The utility of speckle tracking imaging in the diagnostic of acute myocarditis, as proven by endomyocardial biopsy

Mario Kasner [a,1], David Sinning [a,1], Felicitas Escher [a], Dirk Lassner [a], Uwe Kühl [a], Heinz-Peter Schultheiss [a], Carsten Tschöpe [a,b,c,*]

[a] Department of Cardiology and Pneumology, Charité-Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany
[b] Berlin-Brandenburg Center for Regenerative Therapies, Berlin, Germany
[c] German Center for Cardiovascular Research (DZHK), Germany

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Acute myocarditis (AMC) accounts for up to 12% of sudden deaths in young adults [1]. Over a 3 to 10 year observation period, a 25 to 56% mortality rate was reported in AMC [2]. Diagnosing AMC at an early stage favorably affects its prognosis, but making the diagnosis remains challenging, because presenting symptoms vary highly, independent of ejection fraction (EF) [3]. Although a recent study showed that new magnet resonance imaging (MRI) techniques are able to offer a 79% accuracy in diagnosing AMC [4], no single parameter can sufficiently confirm the diagnosis or provide prognostic value [3,10]. Endomyocardial biopsy (EMB) serves as a widely accepted method in diagnosing AMC, but it is available at specialized departments only and may not be appropriate in every patient [5]. Strain rate and strain imaging by two dimensional (2D) speckle tracking is a new echocardiographic method to quantitatively characterize myocardial deformation [6]. In the setting of ischemic condition [7] and hypertrophic cardiomyopathy [8] it has been shown to detect left ventricular (LV) dysfunction even when conventional echocardiography shows normal values. It may therefore improve the diagnostic accuracy and provide a prognostic role in AMC patients, especially when EF is still preserved. We investigated this role by performing this method in patients, who presented with symptoms of AMC and in whom EMB was performed, at initial presentation and at 3 month follow-up.

34 patients, admitted to our department with suspected AMC, were enrolled in the study. The clinical diagnosis of AMC was met if the following criteria were satisfied: acute or newly developed symptoms (dyspnea, chest pain, exercise intolerance, fever, (pre-) syncope) and/or an evidence of myocardial damage (elevated biomarker Troponin T or CK/MB) with or without ECG abnormalities. EMB was performed in all patients. Echocardiographic examinations were performed prior to EMB and repeated at 3 month follow-up. All patients gave written consent for invasive diagnostic procedures. The research protocol was approved by the local institutional review committee.

According to the findings from EMB analyses, patients were divided into three groups:

1. No Inflammation: infiltrating lymphocytes < 7.0 cells/mm^2 (median cell count), macrophages < 35.0 cells/mm^2 (median cell count), absence of myocyte lysis, and no detection of viral genomes
2. Acute Myocarditis (AMC): infiltrating lymphocytes > 7.0 cells/mm^2 (median cell count), macrophages > 35.0 cells/mm^2 (median cell count), presence of myocyte lysis, and detection of viral genomes
3. Borderline Myocarditis (BL): infiltrating lymphocytes > 7.0 cells/mm^2 (median cell count), macrophages > 35.0 cells/mm^2 (median cell count), absence of myocyte lysis, and no detection of viral genomes

Patient characteristics are presented in Table 1. According to findings from EMB analyses 12 patients showed no myocardial inflammation, 14 showed acute myocardial inflammation, and 8 showed borderline inflammation. Echocardiographic results are also presented in Table 1. Patients, in whom AMC or BL was verified in EMB analyses, showed a significantly lower global longitudinal strain rate (GLSR) compared with those patients in whom no inflammation was seen. AMC and BL patients also showed a significantly reduced global longitudinal strain (GLS). Results of 2D strain as obtained by speckle tracking imaging at 3 month follow-up are presented in Fig. 1. GLSR and GLS did not significantly change at 3 month follow-up in the No Inflammation group, but were significantly reduced at 3 month follow-up in the AMC group. In the BL group GLSR was significantly reduced at 3 month follow-up compared with baseline results, whereas GLS did not change significantly. Out of the 14 patients, in whom AMC was confirmed in EMB analyses, 9 patients showed an improved EF at 3 month follow-up. Retrospective analysis revealed a significantly higher GLSR at baseline in these patients.

The distinct value of this study is the correlation of myocardial deformation imaging results with immunohistological findings as obtained by EMB in patients with suspected AMC. We showed that strain rate and strain imaging by 2D speckle tracking provides incremental diagnostic and prognostic information. GLSR and GLS were significantly impaired in patients with myocardial inflammation. This correlation was independent from conventional 2D echocardiographic parameters showing that strain rate and strain imaging is more sensitive in the detection of early changes or mild myocardial damage. Moreover, patients with impaired strain rate and strain at the acute phase of the disease showed worse short-time echocardiographic follow-up results.

Diagnosing AMC remains challenging. Clinical history, physical examination, ECG, and serology have been shown not to be reliable [3]. Conventional 2D echocardiography is unspecific, particularly in patients with a preserved EF [9]. Cardiac MRI has been found not to be accurate in patients with low level or no inflammation [10,4]. Thus, EMB remains the gold standard in diagnosing AMC. However, prior to performing this invasive procedure it remains essential to non-invasively identify AMC as a differential diagnosis. In our study strain rate and strain imaging by 2D speckle tracking proved to play an additional diagnostic role. Advanced NYHA class, bi-ventricular heart failure and the evidence of Q-wave in the ECG are major clinical predictors for poor outcome [5]. However, only few studies investigated the predictive value of non-invasive imaging tools. According to our follow-up echocardiographic analyses, we found that the level of myocardial deformation impairment might also

* Corresponding author at: Department of Cardiology and Pneumology, Charité-University Medicine Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, 12203 Berlin, Germany. Tel.: +49 30 8445 4780; fax: +49 30 8445 4648.
E-mail address: carsten.tschoepe@charite.de (C. Tschöpe).

Table 1
Patient characteristics, conventional echocardiography, TDI, and speckle tracking strain rate and strain imaging.

	Patient population (n = 34)	No Inflammation (n = 12)	Acute Myocarditis (n = 14)	Borderline Myocarditis (n = 8)	p value
Demographics					
Men, n (%)	28 (82.3)	10 (83.3)	11 (78.6)	7 (87.5)	NS
Age, y	41.06 [± 14.32]	39.67 [± 13.21]	44.14 [± 15.85]	37.75 [± 13.84]	NS
BMI, kg/m^2	26.81 [± 5.21]	25.82 [± 4.43]	27.23 [± 5.59]	27.5 [± 6.05]	NS
NT-proBNP, pg/ml	1554.25 [± 1508.43]	1387.2 [± 1545.98]	1683.75 [± 2086.58]	1660 [± 1040.96]	NS
Concomitant disease					
Art. hypertension, n (%)	9 (26.5)	3 (25)	3 (21.4)	3 (37.5)	NS
Diabetes mellitus, n (%)	3 (8.8)	2 (16.7)	1 (7.2)	0	NS
Hyperlipoproteinemia, n (%)	5 (14.7)	2 (16.6)	2 (14.3)	1 (12.5)	NS
Smoker, n (%)	12 (35.3)	5 (41.7)	3 (21.4)	4 (50)	NS
Heart dimensions					
LA, mm	39.7 [± 7.68]	37.10 [± 6.10]	38.43 [± 8.05]	41.5 [± 9.46]	NS
LVEDD, mm	55.32 [± 10.51]	53.53 [± 10.99]	53.5 [± 8.45]	58.5 [± 13.41]	NS
LVESD, mm	39.38 [± 14.57]	38.36 [± 14.46]	37.4 [± 12.12]	45.6 [± 20.33]	NS
Septum, mm	11.36 [± 1.71]	10.56 [± 2.08]	11.43 [± 1.7]	11.5 [± 1.93]	NS
Posterior wall, mm	10.56 [± 1.54]	10.33 [± 1.44]	10.71 [± 1.49]	10.62 [± 1.92]	NS
LV mass index, g/m^2	117.15 [± 48.19]	107.89 [± 33.26]	115.68 [± 28.32]	130.88 [± 49.42]	NS
Conventional echocardiography					
LVEF, %	48.68 [± 19.4]	52.25 [± 19.05]	48.79 [± 22.3]	43.13 [± 14.94]	NS
Mitral flow					
E, m/s	0.82 [± 0.14]	0.87 [± 0.15]	0.78 [± 0.11]	0.8 [± 0.17]	NS
A, m/s	0.6 [± 0.2]	0.59 [± 0.22]	0.6 [± 0.21]	0.6 [± 0.17]	NS
E/A	1.52 [± 0.58]	1.65 [± 0.64]	1.45 [± 0.49]	1.46 [± 0.67]	NS
TDI					
S′, m/s	5.22 [± 2.85]	6.51 [± 2.97]	4.69 [± 2.3]	3.18 [± 2.64]	NS
E′, m/s	3.5 [± 2.18]	6.64 [± 3.76]	3.68 [± 3.17]	5.91 [± 1.98]	NS
A′, m/s	5.35 [± 3.45]	3.71 [± 1.74]	3.83 [± 2.75]	2.25 [± 1.69]	NS
E/E′	14.05 [± 6.21]	13.48 [± 6.78]	15.17 [± 6.62]	13.78 [± 5.1]	NS
Global speckle tracking					
GLSR, 1/s	0.94 [± 0.36]	1.24 [± 0.26]	0.79 [± 0.27]	0.65 [± 0.31]	0.006[a]/0.005 ↑
GLESR, 1/s	1.01 [± 0.45]	1.18 [± .0.43]	0.94 [± 0.51]	0.81 [± 0.32]	NS
GLASR, 1/s	0.64 [± 0.21]	0.71 [± 0.17]	0.65 [± 0.25]	0.48 [± 0.13]	0.034 ↑
GLS, %	12.62 [± 5.74]	17.86 [± 3.86]	10.24 [± 4.12]	8.51 [± 4.88]	0.005[a]/0.008 ↑

↑ No Inflammation vs. Borderline Myocarditis group.
Data are reported as mean ± standard deviation.
Patient characteristics (variable expressed as median [± standard deviation]). BMI indicates body mass index; LA, left atrial parasternal diameter; LVEDD, LV end-diastolic diameter; LVM, LV mass; LVMI, LV mass index; TnT, Troponin T; and NT-proBNP, N-terminal pro-brain natriuretic peptide.
Conventional echocardiography, TDI, and speckle tracking strain rate and strain imaging (variable expressed as median [± standard deviation]). LVEF indicates LV ejection fraction; E, early mitral flow peak velocity; A, late mitral flow peak velocity; S′, systolic diastolic peak velocity of mitral annulus at lateral site; E′, early diastolic peak velocity of mitral annulus at lateral site; A′, late diastolic peak velocity of mitral annulus at lateral site; and E/E′, LV filling index.
[a] No Inflammation vs. Acute Myocarditis group.

provide a prognostic role. Patients with proven myocarditis, who had revealed an impairment of longitudinal strain rate or strain at baseline, showed no recovery of LV function and persistence of symptoms, implicating a progressive myocardial disease; recovered strain values at follow-up examination might indicate a better prognosis.

In conclusion, we were able to prove the additional role of strain rate and strain imaging obtained by 2D speckle tracking in patients with suspected AMC. This holds true particularly in patients with a preserved EF [6]. ?twb=0.28w?>Applying this echocardiographic method can help to prevent overlooking the diagnosis and could be helpful in deciding whether MRI or EMB investigations should be initiated. In addition, it allows easy follow-up investigations to monitor the patient; above a diagnostic role, the method showed a potential predictive value. Performing myocardial deformation analyses should therefore be additionally included into the diagnostic process when suspecting AMC.

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