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Left and right atrial feature tracking in acute myocarditis: A feasibility study

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ABSTRACT

Purpose: The present study aims at evaluating the feasibility and reproducibility of cardiac magnetic resonance (CMR) feature tracking (FT) derived strain and strain rate (SR) parameters of the left and right atrium (LA, RA) in patients with acute myocarditis as well as their potential to detect diastolic dysfunction. In addition, the diagnostic value of LA and RA strain parameters in the setting of acute myocarditis is investigated.

Methods: CMR cine data of 30 patients with CMR-positive acute myocarditis were retrospectively analyzed. 25 age- and gender-matched healthy individuals served as a control. Analysis of longitudinal strain and SR of both atria was performed in two long-axis views using a dedicated FT-software. LA and RA deformation was analyzed including reservoir function (total strain [ε_s], peak positive SR [SR_s]), conduit function (passive strain [ε_e], peak early negative SR [SR_e]) and booster pump function (active strain [ε_a], peak late negative SR [SR_a]). Intra- and inter-observer reproducibility was assessed for all strain and SR parameters using Bland-Altman analyses, intra-class correlation coefficients (ICCs) and coefficients of variation (CV).

Results: FT analyses of both atria were feasible in all patients and controls. Reproducibility was good for reservoir and conduit function parameters and moderate for booster pump function parameters. Myocarditis patients demonstrated an impaired LA reservoir and conduit function when compared to healthy controls (LA ε_s: 32 ± 17 vs. 46 ± 13, $p = 0.019$; LA SR_s: 1.5 ± 0.5 vs. 1.8 ± 0.5, $p = 0.117$; LA SR_e: -1.3 ± 0.5 vs. -1.9 ± 0.5, $p < 0.001$), while LA booster pump function was preserved. In logistic regression and ROC-analyses, LA SR_e proved to be the best independent predictor of acute myocarditis (AUC 0.80), and using LA SR_e with a cut-off of $-1.6\,s^{-1}$ resulted in a diagnostic sensitivity of 83% and a specificity of 80%. Changes in RA phasic function parameters showed a tendency to parallel those of the LA and showed no additional effect with respect to the diagnostic potential in acute myocarditis.

Conclusions: Myocarditis patients exhibit an impaired atrial reservoir and conduit function, what might be indicative of ventricular diastolic dysfunction. LA SR_e was the best predictor for the presence of acute myocarditis in our study, pointing towards the discriminative power of atrial strain analysis in the CMR-based diagnosis of acute myocarditis.

1. Introduction

The left atrium (LA) plays an important role in overall cardiovascular performance [1] as well as in the diagnostic and prognostic assessment of various cardiac diseases [2]. Instead of being a passive chamber, it exhibits three phasic functions modulating ventricular filling, i.e. the systolic reservoir, the early diastolic conduit, and the late diastolic booster pump function [1]. Thus, an interactive and dynamic relationship exists between the atrium and the ventricle [2], leading to an increasing interest in LA function in the cardiology and cardiac imaging community.

LA phasic volumes and function are traditionally measured by echocardiography [2] or, more recently, by cardiovascular magnetic resonance (CMR) [3]. However, increasing evidence exists that myocardial strain and strain rate (SR) imaging might provide more

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sensitive and detailed data on myocardial deformation as compared to volumetric measurements [2].

Echocardiographic speckle tracking thereby has provided feasible and reproducible measurements in order to evaluate phasic LA longitudinal strain and SR [4]. More recently, Kowallick et al. demonstrated the feasibility of CMR feature tracking (FT) for the assessment of LA strain and SR parameters [5], a technique analogous to echocardiographic speckle tracking, which is retrospectively applied on routinely acquired CMR cine data [6].

So far, several studies have demonstrated a potential diagnostic value of left ventricular [7,8] or even biventricular [9] strain analysis in patients with acute myocarditis. As ventricular mechanics have been shown to be diffusely impaired despite preserved ejection fraction (EF), an analysis of atrial mechanics is of great interest in order to allow a deeper understanding of the pathophysiology of this relevant and difficult-to-diagnose disease [10]. In addition, altered atrial mechanics might lead to potential novel diagnostic parameters, addressing the limitations of the current diagnostic tools, i.e. especially their limited diagnostic accuracy [11].

Therefore, the aim of the present study was to evaluate the feasibility of LA FT in patients with CMR-positive acute myocarditis. In addition, the FT algorithm is applied on the right atrium (RA) for the first time in order to test i) whether RA FT is feasible and ii) whether RA mechanics parallel those of the LA or if there is an incremental value of RA FT in acute myocarditis. Finally, the potential diagnostic value of FT derived LA and RA strain and SR parameters is tested in order to identify potential parameters for improving the future non-invasive diagnosis of acute myocarditis and to allow for CMR based insights into potential diastolic dysfunction.

2. Materials and methods

2.1. Study population

After obtaining approval by the local Institutional Review Board, data of 35 patients who had been referred to our department for CMR imaging after a clinical diagnosis of myocarditis and demonstrated preserved EF were retrospectively analyzed. The clinical diagnosis was based upon the current recommendations given by the position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases [10] (Table 1). CMR had been performed within 2 weeks after clinical symptom onset. CMR diagnosis of myocarditis (= "CMR-positive myocarditis") was based upon the presence of ≥2 out of 3 LLC [12], i.e. visually detectable myocardial edema or an increased T2-ratio ≥1.9 [12], a pathological early gadolinium enhancement ratio (EGEr) ≥4 or visually detected LGE with a subepicardial or intramyocardial pattern typical for myocarditis [12]. Two patients were excluded from further analyses due to atrial fibrillation, which were not feasible for consecutive atrial FT analyses. Three additional patients were excluded from further analyses due to mitral regurgitation detected on bSSFP cine images, which is thought to bias atrial volume and function measurements [4]. All remaining 30 patients with stable sinus rhythm and competent mitral valve were included in further analyses.

CMR images from 25 age- and gender-matched healthy subjects served as controls. Inclusion criteria were: i) uneventful medical history, ii) no symptoms of inflammation, iii) absence of any symptoms indicating cardiovascular dysfunction, iv) normal cardiac dimensions and function on cine CMR. For each volunteer written informed consent was obtained prior to the study after approval by the local Institutional Review Board. Characteristics of patients and controls are shown in Table 2.

Table 1
Classification of myocarditis patients according to the current recommendations[a].

	Myocarditis patients (n = 30)
Clinical symptoms consistent with myocarditis [%]	100 (74[b]/52[c]/58[d]/3[e])
Diagnostic criteria consistent with myocarditis [%]	100 (100[f]/84[g]/100[h])
Exclusion of coronary artery disease [%]	100 (84[i]/16[j]/0[k])
CMR LLC [%]	100 (100[l]/0[m]/0[n])

[a]**Current recommendations** [10]: "Clinically suspected myocarditis if ≥1 clinical presentation and ≥1 diagnostic criteria from different categories, in the absence of: (1) angiographically detectable coronary artery disease; (2) known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome. If the patient is asymptomatic ≥2 diagnostic criteria should be met."
Clinical symptoms consistent with myocarditis: [b] Acute chest pain; [c] New-onset (days up to 3 months) or worsening of: dyspnea at rest or exercise/fatigue, with or without left and/or right heart failure signs; [d] Palpitations/arrhythmia symptoms/syncope/aborted sudden cardiac death; [e] Cardiogenic shock.
Diagnostic criteria consistent with myocarditis: [f] ECG/Holter/stress test features; [g] Elevated TnT/TnI; [h] Functional and structural abnormalities on cardiac imaging (echo/angio/CMR).
Exclusion of coronary artery disease: [i] cardiac catheterization; [j] cardiac computed tomography angiography; [k] clinically.
CMR LLC (Lake Louise Criteria): [l] any 2 out of 3; [m] 1 out of 3; [n] 0 out of 3.

Table 2
Characteristics of myocarditis patients and controls.

Parameter	Controls	Myocarditis patients	p-value
Number	25	30	n.a.
Females/Males	5/20	6/24	n.a.
Age [years]	37 ± 12	36 ± 13	0.716
Height [cm]	177 ± 11	178 ± 10	0.546
Weight [kg]	75 ± 14	80 ± 16	0.281
Initial TnT [μg/l]	n.a.	0.56 ± 0.68	n.a.
Heart rate [bpm]	63 ± 13	65 ± 13	0.743
Atrial fibrillation (n)	0	0	n.a.
LV ED volume/BSA [ml/m^2]	82 ± 13	84 ± 21	0.475
LV ES volume/BSA [ml/m^2]	30 ± 9	33 ± 10	0.093
LV EF [%]	63 ± 6	60 ± 7	0.155
LV ED wall mass/BSA [g/m^2] (without papillary muscles)	46 ± 12	54 ± 15	**.045**
LAV max/BSA [ml/m^2]	34 ± 12	39 ± 11	0.150
LAV preac/BSA [ml/m^2]	18 ± 9	24 ± 9	**.029**
LAV min/BSA [ml/m^2]	12 ± 7	16 ± 7	0.078
LA EF total [%]	66 ± 9	61 ± 9	0.054
LA EF passive [%]	48 ± 14	39 ± 9	**.031**
LA EF booster [%]	34 ± 13	36 ± 10	0.068

Continuous variables are expressed as mean ± standard deviation; TnT: Troponin T; LV: left ventricle; ED: end diastolic; BSA: body surface area; ES: end systolic; EF: ejection fraction; LAV max: maximum left atrial volume; LAV min: minimum left atrial volume; LAV preac: left atrial volume prior to atrial contraction.
Bold values means statistically significant.