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3D-speckle-tracking echocardiography correlates with cardiovascular magnetic resonance imaging diagnosis of acute myocarditis – An observational study

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ABSTRACT

Background: The diagnostic importance of three-dimensional (3D) speckle-tracking strain-imaging echocardiography in patients with acute myocarditis remains unclear. The aim of this study was to test the diagnostic performance of 3D-speckle-tracking echocardiography compared to CMR (cardiovascular magnetic resonance imaging) for the diagnosis of acute myocarditis.
Methods and results: 45 patients with clinically suspected myocarditis were enrolled in our study (29% female, mean age: 43.9 ± 16.3 years, peak troponin I level: 1.38 ± 3.51 ng/ml). 3D full-volume echocardiographic images were obtained and offline 2D as well as 3D speckle-tracking analysis of regional and global LV deformation was performed. All patients received CMR scans and myocarditis was diagnosed in 29 subjects based on original Lake-Louise criteria. The 16 patients, in whom myocarditis was excluded by CMR, served as controls. Regional changes in myocardial texture (diagnosed by CMR) were significantly associated with regional impairment of circumferential, longitudinal, and radial strain, as well as regional 3D displacement and total 3D strain. Interestingly, the 2D and 3D global longitudinal strain (GLS) showed higher diagnostic performance than well-known parameters associated with myocarditis, such as LVEF (as obtained by echocardiography and CMR) and LVEDV (as obtained by CMR).
Conclusions: In this study, we examined the use of 3D-speckle-tracking echocardiography in patients with acute myocarditis. Global longitudinal strain was significantly impaired in patients with acute myocarditis and correlated with CMR findings. Therefore, 3D echocardiography could become a useful diagnostic tool in the primary diagnosis of myocarditis.

1. Introduction

Myocarditis is an inflammatory disease of the heart muscle frequently resulting from viral infection and/or post viral immune-mediated responses. Its clinical manifestation can range from essentially asymptomatic presentations showing symptoms of myocardial infarction to severe illness, including cardiogenic shock due to chronic or acute heart failure (HF) [1]. Due to this broad variety of presentations, the diagnosis of myocarditis cannot usually be made solely based on clinical findings. Myocarditis can result in dilated cardiomyopathy (DCM) and is currently the leading cause for heart transplantation.

The diagnostic accuracy of clinical history, physical examination, electrocardiography, and serology are generally not adequate for an accurate diagnosis of myocarditis. Furthermore, findings during acute myocarditis in conventional echocardiography are not specific [2]. Endomyocardial biopsy, with further immunohistochemical and biochemical workup, remains the most widely accepted diagnostic

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technique. However, biopsy may be deemed too invasive and therefore inappropriate for many patients, especially those with less severe disease. Regarding noninvasive imaging techniques, cardiac magnetic resonance imaging (CMR) has become the most important diagnostic tool for myocarditis [3].

Consensus CMR criteria for myocarditis (including visualization of edema with cellular swelling and using early and late enhancement methods) have standardized CMR protocols for assessing myocarditis [3,4]. Echocardiography is currently recommended in the initial diagnostic evaluation of all patients with suspected myocarditis [5]. Echocardiography in myocarditis is typically performed to visualize the associated functional abnormalities, such as wall thickness and pericardial effusion. However, many patients with less severe cases of myocarditis present with a normal echocardiogram or unspecific echocardiographic findings, which diminishes the diagnostic value of this technique, owing to poor specificity and high variability [2].

Two-dimensional speckle-tracking echocardiography can quantitatively measure myocardial mechanics (strain and strain rate) in longitudinal, radial, and circumferential directions [6–8]. In many clinical settings, such as cardiomyopathy or coronary artery disease, a decrease in the longitudinal strain shown by two-dimensional speckle-tracking echocardiography has been found to indicate left-ventricular dysfunction before the occurrence of changes in left-ventricular ejection fraction [9,10]. Hsiao *et al.* demonstrated in acute myocarditis that left-ventricular strain and strain rate may be promising diagnostic and prognostic tools, even in patients with preserved left-ventricular ejection fraction [11]. However, the diagnostic importance of a novel technique, three-dimensional (3D) speckle-tracking strain imaging echocardiography, in patients with acute myocarditis remains unclear. The aim of this study was to test the diagnostic performance of 3D-speckle-tracking echocardiography versus CMR in the diagnosis of acute myocarditis.

2. Methods

We analyzed acquired data sets of 45 patients with suspected acute myocarditis in this retrospective, observational study. Ethical approval was waived by the local Ethics Committee in view of the retrospective nature of the study design. Inclusion criteria were (a) clinical symptoms compatible with a diagnosis of acute myocarditis, such as fever, viral prodromes, chest pain, palpitations, or dyspnea within six weeks of admission, (b) evidence of structural or functional abnormalities by echocardiography or evidence of myocardial damage as indicated by an elevation of at least one biomarker (troponin I level $>$ 0.1 ng/ml or creatine kinase MB fraction $>$ 3.6 μg/l), and (c) absence of coronary artery disease by coronary angiography. The exclusion criteria were known coronary artery disease (CAD), severe valvular disease, prior cardiac surgery, and a poor echocardiographic window. Controls were individuals in whom myocarditis was excluded by CMR.

2.1. Two-dimensional transthoracic echocardiography

Each patient underwent standardized two-dimensional (2D) transthoracic echocardiography for the determination of left- and right-ventricular functional parameters and dimensions, according to the recommendations of the American Society of Echocardiography, using a commercially available ultrasound scanner (Vivid 7, General Electric Medical Health, Waukesha, Wisconsin, USA) with a 2.5 MHz phased-array transducer [12,13]. Echocardiographic views, including apical four-, three- and two-chamber views (4CV, 3CV, 2CV) and parasternal (long- and short-axis views), with the patient in the left lateral decubitus position, were obtained in two-dimensional, three-dimensional, and color tissue Doppler imaging (TDI) modes. The 2D ejection fraction (EF) was calculated by using Simpson's rule from the 4CV image. The E/e' ratio was determined by measuring the TDI-derived systolic and diastolic velocities of the septal mitral valve annulus, according to the recommendations of the American Society of Echocardiography. Furthermore 4CV, 3CV and 2CV were used to perform offline 2D global longitudinal strain (GLS) analysis in commercially-available software (TomTec Imaging Systems GmbH, Unterschleissheim, Germany).

2.2. Three-dimensional speckle-tracking analysis

A 3D full-volume data set of the ventricle was obtained with gated (five beats) acquisition and stored on an echocardiographic imaging server (XCELERA, Philips Medical Systems, Koninklijke N.V.). Offline 3D speckle-tracking analyses of the gray-scale images obtained by 3D echocardiography were performed with commercially-available software (TomTec Imaging Systems). Sector size and depth were optimized to obtain the highest possible volume rates, reaching 17 to 20 frames/sec in the contrast 3D full-volume mode. Radial strain values were obtained by 3D-speckle-tracking echocardiographic analysis of both basal and apical LV short-axis views. The best real-time 3D echocardiography datasets were selected and analyzed offline by an experienced investigator who was blinded to the results of the CMR and 2D echocardiographic measurements.

2.3. Cardiovascular magnetic resonance imaging

All patients received CMR-scans within 72 h of admission in accordance to our site-specific standard operating procedure (SOP). All examinations were performed on a 1.5 Tesla system (Ingenia 1.5 T; Philips Healthcare, Best, The Netherlands). A 16-channel torso coil with digital interface was used for signal reception. ECG-gated steady-state free precession cine images were obtained, including short axis (SA), vertical long axis (VLA), horizontal long axis (HLA), and left-ventricular outflow track (LVOT) stacks. The left ventricle was fully covered in the SA stack. Edema-sensitive black blood T2-weighted short-tau inversion recovery (STIR) sequences were performed in SA and transverse orientations. Early gadolinium enhancement was assessed using transverse free-breathing fast-spin echo T1-weighted images, which were acquired in three identical slices taken both before and after intravenous injection of a double-dose bolus of 0.2 mmol/kg of body weight of gadobutrol (Gadovist, Bayer Healthcare, Leverkusen, Germany). Late gadolinium enhancement (LGE) imaging was achieved by segmented inversion recovery gradient-echo sequences in SA, VLA, and HLA orientations. The optimal inversion time was determined by using the Look-Locker technique. Cardiac analyses were performed according to general recommendations and diagnosis of acute myocarditis was based on original Lake-Louise criteria [14,15].

2.4. Statistical analysis

We used the Kolmogorov-Smirnov test to examine the normal distribution of continuous variables. Continuous data were expressed as mean values ± standard deviation. Categorical data were presented as percentages. Two-tailed p-values were calculated and were considered to be significant if they ranged below 0.05. For comparison between two groups, we used the Student *t* test for paired samples. To evaluate the results, in particular their predictive diagnostic value, and to enable a comparison between the results obtained from the CMR with the results from the speckle-tracking analysis and the control group, we used the following parameters and methods:

To analyze the collected data and its predictive value, we used receiver operating characteristic (ROC) curves and the Youden index (J). The resulting values ranged between 0 and 1, with values near 0 indicating only low diagnostic value and values near 1 showing very good diagnostic value. For ROC curves, the corresponding areas under the curve (AUC) and their 95% confidence intervals (CIs) were calculated.

Spearman's Rank correlation analysis was performed to evaluate strength and direction of monotonic relationship between parameters of myocardial injury / inflammation and GLS.

Statistics were performed using SPSS (PASW statistic, Version 25.0.0.0, SPSS Inc., Chicago, Illinois, USA) and MedCalc Statistical Software (Version 19.2, MedCalc Software Ltd, Ostend, Belgium).

3. Results

The study design is depicted in Fig. 1. A total of 45 patients with clinically suspected myocarditis who met the inclusion criteria were enrolled in the study. Initially, conventional two-dimensional echocardiography and 3D full-volume echocardiographic images were obtained with offline speckle-tracking analysis of regional and global LV deformation. All patients were subjected to CMR scans, and myocarditis was diagnosed in 29 of the subjects (age 47.7 ± 17 years, female 28%). There were 16 patients in whom myocarditis was excluded by CMR, and these patients then served as controls for the study (age 40.4 ± 15.6 years, female 37%). The baseline characteristics of the patients are shown in Table 1. Body weight, blood pressure, and smoking rates were similar in both groups. The peak troponin and peak CK-MB levels were elevated in patients with myocarditis without reaching significance (peak troponin I 2.15 ± 5.44 ng/ml vs 0.61 ± 1.58 ng/ml; p = 0.28, CK-MB 20.6 ± 51.3 µg/l vs 20.4 ± 63.6 µg/l; p = 0.17). The inflammation status of the patients was detected by measuring the peak leukocytes (WBC) and peak hsCRP (high sensitivity C-reactive protein) levels and did not differ between the two groups. Biochemical parameters of myocardial injury and inflammation were also not correlated to 3D GLS, as shown in Table 3.

The two-dimensional and 3D-echocardiograms were performed within 24 h after admission to our clinic. The main conventional echocardiographic findings are shown in Table 2. In patients with myocarditis left ventricular ejection fraction (LVEF) was significantly reduced (44.4 ± 3.2% vs. 54.3 ± 4.2; p = 0.03). In addition, this was associated with significantly larger left ventricular enddiastolic volume (LVEDV) (159.3 ± 14.3 ml vs. 118.8 ± 14.4 ml (p = 0.02), higher E/A ratios (1.9 ± 0.22 vs. 1.05 ± 0.09; p = 0.03), and elevated septal E/e' ratios (12.76 ± 1.9 vs. 4.9 ± 0.67; p = 0.004). There was no difference in interventricular septum diameter (IVSd), systolic pulmonary artery pressure (sPAP), or tricuspid annular plane systolic excursion (TAPSE) measurements between the two groups. Furthermore, no difference was detected in the primary ECG findings (Table 2).

Regional changes in myocardial texture, as diagnosed by CMR, were significantly associated with regional impairment of circumferential, longitudinal, and radial strain as well as regional 3D displacement and total 3D strain as depicted in Fig. 2. The bulls-eye plots represent a 16-

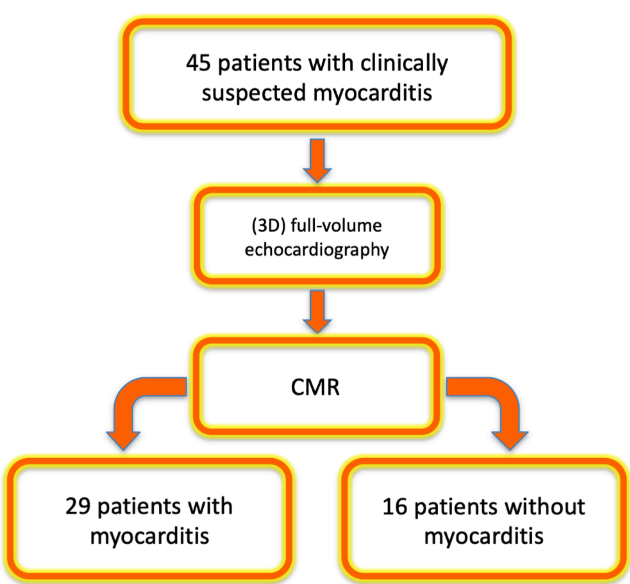


Fig. 1. Study design. 45 patients with suspected acute myocarditis were included in this observational study. Each patient underwent standardized two-dimensional transthoracic echocardiography and a 3D full-volume data set of the ventricle was obtained and analyzed by using commercially available software (TomTec Imaging Systems GmbH). All patients received CMR and myocarditis was diagnosed in 29 subjects. 16 patients with exclusion of myocarditis by CMR served as controls.

Table 1
Baseline clinical characteristics. Groups are divided with regard to the findings from CMR. Data are expressed as mean or as percentage. CK: creatine kinase, CK-MB: muscle-brain type creatine kinase, hsCRP: high sensitivity C-reactive protein, SBP: systolic blood pressure, DBP: diastolic blood pressure.

	All (n = 45)	Myocarditis (n = 29)	Controls (n = 16)	P
Age (years)	43.9 ± 16.3	47.4 ± 17.0	40.4 ± 15.6	0.18
Sex (male/female)	71/29% (39/16)	72/28% (21/8)	63/37% (10/6)	
Bodyweight (kg)	86 ± 18	90 ± 23	81 ± 12	0.37
Height (cm)	176 ± 12	175 ± 12	177 ± 13	0.78
Peak Troponin I (ng/l)	1.38 ± 3.51	2.15 ± 5.44	0.61 ± 1.58	0.28
Peak CK (U/l)	185.2 ± 242.5	218.4 ± 331.7	151.9 ± 153.2	0.45
Peak CK-MB (µg/l)	20.5 ± 35.8	20.6 ± 51.3	2.4 ± 2.3	0.17
Peak hsCRP (mg/ml)	35.4 ± 56.6	39.5 ± 49.6	31.3 ± 63.6	0.81
Peak Leucocytes (G/l)	9.72 ± 3.94	10.13 ± 3.55	9.3 ± 4.33	0.49
SBP (mmHg)	133 ± 30	131 ± 25	135 ± 35	0.71
DBP (mmHg)	79 ± 12	81 ± 16	77 ± 7	0.41
Diabetes (n, %)	3 (5.5%)	3 (10,3%)	0 (0%)	0.77
Hypertension (n, %)	13 (23.6 %)	8 (27,6%)	3 (18,7%)	0,09
Dyslipidemia (n, %)	20 (36.4%)	10 (34,5%)	6 (37,5%)	0.24
Smoking (n, %)	11 (20%)	6 (20,7%)	3 (18,75%)	0.44

Table 2
Conventional echocardiographic characteristics and primary ECG findings. LV, left ventricle; LVEF, left-ventricular ejection fraction; LVEDV, left-ventricular end-diastolic volume; IVSd, inter-ventricular septum diameter; E, early; A, atrial; sPAP, systolic pulmonary arterial pressure; TAPSE, tricuspid annular plane systolic excursion; RBBB, right bundle branch block; LBBB, left bundle branch block. Data are expressed as the mean or as a percentage. A total of 37 patients were analyzed regarding GLS (Myocarditis n = 21; Controls n = 15).

	All (n = 45)	Myocarditis (n = 29)	Controls (n = 16)	P
Echocardiographic findings				
LVEF (%)	49.4 ± 3.7	44.4 ± 3.2	54.3 ± 4.2	0.03
LVEDV (ml)	135.6 ± 14.4	159.3 ± 14.3	111.8 ± 14.4	0.02
LV length (cm)	8.7 ± 0.3	8.9 ± 0.2	8.4 ± 0.3	0.08
IVSd	1.2 ± 0.07	1.2 ± 0.04	1.1 ± 0.09	0.22
E wave (m/sec)	0.86 ± 0.06	0.83 ± 0.05	0.88 ± 0.07	0.56
A wave (m/sec)	0.87 ± 0.05	0.55 ± 0.04	0.69 ± 0.05	0.08
E/A ratio	1.48 ± 0.16	1.9 ± 0.22	1.05 ± 0.09	0.03
Septal e' (cm/sec)	0.26 ± 0.06	0.19 ± 0.04	0.33 ± 0.08	0.10
Septal E/e' ratio	8.83 ± 1.33	12.76 ± 1.9	4.9 ± 0.76	0.004
sPAP (mmHg)	16.75 ± 2.85	16.7 ± 2.1	16.8 ± 3.6	0.99
TAPSE (cm)	2.05 ± 0.1	1.9 ± 0.1	2.2 ± 0.1	0.08
GLS 2D (%; n = 22/15)	−13.77 ± 6.4	−12.6 ± 5.6	-15.9 ± 7.3	0.049
GLS 3D (%; n = 22/15)	−13.26 ± 6.5	−10.3 ± 4.97	-17.7 ± 6.1	0.0003
Primary ECG findings				
Normal n (%)	28 (62.2)	18 (62.1)	10 (62.5)	0,77
ST-segment elev. (%)	1 (2.2)	1 (3.45)	0 (0)	0.45
T-wave changes (%)	7 (15.6)	5 (17.2)	2 (12.5)	0.93
RBBB (%)	4 (8.89)	3 (10.34)	1 (6.25)	0.68
LBBB (%)	5 (11.1)	3 (10.34)	2 (12.5)	0.88

Table 3

Correlation of GLS and biochemical markers of myocardial injury / inflammation. No correlation could be shown between markers of myocardial injury and inflammation in patients with myocarditis and GLS as shown by Spearman's rank correlation coefficient (r) and p value (all p > 0,05; not significant).

Biochemical marker	Spearman's rank correlation coefficient (r)	Significance level P
Troponin base	-0.008	0.96
Troponin peak	0.082	0.64
CK-MB base	0.049	0.79
CK-MB peak	0.077	0.69
CRP base	-0.144	0.43
CRP peak	-0.055	0.77
WBC base	0.122	0.47
WBC peak	0.054	0.75

segment model of the left ventricle, where each segment was compared between 3D strain-echocardiography and CMR. Significant correlations of segmental changes in myocardial texture (as diagnosed with CMR) and impaired strain (as diagnosed with 3D strain echocardiography) are marked green. The 3D diastolic strain index was not associated with pathological findings in the CMR (Fig. 2).

To assess the association of global longitudinal strain (GLS) with the diagnosis of myocarditis in CMR, 3D GLS as well as 2D GLS (reconstructed from 4CV, 3 CV and 2CV) was analyzed. Due to image quality, 8 patients had to be excluded from the strain analysis (7 in the myocarditis group and 1 in the control group). 3D GLS showed higher diagnostic performance/AUCs (area under the curve) than well-known parameters associated with myocarditis, such as LVEF and LVEDV (Fig. 3) and was slightly superior to 2D GLS. The diagnostic value of 3D GLS was confirmed by comparing ROC curves, which demonstrated an area under the curve (AUC) of 0.826 (95% confidence interval [CI] 0.62 to 0.95; p = 0.0003), while the 2D GLS ROC curve analysis showed an AUC of 0.771 (95% CI 0.56 to 091; p = 0.016). Both 3D and 2D GLS ROC curves reached statistical significance (p < 0.05), whilst LVEF only displayed an AUC of 0.635 (95% CI 0.42 to 0.81; p = 0.163) when obtained by echocardiography and an AUC of 0.688 (95% CI 0.47 to 0.86; p = 0.103) when calculated from CMR findings. LVEDV demonstrated the worst predictive capacity with an AUC of 0.59 (95% CI 0.38 to 0.78; p = 0.299). Neither LVEF or LVEDV reached statistical significance in our patient cohort (Fig. 3). Global torsion and twist were also not associated with myocarditis in our collective (data not shown).

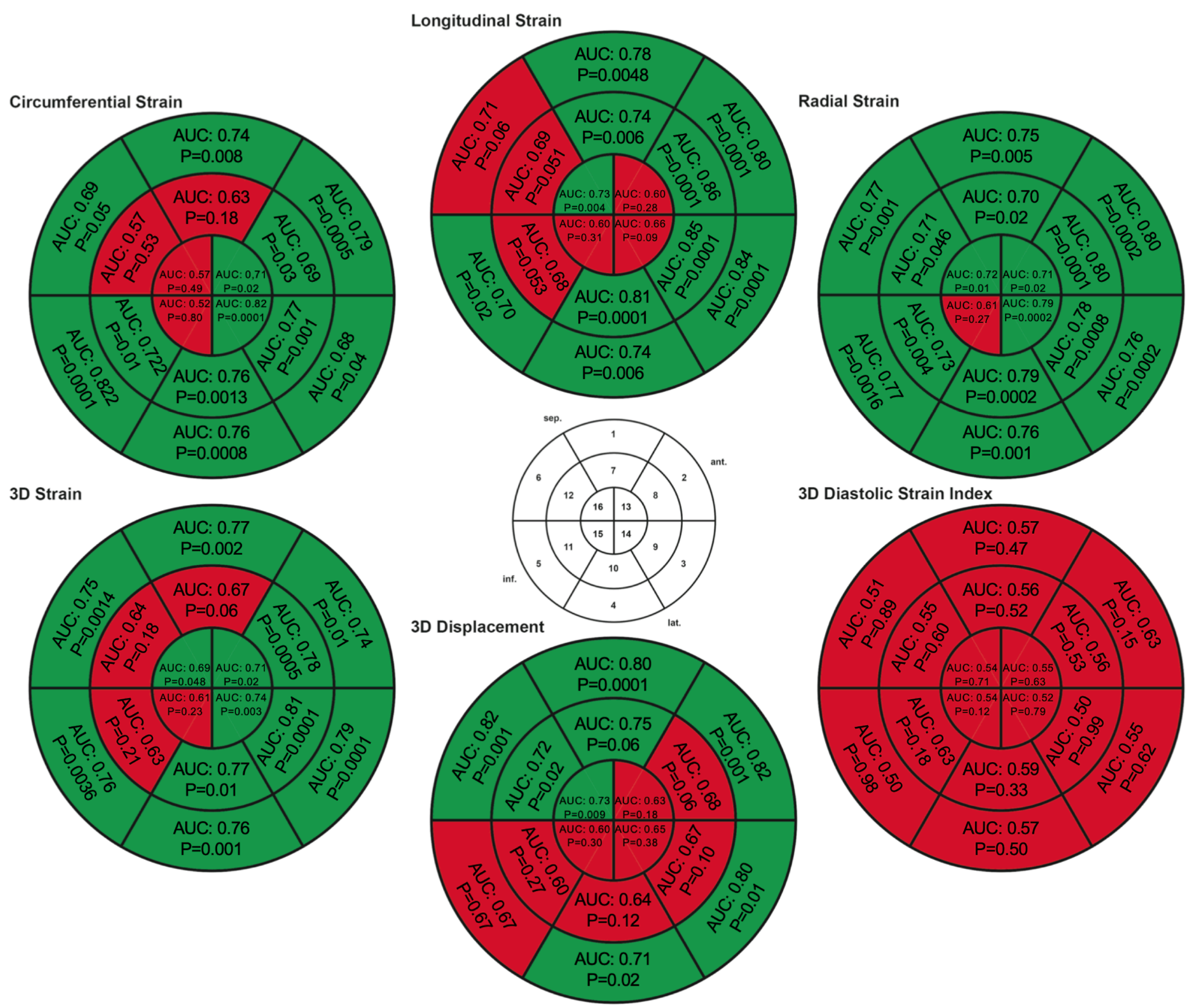
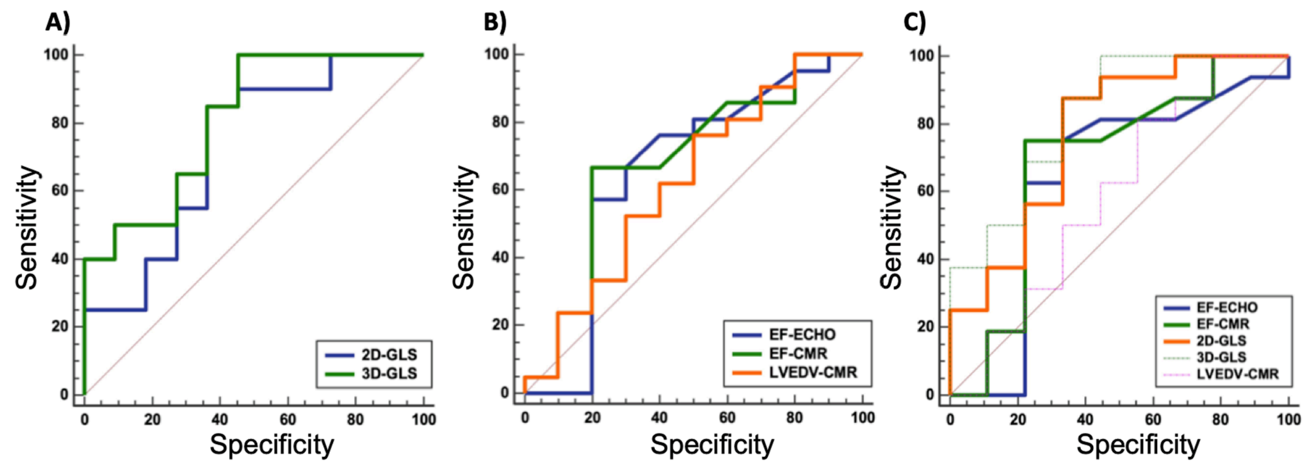


Fig. 2. Correlation of CMR findings with the regional changes detected in 3D-speckle-tracking echocardiography. Regional changes in myocardial texture as diagnosed by CMR, were significantly associated with regional impairment of circumferential, longitudinal, and radial strain as well as regional 3D displacement and total 3D strain, as demonstrated by AUCs displayed in a 16 segment model of the left ventricle. The 3D diastolic strain index was not associated with pathological findings in the CMR. Green, significantly associated (p≦0.05); red, no significant association (p > 0.05).



	3D GLS	2D GLS	EF (Echo)	EF (CMR)	LVEDV (CMR)
AUC	0.826	0.771	0.635	0.688	0.590
95 % CI	0.62 to 0.95	0.56 to 0.91	0.42 to 0.81	0.47 to 0.86	0.38 to 0.78
Significance level P	0.0003	0.016	0.163	0.103	0.299
Associated criterion	-19.5%	-17.87%	≤52%	≤50%	>130ml
Specificity	84.5%	80.7%	66.7%	80.0%	50.0%
Sensitivity	100%	80.0%	68.0%	63.6%	77.3%

Fig. 3. Predictive value of 3D- and 2D global longitudinal strain (GLS) as well as LVEF and LVEDV for determination of acute myocarditis. Receiver operating characteristic curves for **A)** 3D GLS compared to 2D GLS; **B)** Comparison of LVEF (as obtained by echocardiography and CMR) and LVEDV (CMR); **C)** Comparison of 3D GLS, 2D GLS, EF (MRI and Echo) and LVEDV (MRI). A total of 37 patients were analyzed regarding GLS (Myocarditis n = 21; Controls = 15).

4. Discussion

3D echocardiography has been widely used in clinical settings since its introduction in commercially available 3D-speckle tracking systems. 3D-speckle-tracking has not been regarded as a routine tool for analysis of cardiac function, despite its various advantages compared to two-dimensional (2D) imaging [16]. 3D-speckle-tracking is a novel echocardiographic technique that allows digital tracking and quantification of myocardial deformation as a function of time. The deformation can be assessed as three orthogonal strain values: radial strain (RS), longitudinal strain (LS), and circumferential strain (CS). Strain and strain-rate imaging can assess both circumferential deformation (a negative value in systole, as the circumference of the LV decreases) and radial deformation (a positive value in systole, as the LV wall thickness increases) [17].

Acute myocarditis is characterized by inflammatory myocardial damage that can result in severe left-ventricular wall motion abnormalities [1]. However, the myocardial damage is mainly circumscribed to the subepicardial layers, whether or not it is associated with any wall motion abnormality. Previous echocardiographic studies of patients with myocarditis have shown a variety of findings [18]. In addition to systolic function, regional wall motion abnormalities, diastolic dysfunction, and changes in echocardiographic image texture have been reported [2,6,19–21]. In this study, routine parameters such LVEDV and septal E/e' ratio are significantly elevated due to acute inflammatory left-ventricular damage. Furthermore, LVEF was significantly reduced in patients with acute myocarditis.

The most important result of this study is that global longitudinal strain (GLS) analysis demonstrates better predictive values for the diagnosis of myocarditis than conventional parameters such as LVEF and LVEDV [2]. In our patient cohort, 2D GLS was slightly inferior to 3D GLS for the discrimination of myocarditis. However, both 2D and 3D GLS were statistically significant and superior to LVEF (as quantified by echocardiography or CMR) or LVEDV (as quantified by MRI), which failed to be predictive for myocarditis and did not reach statistical significance. GLS assessment using automated speckle-tracking echocardiography is a technique for detecting and quantifying subtle disturbances in the LV systolic function [22]. GLS reflects the longitudinal deformation of the myocardium, and its accuracy has been validated against CMR tagging [23]. In the general population and patients with heart failure, GLS was shown to be a superior predictor of cardiac events and all-cause mortality compared to LVEF [24,25]. Furthermore, it has also been shown that GLS is a robust prognostic marker following myocardial infarction as well as in patients with cardiomyopathy and aortic stenosis [26–28].

The second relevant finding is that regional changes in myocardial texture, as diagnosed by CMR, were significantly associated with regional impairment of circumferential, longitudinal, and radial strain as well as regional 3D displacement and total 3D strain. Our results also showed that radial strain correlated with most segments affected by myocarditis (15 of 16 segments). Radial strain represents radially-directed myocardial deformation toward the center of the LV cavity, and thus indicates the degree of LV thickening and thinning motions during the cardiac cycle.

Routinely, echocardiography is the first imaging technique used in a clinical setting especially in patients with angina. In patients with normal LV size and overall function, standard echocardiography has poor diagnostic accuracy. The gold standard for noninvasive diagnosis of myocarditis is cardiac magnetic resonance imaging (CMR). CMR or invasive diagnostics, such as myocardial biopsy, are often not available in the setting of an acute presentation. It has been shown that 2D echocardiography with strain imaging can help with differential diagnosis and lead to an optimal treatment path for these patients [10,29].

A representative case (shown in Fig. 4) demonstrates that decreased myocardial 3D longitudinal strain, as assessed by 3D-speckle tracking, is associated with the CMR findings. However, the major pitfalls of 3D-speckle-tracking are its dependency on image quality and its ability to define the endocardial and epicardial boundaries by random noise and a relatively low temporal resolution. The acquisition of the 3D full-volume dataset is fast and simple. For this purpose, a standard apical four chamber-view is acquired and can then be analyzed offline with commercially-available software which allows for automated analysis. Image acquisition and automated analysis only takes approximately two

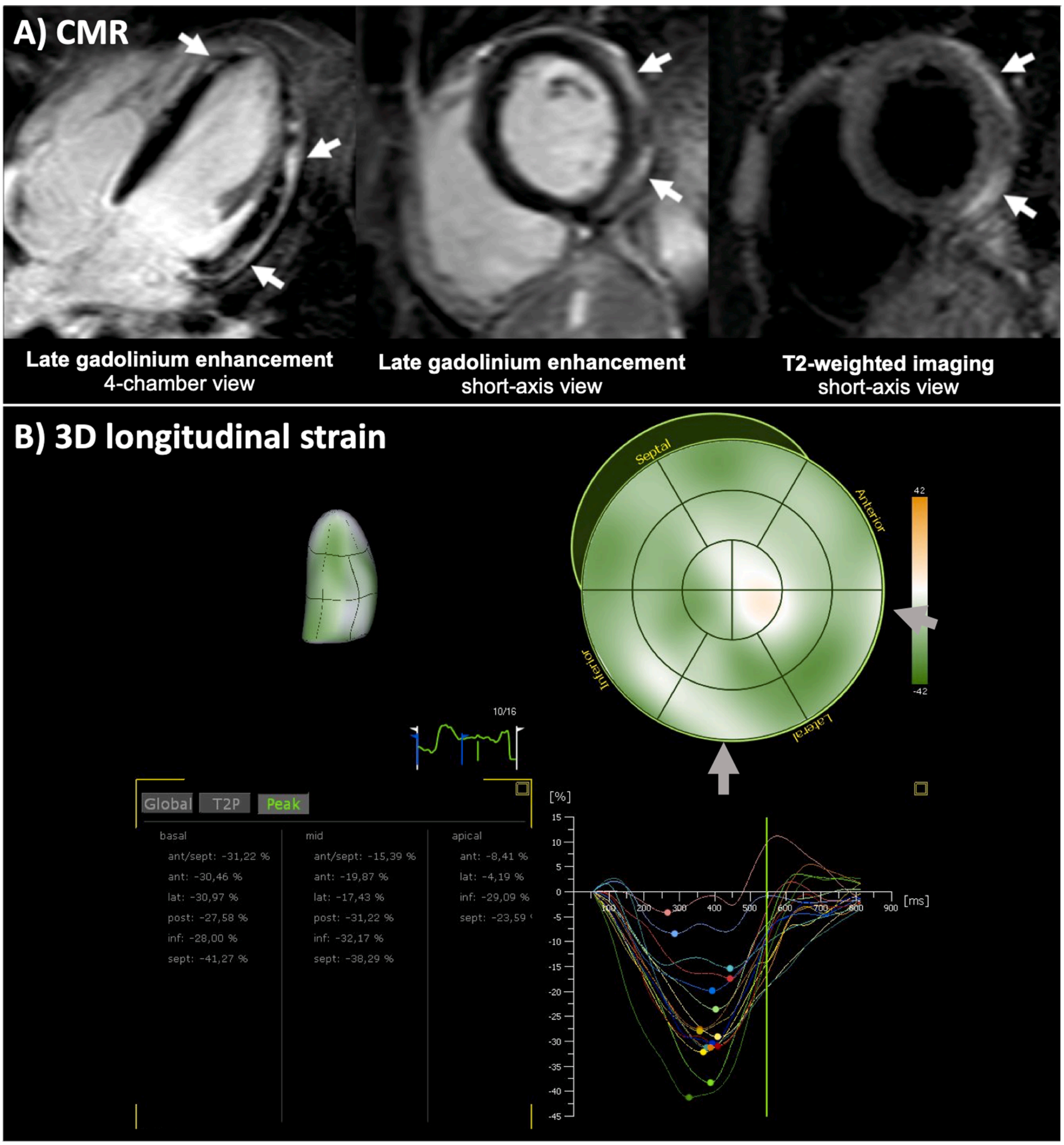


Fig. 4. Example of correlation of 3D longitudinal strain parameters with CMR findings in a patient with myocarditis. A) Cardiac magnetic resonance images of a 22-year-old patient with acute myocarditis. Late gadolinium enhancement imaging in 4-chamber and short-axis views show subepicardial and midmyocardial hyperenhancement at the left ventricular lateral wall and the apical septum. T2-weighted image shows corresponding myocardial edema (LGE and edema marked with white arrows). **B)** Example of a 3D longitudinal strain analysis which correlates with CMR findings. Lighter areas in the bullseye plot represent impairment of longitudinal strain (marked exemplary with grey arrows).

minutes. The two-dimensional speckle-tracking approach, requires the acquisition of standard apical four-, three- and two-chamber views. The speckle tracking analysis is then performed in each echocardiographic window and the results can be combined to obtain global strain parameters. The 2D approach is more time-consuming and inter-examiner dependent than the 3D full volume dataset approach.

2D echocardiography has generally played only a minor role in confirming the diagnosis of acute myocarditis. The underlying reasons are the apparently normal findings that it gives and a lack of specific features for less severe forms of myocarditis.

The advent of novel echocardiographic modalities, such as strain echocardiography, has dramatically expanded the scope of echocardiography, which can provide an accurate bedside assessment of regional contractility and can identify global longitudinal myocardial dysfunction derived from edema in acute myocarditis. Interestingly, a decrease in myocardial GLS, as assessed by the 3D-speckle-tracking technique, in the absence of wall-motion abnormalities, may represent a useful additional diagnostic finding in acute regional myocarditis.

Even though our sample size was small, we believe that the findings can be applied to patients with clinically suspected myocarditis. Systematic endomyocardial biopsy was not available as a reference standard because it is not part of the standard clinical workup of acute myocarditis at our institution. The main limitations of this study are the rather small sample size as well as the observational character and lack of long-term endpoints, such as cardiovascular mortality. Further, randomized prospective studies on a larger collective with subdivision into different entities and follow-ups are required to confirm our results.

5. Conclusions

This study aimed to investigate the diagnostic value of 3D-speckle-tracking echocardiography in patients with acute myocarditis. Global parameters, such as 3D and 2D global longitudinal strain, were significantly associated with the prevalence of myocarditis and had a better discriminatory capacity than LVEF (Echo and CMR) and LVEDV (CMR). 3D radial strain allows the visualization and analysis of regional wall mechanics, and therefore, this new imaging modality could become a useful tool in the diagnosis of myocarditis. A definitive diagnosis would still be based on clinical presentation and other noninvasive imaging modalities, such as CMR.

Ethics statement

Ethical approval was waived by the local Ethics Committee in view of the retrospective nature of the study design.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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