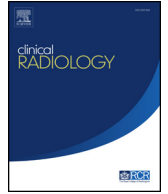


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Early diastolic septal movement in patients with myocarditis

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AIM: To evaluate early diastolic septal relaxation as a parameter in the diagnostic workup via cardiovascular magnetic resonance imaging (CMRI) in patients with myocarditis.

MATERIALS AND METHODS: Early diastolic septal movement was evaluated (EDS) prospectively via frame-by-frame analysis in 255 consecutive patients with presenting signs of myocarditis and in 64 controls matched 4:1 for gender and age. ECG-triggered, T2-weighted, fast spin echo triple inversion recovery sequences and late gadolinium enhancement were obtained, as well as left ventricular (LV) function and dimensions in patients and controls.

RESULTS: EDS was detected in 66.7% of the patients and 18.7% of the controls ($p < 0.001$). Sensitivity was 69.4% and specificity 79.7%. Patients with EDS had a significant lower LV ejection fraction (LV-EF) of $61.1 \pm 0.6\%$ and significant higher end-diastolic volume (EDV) of 158.5 ± 2.7 ml than in patients without EDS (LV-EF $65.3 \pm 0.9\%$, $p = 0.0001$; EDV 148.4 ± 3.9 ml, $p = 0.04$). A significant negative correlation was observed between LV-EF and EDS in patients, and a lower LV-EF correlated with a more frequent occurrence of EDS ($r = -0.24$, $p = 0.0001$). Scar tissue was also more frequent in patients than controls (63.1% and 7.8%, $p = 0.007$).

CONCLUSIONS: EDS is a parameter obtained non-invasively by CMRI and is present in a high percentage of patients with myocarditis. Cardiac functional parameters are significantly altered in patients with EDS. EDS is a feasible parameter that can play an important role in the diagnosis of myocarditis.

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Introduction

Clinical presentations of myocarditis range from non-specific systemic symptoms (fever, myalgia, palpitations, or exertional dyspnoea) to fulminant haemodynamic collapse and sudden cardiac death.^{1,2} Myocarditis is pathologically defined as “inflammation of the myocardium”;

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however, despite this seemingly rather clear-cut definition, its diagnosis continues to be a challenging task in clinical practice.³

Diagnosing myocardial involvement after viral infection is usually difficult, as electrocardiogram (ECG) and echocardiographic abnormalities are usually transient or non-specific. Some patients even present without any electro- or echocardiographic abnormalities,^{4–6} and their troponin and/or creatinine kinase levels are normal.^{2,7}

During the past two decades, cardiovascular magnetic resonance imaging (CMRI) has evolved from being a research tool to a clinically validated, safe, and comprehensive imaging method. CMRI provides anatomical and functional information in acquired and congenital heart disease, and is the most precise technique for quantifying ventricular volumes, function, and mass.⁸ Delayed contrast enhancement is an accurate method with which to diagnose ischaemic and non-ischaemic cardiomyopathies, as well as myocarditis.^{8–10}

Early systolic and diastolic motion of the septum has been examined via echocardiography^{11–15} in different patient collectives. To the authors' knowledge, early diastolic septal movement (EDS) has not been systematically examined via CMRI in patients with myocarditis. EDS describes a sudden, asynchronous motion of the left ventricle's (LV) septal or antero-septal middle to apical portion during early diastole prior to or at the beginning of mitral valve opening. The aim of the present study was to evaluate EDS in patients with myocardial involvement after viral infection of the respiratory or gastrointestinal tract as a feasible parameter that may play an important role in the diagnosis of myocarditis. The prespecified hypothesis of the present study was that EDS would occur more frequently in patients than in controls.

Materials and methods

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Patients

Two hundred and fifty-five patients with myocardial involvement after viral infection of the respiratory or gastrointestinal tract were studied prospectively. This group of patients was compared with 64 age- and sex-matched controls. Patients and controls were examined between 1 January 2007 and 16 December 2015 (inclusion of the last patient). Data collection concluded in July 2016. Patients and controls were examined by experienced cardiologists, underwent 12-lead ECG, transthoracic echocardiography, and a non-invasive stress test (bicycle exercise and/or dynamic stress echocardiography or adenosine CMRI) or computed tomography of the coronary arteries to rule out coronary artery disease. The patient inclusion criteria were documented non-ischaemic scarring of the myocardium and/or myocardial oedema. The controls were examined during a check-up or for atypical

thoracic pain. Patients and controls were excluded if they had a history or findings suggestive of coronary artery disease (signs of ischaemia on resting ECG or stress tests), left or right bundle branch block, atrial fibrillation, dilated cardiomyopathy, congenital heart disease, right heart failure, signs of pulmonary hypertension on continuous wave (CW) Doppler, LV hypertrophy (diameter of the septum and/or inferior wall suggestive of coronary artery disease (signs of ischaemia on resting ECG or stress CMRI) or valvular stenosis, renal failure (creatinine ≥ 1.8 mg/dl) or known history of claustrophobia. All patients had a previous viral infection of the respiratory or gastrointestinal tract and the majority of patients complained of symptoms such as dyspnoea, thoracic pain, fatigue, and/or palpitations. Fifty-nine percent of the patients had documented premature ventricular beats. The diagnostic CMRI criteria of myocarditis were oedema and/or non-ischaemic contrast enhancement of the myocardium. All patients and controls gave written informed consent.

CMRI

All images were acquired using a 1.5 T MRI system (Intera CV 1.5T, Phillips Medical Systems, Best, The Netherlands) and specifically designed software (Release 11). A five-element cardiac phased-array coil was used combined with a homogeneity correction algorithm (Constant Level AppeaRance; CLEAR). This algorithm generates sensitivity maps for each synergy coil element (relative to the body coil sensitivity) to calculate uniformity correction.¹⁶ Data acquisition was ECG triggered.

Functional and morphological data were evaluated using view forum 6.5. (Phillips Medical Systems, Best, The Netherlands). Regions of interest were drawn manually. To evaluate LV function and dimensions, two-, three- and four-chamber long-axis views were taken, and three-dimensional (3D) short-axis volume data assessed by steady-state free precession imaging as previously described.^{7,17} Phase-contrast velocity images in the ascending aorta were obtained to measure stroke volume and rule out significant aortic insufficiency. ECG-triggered, T2-weighted and short-inversion time (TI) triple inversion recovery fast spin echo sequences (STIR+) were carried out in all patients and controls as described previously.^{7,17}

Late gadolinium enhancement (LGE) imaging was obtained in all patients and controls 10 minutes after the intravenous administration of 0.2 mmol/kg intravenous gadolinium-diethylenetriamine-pentaacetate. A contiguous stack of sections was obtained covering the entire LV without gap during two breath holds. In addition, a four-chamber view was obtained in all patients. The ability of this inversion recovery sequence to detect mid-myocardial or subepicardial LGE was tested at the beginning of the examinations and reported previously.⁷ Mid-myocardial or subendocardial contrast enhancement was regarded as positive. Signal intensity and standard deviations were not obtained. 3D inversion recovery turbo gradient echo sequences were taken as reported¹⁷ and a contiguous stack of sections obtained covering the entire LV with no gap during

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