Altered energy metabolism after myocardial infarction assessed by 31P-MR-spectroscopy in humans

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Abstract. The value of 31P-magnetic resonance spectroscopy (MRS) as a possible tool to distinguish viable from non-viable tissue after myocardial infarction was analysed in humans. Fifteen patients 3 weeks after anterior myocardial infarction were studied with breath-hold cine MRI and 3D-CSI MRS (1.5 T system). 31P-spectra were obtained from infarcted as well as non-infarcted myocardium (voxel size 25 cm3 each). Gold standard for viability was recovery of regional function, as determined by a control MRI 6 months after revascularization. Ten age-matched healthy volunteers served as control group. No significant difference was found between the phosphocreatine to adenosinetriphosphate (PCr/ATP) ratio of volunteers (SD 1.72 ± 0.31) and non-infarcted septal myocardium of patients. Cine MRI demonstrated recovery of regional function in 10 patients, i.e. 10 patients showed viable and 5 non-viable myocardium. In viable myocardium, the PCr/ATP ratio was 1.47 ± 0.38 (non-significant vs volunteers; p > 0.05). In the 5 patients with akinetic myocardium, PCr peaks could not be detected. Therefore, calculation of PCr/ATP ratios was not possible. However, a significant reduction of the ATP signal-to-noise ratio (SNR) was observed (2.92 ± 0.73 vs 6.68 ± 0.80; patients vs volunteers; p <0.05). The SNR of ATP of akinetic regions may predict recovery of function after revascularization in patients with myocardial infarction.

Key words: Heart – Ischaemia – MR imaging – MR spectroscopy – High-energy phosphates

Introduction

After myocardial infarction, differentiation between viable (hibernating or stunned) and non-viable (scar) tissue is crucial for the decision whether revascularization is required [1, 2]. Currently, stress echocardiography, thallium scintigraphy and, more recently, positron emission tomography (PET) and MRI are used for the diagnosis of myocardial viability. However, these methods have constraints such as investigator dependence, use of external tracers or high costs [1, 2, 3]. Magnetic resonance spectroscopy (MRS) offers the unique possibility to study non-invasively cardiac energy metabolism [4, 5]. Experimental data using 31P-MRS have shown that normal myocardium contains high amounts, whereas non-viable (scar) tissue contains negligible amounts of high-energy phosphates (HEP) [6, 7].

However, only few reports are available on the clinical use of MRS for ischaemic heart disease [8, 9, 10, 11]. This may be due to three main problems of human cardiac spectroscopy: (a) a low spatial resolution with large voxels due to low sensitivity; (b) contamination by surrounding tissue other than the heart; and (c) problems with determination of absolute values of metabolites [4]. Different spectroscopic localization techniques are used to overcome these problems such as chemical-shift imaging (CSI). Chemical-shift imaging allows (a) a spatial resolution of approximately 25 cm2, and (b) adaptation of double-angulated voxels to cardiac tissue decreasing contamination by surrounding tissue. Reports on the use of CSI for absolute quantification of energy metabolites in humans are limited [10, 12, 13, 14]. However, as a multivoxel technique, CSI allows comparison of injured and non-injured myocardium during one examination using the non-injured myocardium as internal reference.

31P-MRS with CSI was used to test the hypothesis that the PCr/ATP ratio or PCr- and ATP signal-to-noise ratio (SNR) may allow differentiation between viable and non-viable myocardium in patients after anterior myocardial infarction.
Subjects and methods

Patients

Fifteen patients were examined 22 ± 10 days (range 14–50 days) after anterior myocardial infarction. There were 12 men and 3 women with an age range of 37–78 years (mean age 60.5 ± 12.0 years). Coronary angiography and left ventriculography were performed in all patients using standard techniques and a combined study with MRI and MRS was performed. Both examinations were performed on the same day. The total MR investigation time was approximately 90 min for each patient.

None of the patients had a pacemaker, a history of metal fragments, implants or vascular clips, severe arrhythmias, unstable angina pectoris or claustrophobia. All patients underwent revascularization of the coronary lesions. Ten patients had percutaneous transluminal coronary angioplasty (PTCA), and 5 of them had coronary artery bypass grafting (CABG). Patients were reexamined 6 months after revascularization with MRI to determine recovery of regional function for assessment of viability. Written informed consent was obtained from all patients and volunteers, and the study was approved by the Ethics Committee of the University of Würzburg.

Volunteers

Ten healthy volunteers (6 men and 4 women; age range 21–69 years, mean age 41 ± 17 years) were examined as a control group with MRI and MRS. None of them had a history of heart disease and global functional analysis by MRI was normal. Voxel of size of 25 cm³ were positioned in the septal myocardium as well as in the anterior myocardium of each volunteer. The PCR/ATP values were compared in a separate study. For nuclear Overhauser enhancement (NOE), correction factors were determined using two consecutive measurements with and without NOE [15].

Cardiac MR imaging

Magnetic resonance imaging as well MRS were performed on a 1.5-T scanner (Magnetom Vision, Siemens, Erlangen, Germany). For imaging, subjects were studied in supine position, using a phased-array body coil. Short- and long-axis cine MRI was performed using an ECG-triggered cine 2D-FLASH sequence. Slice thickness was 8 mm using a breathhold technique in end-expiratory position with TR of 100 ms, TE of 4.8 ms and flip angle of 30°. For functional analysis all short-axis slices from the base to the apex were analysed using the Argus software version VB31B (Siemens, Erlangen, Germany).

In order to evaluate regional function, the short-axis views of the left ventricle were equally divided into eight segments [16] with a reference sector put at the anterior border of the free right ventricular wall to the left ventricular wall. Depending on the heart size, the number of segments per patient ranged from 63–79. Regional wall motion was assessed visually by consensus reading of two observers. Myocardial viability was defined as an improvement of systolic wall thickening at rest 6 months after revascularization. Criterion for viability was regained motion of the majority of segments, i.e. of more than 50% of segments, which had former wall-motion abnormalities.

13P-MR spectroscopy

Data acquisition

For MRS, patients were positioned in prone position in order to decrease breathing artifacts. 13P-spectra were acquired using a double resonant 13P/1H-surface coil. Using a 2D turbo-FLASH sequence with a field of view (FOV) of 400 × 400 mm² (30 adjacent 8-mm slices each, 128 × 256 matrix, 4 acquisitions, dark-blood technique) 1H images were obtained from the short- and the two long-heart axes. Next, an automatic phase-sensitive map shim was performed. The full width half maximum (FWHM) was less than 70 Hz. Afterwards, a 13P-3D-CSI sequence was started, consisting of 8 × 8 × 8 phase-encoding steps with a FOV of 200 × 200 × 320 mm³. Five hundred twelve spectral data points were acquired in 256 ms. Trigger delay was 50 ms after the R-wave; four averages were obtained in 45 up to 60 min. In order to increase the SNR of the spectra, NOE was applied [15] depending on the heart rate.

Data processing

The software package “Luise” (Siemens, Erlangen, Germany) was used for postprocessing. In the spatial dimensions no filter was applied. The time-domain signal underwent baseline correction (the last 20% of the FID were used), zero-filling to 1024 data points, and an exponential filter having a time constant of 50 ms. After Fourier transformation of the free induction decay (FID), zero and first-order phase correction, baseline correction was applied by polygonal subtraction. After processing, the area under each peak was determined by manual fit with computer assistance. The calculation of the PCR/ATP ratios was based on the areas of the PCR- and γ-ATP-signal. The SNR of PCR and γ-ATP were calculated using the Matlab software package Amares for the determination of the signal amplitudes [17]. Noise was determined via the standard deviation of the last 100 points of the FID signal.

The effect of saturation was considered using the mean TR of each experiment and published T1-values [18]. The NOE correction factors were obtained from healthy volunteers. Blood contamination of the spectra was corrected using the 2,3 diphosphoglycerate (2,3-DPG) resonances from blood as a reference. As described previously [19], 15% of the integral area of the