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Diagnostic Performance of Cardiovascular Magnetic Resonance in Patients With Suspected Acute Myocarditis

Comparison of Different Approaches

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OBJECTIVES The aim of this research was to identify the diagnostic performance of gadolinium-enhanced and T2-weighted cardiovascular magnetic resonance (CMR) in suspected acute myocarditis.

BACKGROUND Acute myocarditis is difficult to diagnose; CMR provides various means to visualize myocardial inflammatory changes. A CMR approach with clear-cut diagnostic criteria would be desirable.

METHODS We investigated 25 patients with suspected acute myocarditis (18 males, 44 $\pm$ 17 years) and 23 healthy controls (13 males, 29 $\pm$ 10 years). Cardiovascular magnetic resonance studies included the following sequences: 1) T2-weighted triple inversion recovery; 2) T1-weighted spin echo before and over 4 min after gadolinium injection; and 3) inversion recovery-gradient echo 10 min after gadolinium injection. Qualitative and quantitative image analysis was performed for: 1) focal and global T2 signal intensity (SI); 2) myocardial global relative enhancement (gRE); and 3) areas of late gadolinium enhancement (LGE).

RESULTS Both global T2 SI and gRE were higher in patients than in controls (T2: 2.3 $\pm$ 0.4 vs. 1.7 $\pm$ 0.4; $p < 0.0001$, gRE: 6.8 $\pm$ 4.0 vs. 3.7 $\pm$ 2.3; $p < 0.001$). The sensitivity, specificity, and diagnostic accuracy for T2 (cutoff value of 1.9) were 84%, 74%, and 79%, respectively; gRE: (cutoff value of 4.0) 80%, 68%, and 74.5% respectively; LGE: 44%, 100%, and 71%, respectively. The best diagnostic performance was obtained when "any-two" of the three sequences were positive in the same patient yielding a 76% sensitivity, 95.5% specificity, and 85% diagnostic accuracy.

CONCLUSIONS A combined CMR approach using T2-weighted imaging, early and late gadolinium enhancement, provides a high diagnostic accuracy and is a useful tool in the diagnosis and assessment of patients with suspected acute myocarditis. (J Am Coll Cardiol 2005;45: 1815–22) © 2005 by the American College of Cardiology Foundation

Identifying patients with acute myocarditis is a challenging task. Clinical presentations often mimic other disorders and may vary from flu-like symptoms or subclinical disease to acute heart failure and sudden cardiac death (1). Of the imaging approaches utilized to diagnose the disease, cardiovascular magnetic resonance (CMR) has emerged as an important tool. The two relevant gadolinium-enhanced CMR approaches described so far depend on the measurement of myocardial global (early) relative enhancement (gRE) (2) or the visualization of late gadolinium enhancement (LGE) (3). Each of these approaches monitors a different aspect of myocardial injury in myocarditis. Whereas gRE likely reflects myocardial hyperemia and increased capillary permeability as features of present inflammation, LGE mostly indicates irreversible myocardial injury. Another interesting and yet inadequately studied noncontrast CMR approach in myocarditis is T2-weighted imaging, which almost exclusively depends on the detection of myocardial edema. It has been shown to be of diagnostic value (4), but experience has been reported only sparsely. The diagnostic performance of these techniques to identify myocarditis is not well-defined. For example, the reported sensitivity of LGE to detect acute myocarditis varies from 44% to 88% (3,5). Furthermore, a comprehensive CMR protocol combining data obtained from each approach has not reached the clinical arena and yet appears promising for two reasons: first, the spectrum of myocardial injury caused by the disease is diverse, ranging from mild inflammation with hyperemia or edema to frank necrosis (6). One would then expect that an imaging approach designed to detect only one of these injuries would lack sufficient sensitivity. Second, providing information on the various myocarditis-induced injuries could help identify patients with a severe form of the disease or those with a potentially unfavorable prognosis.

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METHODS

Patients. Inclusion criteria:

1) Symptoms and signs suggestive of cardiac disease (angina pectoris, dyspnea, palpitations).

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Abbreviations and Acronyms

CK = creatine kinase
CMR = cardiovascular magnetic resonance
gRE = global relative enhancement
LGE = late gadolinium enhancement
SI = signal intensity

2) Evidence for myocardial injury as defined by electrocardiogram (ECG) changes (ST-segment changes, conduction defects) and elevated serum markers (creatine kinase [CK], troponin T or I).
3) Exclusion of coronary artery disease by angiographic and/or clinical criteria.

Criteria of exclusion were previous myocardial infarction, evidence of chronic myocarditis, and known contraindications to CMR.

Control group. Twenty-three healthy volunteers (13 males, age 29.3 ± 10 years) with no current or past evidence of cardiovascular disorders served as our control group.

A written informed consent was obtained from each subject, and the local ethics committee approved the study.

CMR. Cardiovascular magnetic resonance studies were performed in a 1.5-T system (Signa CV/*i*, GE Medical Systems, Milwaukee, Wisconsin). Localization was performed using breath-hold real time and steady-state free precession images of true anatomical axes of the heart. For the T2- and T1-weighted spin echo sequences, which were used for a quantitative evaluation, the body coil was used. We applied a breath-hold, black-blood, T2-weighted, triple inversion recovery sequence (TR 2 × RR, TE 65 ms, TI 140 ms) in three (basal, midventricular, and apical) short-axis slices (slice thickness 15 mm, gap 5 mm, field of vision 34 to 38 cm, matrix: 256 × 256). Breath-hold steady-state free precession images (TR 3.8 ms, TE 1.6 ms) were acquired in two- and four-chamber views to assess global ventricular function. We then applied a free breathing spin echo sequence in four identical axial slices both before and after (without any change in parameters in between) intravascular injection of 0.1 mmol gadolinium-diethylenetriaminepentaacetate (DTPA) (Magnevist, Schering, Germany) using an automated injector (Medrad, Indianola, Pennsylvania). The sequence was started immediately after injection and lasted 3 to 4 min; thus, the images reflect gadolinium enhancement at a mean of 2 min. After the acquisition of spin echo images, an additional dose (0.1 mmol) of gadolinium-DTPA was injected, and a breath-hold contrast-enhanced inversion-recovery gradient-echo sequence (TR 5.5 ms, TE 1.4 ms, TI 225 to 275 ms as individually optimized to null myocardial signal, matrix 256 × 192, slice thickness/gap 15/5 mm) was applied after a delay of 10 min in three short- and three long- (two-, three-, and four-chamber views, respectively) axis slices.

Coronary angiography. Coronary angiography was performed on a standard angiography suite (Hicor, Siemens, Erlangen, Germany) in 21 patients to exclude the presence of significant coronary artery disease (>70% stenosis).

Clinical analysis. Two observers (A.Z. and P.B.), who were blinded to CMR data, assessed the clinical course of the patients during their hospital stay.

Image analysis. SPIN ECHO IMAGES. Regions of interest covering the left ventricular myocardium as well as within a skeletal muscle (erector spinae or lattisimus dorsi) in the same slice were manually drawn in the precontrast images and were copied to the postcontrast images (Fig. 1), and gRE was calculated as previously described (2).

T2-WEIGHTED IMAGES. Quantitative analysis: regions of interest were drawn covering the left ventricular myocardium and within a skeletal muscle in the same slice. The myocardial signal intensity (SI) was related to that of the skeletal muscle:

$$\text{Relative myocardial T2 SI} = SI_{\text{myocardium}} / SI_{\text{skeletal muscle}}$$

Endocardial and epicardial contours were manually drawn, and focal areas of high T2 SI (those with SI more than the normal myocardium plus two standard deviations) were identified (MASS 6, Medis, Leiden, the Netherlands).

QUALITATIVE ANALYSIS. This was performed by the consensus agreement of two observers (J.S-M. and H.A-A.) who were blinded to the patients' clinical data. Images were evaluated for the presence or absence of focal or segmental areas of high T2 SI.

LGE. QUALITATIVE ANALYSIS. This was done for the presence, number, and transmurality of LGE areas.

QUANTITATIVE ANALYSIS. Areas of LGE (those with SI more than the normal myocardium plus two standard deviations) were delineated similar to that in T2 imaging. Regions of interest were also drawn within background air. The contrast-to-noise ratio (CNR) and the signal-to-noise ratio (SNR) of LGE were then calculated as follows:

$$CNR = (SI_{LGE} - SI_{\text{myocardium}}) / SI_{\text{noise}}$$

$$SNR = SI_{LGE} / SI_{\text{noise}}$$

Foci of high signal in delayed enhancement and T2 images were traced, and their volume expressed as a percentage of the total myocardial slice volume.

Statistics. All statistical tests were performed using a commercially available statistical program (SPSS 11 for Macintosh, SPSS Gmbh Software, Munich, Germany). Data are presented as mean ± SD. Continuous variables were compared using the Mann-Whitney *U* test and noncontinuous data using the chi-square test. Data were correlated using the Spearman correlation coeffecient. Reciever operating charcteristic curves were used to identify the cutoff values of gRE and global T2 signal changes. A p value <0.05 was considered significant.