualized in *Figure 2*. As shown in the figure, within the basal parts of the LV (AHA segments 1–6), myocardial oedema was more pronounced in the inferolateral and inferior segments than in the anterior, anterolateral, anteroseptal, and inferoseptal segments. In the mid LV segments (AHA segments 7–12), myocardial oedema was more pronounced in the anterior, anterolateral, and inferolateral segments.

We found no significant correlation between the peak values of cardiac necrosis markers and the amount of myocardial oedema as

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Table 1 Baseline characteristics

	Values
Age, years	31.9 ± 12.6
Gender, F/M	6/22
Height, cm	178 ± 11
Weight, kg	83.9 ± 19.3
Systolic blood pressure, mmHg	119.7 ± 12.9
Diastolic blood pressure, mmHg	74.3 ± 9.6
Pulse, bpm	78 ± 16
Temperature at admission, °C	37.7 ± 0.9
Paraclinical parameters[a]	
Haemoglobin, mmol/L	8.6 ± 1.3
Potassium, mmol/L	3.9 ± 0.3
Sodium, mmol/L	139 ± 28
Creatinine, μmol/L	73.7 ± 14.1
Plasma glucose, mmol/L	6.5 ± 1.6
C-reactive protein, mg/L	86.3 ± 106.7
Leucocytes, 10^9/L	9.6 ± 3.7
Peak troponin-T, μg/L	966.9 ± 768.5
Peak CK-MB, μg/L	38.5 ± 33.7
Total creatinine kinase, U/L	676.3 ± 1114.7

[a]Local laboratory reference intervals: haemoglobin (mmol/L): 8.3–10.5; potassium (mmol/L): 3.5–4.6; sodium (mmol/L): 137.145; creatinine (μmol/L): 45–90; plasma glucose (mmol/L): 4.2–7.8; C-reactive protein (mg/L): <8; leucocytes (10^9/L): 3.5–10.0; troponin-T (μg/L): >14; CK-MB (μg/L): <7; creatinine kinase (U/L): 50–200.

Table 2 Echocardiographic parameters

	Values
IVS diastolic, cm	0.9 ± 0.1
IVS systolic, cm	1.1 ± 0.1
LVIDD, cm	4.6 ± 0.5
LVIDS, cm	3.4 ± 0.8
LA diameter, cm	3.5 ± 0.5
Ejection fraction, %	54.4 ± 11
LVEDV, mL	120.1 ± 26.8
LVESV, mL	56.7 ± 17.3
WMSI	1.16 ± 0.1
Global deformation analysis	
Global longitudinal systolic strain, %	−16.2 ± 3.6
Global longitudinal systolic endocardial strain, %	−19.4 ± 3.9
Global longitudinal systolic epicardial strain, %	−14 ± 3
Circumferential strain (papillary muscle level), %	−16.5 ± 4.6
Circumferential endocardial strain (papillary muscle level), %	−24.4 ± 6.4
Circumferential epicardial strain (papillary muscle level), %	−11.4 ± 3.7

IVS, interventricular septum; LVIDD, left ventricular internal diameter diastolic; LVIDS, left ventricular internal diameter systolic; LA, left atrium; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume.

assessed by CMR (troponin-T: $r = 0.3$; $P = 0.05$ and CK-MB: $r = 0.1$; $P = 0.3$).

Using the conventional echocardiographic parameter LV EF, we found a significant correlation to the oedema amount assessed by CMR in the univariate analysis ($r = -0.44$; $P = 0.04$); however, in the multivariate analysis, it turned out to be non-significant ($P = 0.35$) (*Table 3*). We found that the wall motion score index (WMSI) correlated significantly with the oedema amount, although only in patients with oedema constituting >11% of the left ventricle (*Figure 3*).

In the univariate analysis, the GLS correlated significantly with the amount of oedema ($r = 0.65$; $P < 0.001$, *Figure 4*). Correcting in the multivariate analysis for blood pressure, heart rate, age, gender, cardiac necrosis markers, and days between echocardiography and CMR, we found a significant correlation between GLS and oedema assessed by CMR ($P = 0.004$) (*Table 3*). Furthermore, we found that both epicardial longitudinal- and endocardial longitudinal systolic strains significantly correlated with oedema ($r = 0.55$; $P = 0.003$ and $r = 0.54$; $P < 0.001$) (*Table 2*).

Segmental strain analysis is demonstrated in *Table 4*. Compared with segments without myocardial oedema, we observed a significant decrease in RLS in segments with oedema assessed by CMR according to AHA segment numbers 3, 5, and 11, and an almost significant difference in segment 9. We divided the segmental strain into the following regions: septal (AHA segments 3 + 4 + 9 + 10), anterior (AHA segments 1 + 2 + 7 + 8), and inferior (AHA segments 5 + 6 + 11 + 12). In the septal region, we found that deformation significantly decreased in segments with oedema vs. no oedema (−16.6 ± 3.2 vs. −18.1 ± 2.8; $P = 0.0001$). In the anterior region, we found no significant difference in deformation according to the presence of oedema (−15.7 ± 3.3 vs. −15.2 ± 3; $P = 0.2$). Finally, in the inferior region, there was a highly significant difference (−14.9 ± 2.8 vs. −17.1 ± 2.9; $P < 0.0001$). According to the inferior region, we observed a significant decrease in deformation in segments with oedema compared with the other regions [−14.9 ± 2.8 (inferior) vs. −16.6 ± 3.2 (septal); $P < 0.0001$ and −14.9 ± 2.8 (inferior) vs. −15.7 ± 3.3 (anterior); $P = 0.04$].

No significant correlation was observed between the amount of oedema and decreased deformation when analysing circumferential strain (global: $r = 0.3$, $P = 0.13$; epicardial: $r = 0.26$, $P = 0.19$; and endocardial: $r = 0.32$, $P = 0.1$). On the segmental circumferential strain level, we observed a more pronounced decrease in the inferolateral strain (−14.3 ± 6.6) according to location than in the other segments (anteroseptal: −18.1 ± 6.7; anterior: −17.2 ± 6.4; anterolateral: −15.6 ± 5.9; inferior: −16.1 ± 6.6; and inferoseptal: −18 ± 5.8). However, on segmental level, no correlation was observed between the amount of oedema and segmental strain values.

There was good inter-observer agreement for GLS with an ICC of 0.91 (95% CI 0.88–0.93). Intra-observer agreement for GLS was also very good with an ICC of 0.95 (95% CI 0.92–0.97).

Discussion

The present study represents a detailed analysis of global, regional, and layer-specific myocardial deformation by echocardiography in

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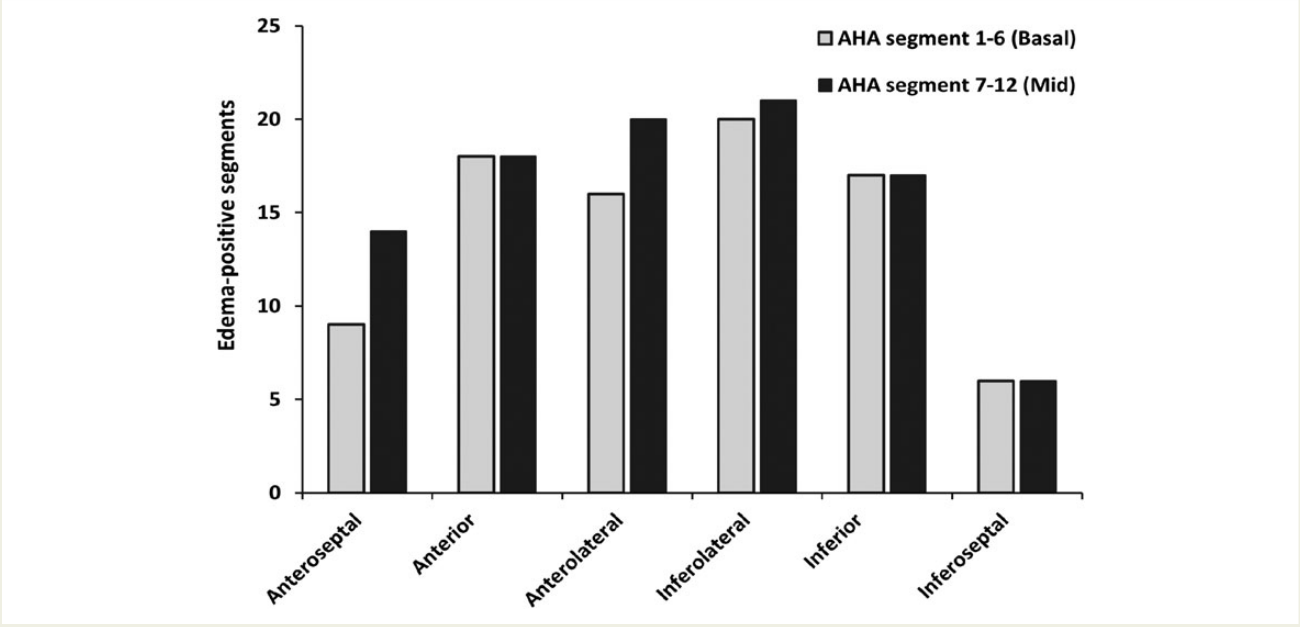

Figure 2 The regional distribution of oedema-positive segments by CMR.

Table 3 Univariate and multivariate predictors of oedema amount by CMR

	Univariate analysis *P*-value	Multivariate analysis[a] *P*-value
Age, years	0.7	
Gender, F/M	0.5	
Systolic blood pressure, mmHg	0.3	
Diastolic blood pressure, mmHg	0.3	
Heart rate, bpm	0.4	
Peak troponin-T, µg/L	0.13	
Days between CMR and echocardiography, *n*	0.3	
Left ventricular EF, %	0.04	0.35
WMSI	0.002	0.009
Global longitudinal systolic strain, %	<0.0001	0.004

[a]Correction for systolic blood pressure, diastolic blood pressure, heart rate, peak troponin-T, and days between CMR and echocardiography.

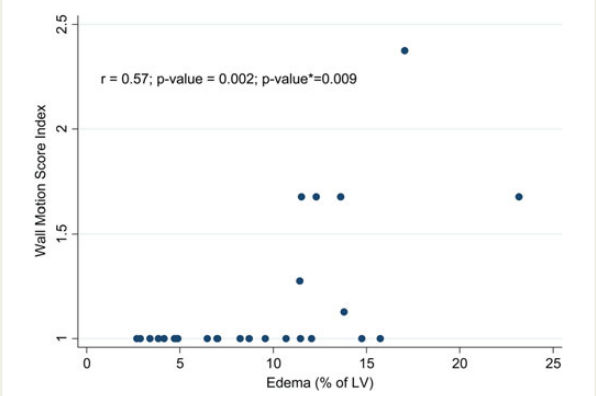

Figure 3 Correlation between WMSI and oedema in the left ventricle estimated by CMR. *Correction in multivariate regression model for systolic blood pressure, diastolic blood pressure, heart rate, peak troponin-T, and days between CMR and echocardiography.

patients with acute myocarditis, including an evaluation of myocardial oedema by CMR. The major finding of this study

(i) suggests that global and regional deformation analysis is more informative than conventional echocardiographic parameters for assessing the mechanics of LV function during acute myocarditis. The present findings confirm that longitudinal strain is a more significant indicator/determinant than visual assessment and EF to detect myocardial injury,

(ii) suggests no differences in the strain values obtain according to layer-specific myocardial deformation in acute myocarditis.

Global and regional longitudinal systolic strain analysis according to oedema

In keeping with previous studies, global and regional myocardial deformation was reduced in our patients.[13,14] We found a significant correlation between GLS and the amount of oedema independently

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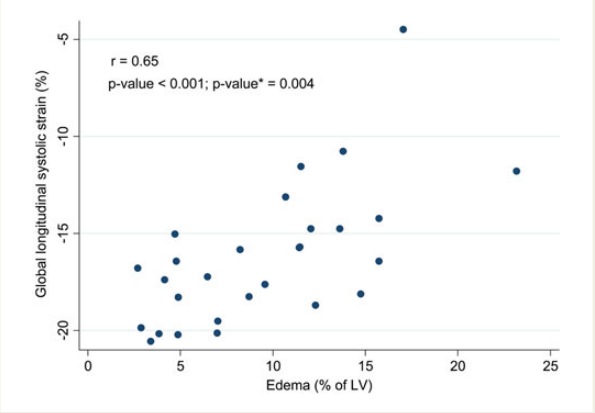

Figure 4 Correlation between global longitudinal systolic strain and oedema in the left ventricle estimated by CMR. *Correction in multivariate regression model for systolic blood pressure, diastolic blood pressure, heart rate, peak troponin-T, and days between CMR and echocardiography.

Table 4 Regional strain in segments according to the presence of oedema

AHA segment number	RLS (%) in segment with oedema	RLS (%) in segments without oedema	*P*-value
1	−14.4 ± 5	−14.5 ± 5.1	0.96
2	−15.5 ± 4.6	−14.9 ± 5.1	0.8
3	−13.8 ± 2.5	−16.3 ± 3	0.04
4	−16.4 ± 4.2	−17.3 ± 5	0.7
5	−12.7 ± 5.3	−16.9 ± 3.2	0.01
6	−15.6 ± 5.1	−15.6 ± 4.9	0.99
7	−15.9 ± 5.3	−13.3 ± 5.2	0.3
8	−17.1 ± 4.5	−18.1 ± 4.5	0.6
9	−17.1 ± 4.3	−19.5 ± 2.2	0.08
10	−18.9 ± 4.1	−19.4 ± 4.6	0.8
11	−14 ± 3.8	−16.7 ± 2.8	0.04
12	−17.2 ± 5.3	−19.3 ± 2.7	0.3
13–17	N/A	N/A	N/A

AHA, American Heart Association; GLS, global longitudinal systolic strain.

of conventional echocardiographic parameters, showing that myocardial deformation analysis is more likely to detect subtle changes or mild myocardial damage. Furthermore, we demonstrated that the presence of oedema was mainly localized in the infero-postero-lateral segments of the left ventricle assessed by CMR—which was also visualized by the predominance of an infero-postero-lateral segmental strain decrease by 2D speckle-tracking echocardiography. Although our findings suggest that LV myocardial deformation imaging gives additional information about the degree of cardiac involvement compared with conventional echocardiography, our findings indicate that CMR should also be considered in the diagnostic set-up in patients with suspected acute myocarditis.[15–18] However, we also propose that deformation imaging should be added to the diagnosis of myocarditis—especially in the cases of limited accessibility to CMR.

In the present study, we observed abnormal strain in segments with no oedema in CMR according to *Table 4*. However, comparing strain values on a single segment level should be evaluated with caution due to a great variability measuring individual myocardial segments. In the table, 9 out of 12 segments demonstrated larger strain values in the presence of oedema. Furthermore, it should be kept in mind that any comparison of imaging techniques may be hampered by possible misalignment in segmental analysis. Furthermore, it is possible that myocardial inflammation is present which is not detected by CMR as oedema.

Endocardial- and epicardial layer strain and circumferential strain

In keeping with our findings, previous studies have shown myocardial affection as a patchy distribution predominantly in the epicardial layer of the myocardium on the lateral free wall of the LV by CMR.[19,20] In theory, this would lead us to hypothesize a decreased epicardial strain compared with the endocardial strain values. Surprisingly, we found no direct correlation between either epicardial or endocardial strain and the amount of oedema. We observed alterations in the global strain parameters in terms of GLS reflecting the patchy distribution of myocardial oedema and late enhancement. Furthermore, it is important to recognize that deformation parameters within the ventricle and myocardial layers are not independent. Adjacent segments and myocardial fibres work in a complex way because of constancy of mass and volume. A deformation in the endocardial layer will result in a deformation in the epicardial layer even if this segment/layer is without any function resulting in a passive deformation. Furthermore, as previously observed in the normal human heart, we observed that GLS is higher in the endocardium than in the epicardium.[21]

We found a stronger correlation to oedema with longitudinal strain compared with circumferential strain. According to the constancy of mass and volume, theoretically, one may expect some correlation between longitudinal and circumferential strains.[22,23] An explanation for our observation could be a more pronounced alteration in the longitudinal direction according to oedema 'lesions', and furthermore, we cannot rule out the possibility that a larger sample size would reveal a significant difference also in circumferential strain values. We did observe at numerical difference according to location in circumferential strain values.

Deformation analysis and cardiac necrosis markers

Usually, acute myocarditis is a systematic disease caused by direct viral damage, or it is the consequence of an immune reaction, mediated by T-lymphocytes and antibodies directed against pathogens and similar endogenous heart epitopes and involves all of the myocardium, although without clinical sequels.[24–26] Cardiac necrosis markers such as troponin I have been found to have high specificity (89%) but limited sensitivity (34%) in the diagnosis of acute myocarditis.[27] We observed an increase in heart necrosis biomarkers in all patients; however, we found no correlation between

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the amount of oedema and biomarkers. The reason for this is most likely that the inflammatory process induced by acute myocarditis does not necessarily induce significant myocytolysis in all patients suffering from acute myocarditis. The standard Dallas pathological criteria defining myocarditis require that an inflammatory cellular infiltrate with or without associated myocyte necrosis is present on conventionally stained heart tissue sections.[28] Oedema induced by acute myocarditis may not be detected by conventional echocardiographic parameters unless the amount of oedema is considerable, involving >11% of the myocardium. However, most patients with acute myocarditis have less myocardial oedema involvement, which underlines the value of deformation imaging that detects all degrees of involvement.

Limitations

Our study represents a single-centre experience, using selected patients, and a relatively small sample size. So far, EMB is the gold standard for the diagnosis of myocarditis; but in patients without wall motion abnormalities and preserved EF, this approach seems unnecessary or even contraindicated.[4] Therefore, CMR is the primary tool for non-invasive assessment of myocardial inflammation in patients with acute myocarditis and normal systolic function. However, we acknowledge the lack of histopathological correlation.

The correlation between the GLS and the amount of oedema would probably have been stronger if both tests had been performed within a shorter time period, ideally the same day. This hypothesis, however, will need further testing in a larger, prospectively designed study. Furthermore, the effects of involving various vendors and post-processing software need to be investigated on a larger scale to obtain vendor-specific normative data and cut-offs.

The diagnosis of acute myocarditis on CMR requires multiple techniques, including T2-weigthed imaging to demonstrate myocardial oedema, early contrast enhancement to identify myocardial hyperaemia, and LGE to detect regional necrosis.[11] In terms of differentiating between myocardial oedema and myocardial necrosis in acute myocarditis, it is well recognized that there will often be an overlap between areas with oedema detected by T2-weighted imaging compared with areas with LGE. This is because in the early stages of necrosis, gadolinium enters the cells through acutely injured cell membranes due to an increased distribution volume. After the acute phase, the volume of distribution is increased into the extracellular space due to interstitial fibrosis. In consequence, the amount of myocardial necrosis by late gadolinium enhancement is often overestimated in the acute phase of myocarditis compared with scans performed at follow-up.

Finally, apical segments (AHA segments 13–17) were excluded from the CMR oedema analysis as well-known artefacts from slow-flowing blood in the apex of the LV may mimic oedema.

Conclusion

Myocardial deformation analysis obtained by 2D speckle-tracking echocardiography appears to be useful in evaluating the localization and degree of myocardial involvement in patients with acute myocarditis. The value of deformation analysis is particularly evident in patients with a preserved EF and without left ventricular wall motion abnormalities. Analysis of longitudinal myocardial strain is likely to improve conventional diagnostic investigations in suspected acute myocarditis, especially in cases where assess to CMR and/or myocardial biopsy is limited.

Conflict of interest: None declared.

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Spontaneous thrombosis of the ductus arteriosus in a newborn, complicated by thrombus migration and massive pulmonary embolism

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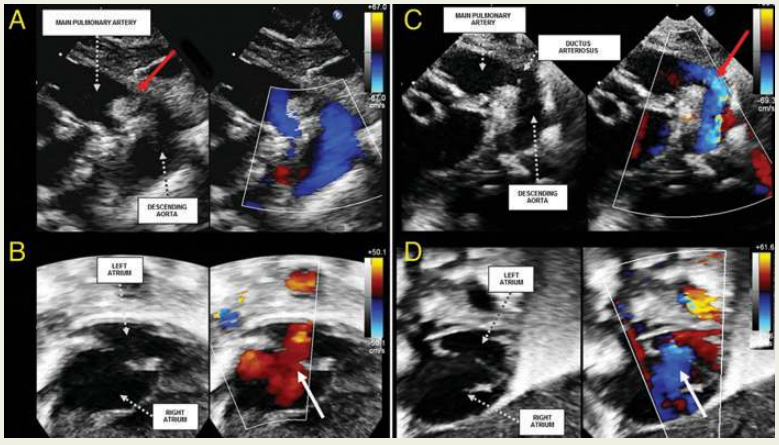

A 1-day-old term baby has been referred to our unit because of respiratory distress. A transthoracic echocardiography (*Panel A*; see Supplementary data online, *Movie S1*) was performed to rule out a congenital heart disease and showed a large thrombus (red arrow) at the pulmonary site of the patent ductus arteriosus, with no shunt. There was an associated secundum atrial septal defect (*Panel B*) with left to right shunt (white arrow). Anticoagulation therapy (subcutaneous enoxaparin) was started. Coagulation screening detected a heterozygous mutation for the methylenetetrahydrofolate reductase (MTHFR) gene, and an umbilical line had been inserted because of respiratory distress.

Twenty-four hours later a sudden clinical deterioration occurred, with acute severe systemic desaturation, increased respiratory distress associated with signs of cardiogenic shock (hypotension, oliguria, and increased lactate level). A new echocardiogram (*Panel C*; see Supplementary data online, *Movie S2*) could no longer demonstrate the presence of the thrombus in the ductal region. Right-to-left shunting across the duct (*Panel C*; red arrow, see Supplementary data online, *Movie S2*) suggested increased pulmonary vascular resistance. There was also right-to-left shunting across the atrial septum (*Panel D*, white arrow). The global RV systolic function was mildly impaired.

The critical clinical status did not allow any further clinical investigation, but the sudden deterioration associated with an acute increase of the pulmonary vascular resistance was very likely due to migration of the thrombus causing massive pulmonary embolism. Thrombolysis was considered but because of its high risk in neonates, we decided to maintain anticoagulation therapy increasing the inotropic support. A few hours later, the clinical condition improved, with increasing oxygen saturation and appearance of mainly left to right shunt across the ductus arteriosus and across the interatrial communication.

Supplementary data are available at *European Heart Journal—Cardiovascular Imaging* online.

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