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Diagnostic implications of magnetic resonance feature tracking derived myocardial strain parameters in acute myocarditis

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ABSTRACT

Purpose: The present study aims to evaluate the diagnostic value of cardiac magnetic resonance (CMR) feature tracking (FT) derived strain-analysis of both ventricles in patients with acute myocarditis (ACM) in order to improve its currently still challenging non-invasive diagnosis.
Methods: CMR cine data of 31 patients with clinically suspected ACM and confirmation of diagnosis by CMR according to the Lake Louise criteria as well as 14 patients with clinically diagnosed ACM but inconspicuous CMR were retrospectively analyzed. 20 healthy volunteers (HV) served as a control. Analysis of global longitudinal, circumferential and radial strain and strain rate of both ventricles was performed in one long-axis and three short-axis slices using a dedicated FT-software (TomTec Imaging Systems).
Results: Patients with ACM showed significantly reduced LV longitudinal strain (-12.7 ± 6.5 vs. $-16.8 \pm 5.9\%$, $p = 0.021$) and LV circumferential strain (LVCirStrain; -22.9 ± 5.7 vs. $-27.8 \pm 4.4\%$, $p < 0.001$) compared to HV. Conversely, they showed improved basal RV circumferential strain rate (BasalRVCirSR; -0.70 ± 0.23 vs. $-0.47 \pm 0.31\ s^{-1}$, $p = 0.009$). In ACM patients with preserved EF, BasalRVCirSR was significantly increased compared to HV while LV strain was not significantly different between both groups. In multinominal logistic regression analysis, LVCirStrain and BasalRVCirSR proved to be the best independent predictors of ACM with preserved EF. A combined cut-off of $-0.53\ s^{-1}$ for BasalRVCirSR and of -29.0% for LVCirStrain allowed a classification of ACM patients with preserved EF with a sensitivity of 89% and a specificity of 80%. Also patients with clinical ACM but inconspicuous CMR showed a significantly improved BasalRVCirSR and a cut-off of $-0.77\ s^{-1}$ allowed a classification of ACM patients with a sensitivity of 70% and a specificity of 90%, while all other CMR parameters were normal.
Conclusions: The defined cut-offs for LVCirStrain and BasalRVCirSR allow a prediction of ACM with high sensitivity and specificity, even in patients with preserved EF and in patients with otherwise completely inconspicuous CMR. Our results point to a discriminative power especially of RV strain analysis in the CMR-based diagnosis of ACM.

1. Introduction

Acute myocarditis (ACM) represents one of the most frequent causes of sudden cardiac death in young patients and up to 30% of cases with biopsy-proven ACM develop a secondary dilatative cardiomyopathy with poor prognosis [1]. The diagnosis of ACM still represents a great challenge due to the heterogeneity of its clinical presentations. The clinical diagnostic criteria of ACM as well as the current gold standard, endomyocardial biopsy (EMB), are limited due to their low sensitivity and specificity [2]. Furthermore, EMB is an invasive method with relevant patient risks.

These diagnostic problems have led to an increasing importance of cardiac magnetic resonance imaging (CMR) in patients with ACM, as recently pointed out in a position paper of the European Society of Cardiology Working Group on myocardial and pericardial diseases [3]. CMR imaging of myocarditis exhibits the unique possibility of myocardial tissue characterization, using specialized technical features of CMR (T2-weighted imaging, Early and Late Gadolinium Enhancement (LGE)). These are referred to as the Lake

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Louise Consensus Criteria (LL Criteria) [1] and are widely used in clinical routine. According to previous studies, however, the LL Criteria exhibit varying sensitivity and specificity [1], and many patients clinically highly suspicious of suffering from ACM demonstrate an inconspicuous CMR study with none of the LL Criteria being positive, especially in cases with low level or no inflammation [4]. Hence, additional diagnostic parameters would be highly desirable to improve the non-invasive diagnosis of ACM.

As shown by echocardiography, many patients with ACM demonstrate an abnormal regional wall contractility [5]. Several studies have shown the superiority of strain imaging—as a means to quantify myocardial deformation—over the conventional functional assessment in early forms of myocardial dysfunction [6]. For patients with ACM, echocardiographic strain analysis could demonstrate a reduced segmental wall contractility even in patients with visually no wall motion abnormalities [7]. While echocardiographic strain analysis represents an observer-dependent examination and is not yet established in the clinical routine, the recently introduced Feature Tracking (FT) algorithm [8] offers the potential to analyze myocardial strain parameters based on routinely acquired cine-MR images in patients with suspected myocarditis.

The goal of the present study was therefore to investigate the potential role of CMR FT-based strain analysis of both ventricles in the diagnosis of ACM especially in patients with preserved left ventricular ejection fraction (EF).

2. Material and methods

2.1. Study population

After obtaining approval by the local ethics committee a retrospective study was performed. We retrospectively analyzed the data of 45 patients who had been consecutively referred to our department for CMR imaging from 2012 to 2014 after a clinical diagnosis of ACM. MRI had been performed within 2 weeks after clinical symptom onset. The clinical diagnosis of ACM was based upon the current recommendations given by the position statement of the European Society of Cardiology Working Group on myocardial and pericardial diseases [3] (Table 1). CMR diagnosis of ACM was based upon the presence of at least two out of three LL criteria [1], i.e., visually detected myocardial edema on T2-weighted images, a pathological early gadolinium enhancement ratio (EGEr) or visually detected LGE. The subjects were divided into two groups based upon CMR imaging results: (1) 31 patients with clinically diagnosed ACM confirmed by CMR according to the LL criteria, and (2) 14 patients with clinically diagnosed ACM but normal CMR (no visual edema or LGE, no pathological EGEr, no pericardial effusion, no functional abnormality). Furthermore, each group was divided into two subgroups according to the left ventricular ejection fraction (EF) (group A—EF > 55%, group B—EF < 55%).

CMR images from 20 healthy volunteers (HV) served as a control. The status "healthy" was based on: (i) uneventful medical history, (ii) absence of any symptoms indicating cardiovascular dysfunction (iii) normal cardiac dimensions and function proven by cine CMR, and (iv) no history of inflammatory disease including common cold virus in the last four weeks before the examination. For each volunteer written informed consent was obtained prior to the study after approval by the local ethics committee. Characteristics of patients and HV are shown in Table 2.

2.2. Magnetic resonance imaging

CMR was performed on a 1.5T MR system (Achieva 1.5T, Philips Healthcare, Best, The Netherlands) using a standard five-element cardiac phased array coil. A balanced steady-state free precession (b-SSFP) sequence in breath-hold technique and with retrospective ECG-triggering was acquired for functional analysis and subsequent FT analysis. Imaging parameters were set as follows: repetition time (TR) 28 ms, echo time (TE) 1.4 ms, flip angle (FA) 60°, field of view (FOV) 343 × 380 mm^2, matrix 256 × 256, slice thickness 8 mm, 30 cardiac phases The sequences were exported in DICOM-Format without special adjustments.

In all patients the MR protocol included three horizontal long axes and a stack of short axes (SAX) covering the left and right ventricle (LV/RV) to assess wall motion and allow for cardiac chamber quantification of LV and RV. Volumetry was performed on a standard post-processing platform (Extended MR WorkSpace, Version 2.6.3.4, Philips Healthcare, Best, The Netherlands).

Edema-sensitive black blood T2-weighted images with fat saturation in SAX orientation were used to visualize inflammatory changes in the myocardium [9]. In order to detect myocardial hyperemia, myocardial early gadolinium enhancement was assessed using fast spin- echo T1-weighted images during the first minutes after 0.1 mmol/kg Gd-DOTA (Dotarem; Guerbet, Villepinte, France) contrast administration as previously described [10]. For the detection of myocardial fibrosis and scarring, LGE imaging was performed 15 min after 0.1 mmol/kg Gd-DOTA (Dotarem; Guerbet, Villepinte, France; cumulative dose 0.2 mmol/kg Gd-DOTA) contrast administration using an inversion-recovery gradient-echo sequence in the horizontal long axis and in the SAX as previously described [11].

2.3. Myocardial strain analysis using CMR feature tracking

Myocardial FT was performed offline based on the acquired bSSFP cine images and using a dedicated software (Image-Arena VA Version 3.0 and 2D Cardiac Performance Analysis MR Version 1.1.0; TomTec Imaging Systems, Unterschleissheim, Germany). The details of the FT algorithm have been published previously [8].

The four-chamber view was used to derive RV and LV longitudinal strain and strain rate values. Circumferential and radial strain and strain rate parameters of both RV and LV were determined in short axis view at a basal, mid-ventricular and apical level of the ventricle. To ensure a standardized analysis for each subject the basal slice in short axis view was defined as the first slice below the atrioventricular level showing a circumferential myocardial enclosing; the mid-ventricular slice was localized at the level of both papillary muscles and the apical slice located equally distant from the mid-ventricular level as the distance between the basal and the mid-ventricular level as reported previously [12]. To obtain global radial and circumferential strain and strain rate estimates values were averaged over all three SAX slices.

For FT analysis, endocardial contours were drawn manually in end-diastolic images with subsequent software-driven automatic tracking of the endocardial contour throughout the entire cardiac cycle. The quality of automatic tracking was checked and contours were manually adjusted and tracking repeated were deemed necessary.

2.4. Analysis of Lake Louise criteria

Image analysis of Lake Louise criteria was performed using a standard post-processing platform (Extended MR WorkSpace, Version 2.6.3.4, Philips Healthcare, Best, The Netherlands). The myocardium was divided into 16 segments according to the AHA 16-segment model. Every segment was visually evaluated for presence of myocardial edema on T2-weighted black-blood imaging. Moreover, T2-ratio was calculated as previously described [1,13]. For calculation of the EGEr, representative myocardial and skeletal muscle ROIs were drawn on one axial slice before and after contrast administration. EGEr was calculated as previously described