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Intraindividual comparison of T1 relaxation times after gadobutrol and Gd-DTPA administration for cardiac late enhancement imaging

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ABSTRACT

Purpose: To evaluate T1-relaxation times of chronic myocardial infarction (CMI) using gadobutrol and gadopentetate dimeglumine (Gd-DTPA) over time and to determine the optimal imaging window for late enhancement imaging with both contrast agents.
Material and methods: Twelve patients with CMI were prospectively included and examined on a 1.5 T magnetic resonance (MR) system using relaxivity-adjusted doses of gadobutrol (0.15 mmol/kg) and Gd-DTPA (0.2 mmol/kg) in random order. T1-relaxation times of remote myocardium (RM), infarcted myocardium (IM), and left ventricular cavity (LVC) were assessed from short-axis TI scout imaging using the Look–Locker approach and compared intraindividually using a Wilcoxon paired signed-rank test ($\alpha < 0.05$).
Results: Within 3 min of contrast agent administration (CA), IM showed significantly lower T1-relaxation times than RM with both contrast agents, indicating beginning cardiac late enhancement. Differences between gadobutrol and Gd-DTPA in T1-relaxation times of IM and RM were statistically not significant through all time points. However, gadobutrol led to significantly higher T1-relaxation times of LVC than Gd-DTPA from 6 to 9 min (220 ± 15 ms vs. 195 ± 30 ms $p < 0.01$) onwards, resulting in a significantly greater ΔT1 of IM to LVC at 9–12 min (-20 ± 35 ms vs. 0 ± 35 ms, $p < 0.05$) and 12–15 min (-25 ± 45 ms vs. -10 ± 60 ms, $p < 0.05$). Using Gd-DTPA, comparable ΔT1 values were reached only after 25–35 min.
Conclusion: This study indicates good delineation of IM to RM with both contrast agents as early as 3 min after administration. However, we found significant differences in T1 relaxation times with greater ΔT1 IM–LVC using 0.15 mmol/kg gadobutrol compared to 0.20 mmol/kg Gd-DTPA after 9–15 min post-CA suggesting earlier differentiability of IM and LVC using gadobutrol.

1. Introduction

Cardiac late gadolinium enhancement (LGE) imaging is a highly sensitive and specific method for assessment of myocardial infarction, allowing direct imaging of myocardial necrosis and fibrosis with high spatial resolution and tissue contrast [1–3]. The extent of LGE has a high prognostic value and may be used to predict functional recovery, cardiovascular events, and response to revascularization or resynchronization therapy following myocardial infarction [4,5]. LGE is measured on T1-weighted images after intravenous administration of T1-shortening extracellular gadolinium chelates [6], which have been shown to accumulate in infarcted myocardium [7]. Accumulation in infarcted myocardium is assumed to be a result of altered wash-in/wash-out kinetics and an increased extracellular volume [1,8].

Most studies on LGE have been conducted with the first approved magnetic resonance (MR) imaging contrast agent, gadopentetate dimeglumine (Gd-DTPA) [2,6,8]. In the last decades,

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several other gadolinium-based MR contrast agents have been approved. They differ in their molecular structure, charge, thermodynamic stability, pharmacokinetics, and T1 relaxivity [9,10]. Gadobutrol is a nonionic macrocyclic extracellular contrast agent, with a higher T1 relaxivity compared to the ionic, linear contrast agent Gd-DTPA [9,11]. These contrast agents have been investigated in comparative studies in different organ systems to evaluate their potential use for specific indications [12–14]. Recent comparative studies evaluated different MR contrast agents also for cardiac LGE imaging at a certain time point after administration [12,15–19]. The contrast agents investigated in these studies were generally found to allow reliable differentiation between infarcted myocardium (IM) and remote myocardium (RM). In contrast, the delineation of IM from the left ventricular cavity (LVC) proved to be challenging and varied significantly for some contrast agents [15,18]. These observations indicate that the pharmacokinetics of the compared contrast agents in IM and LVC differ. Yet, IM-to-LVC contrast is needed for delineating small subendocardial infarcts and measuring infarct transmurality, which are strong prognostic parameters [20]. T1 relaxation times after contrast agent injection determine contrast in T1-weighted images. Unlike signal intensity measurements, the T1 relaxation time is a quantitative measure and its absolute value after contrast agent application seems to be of clinical significance [21]. It relates to the extracellular volume fraction and is reduced in conditions with myocardial fibrosis [30]. Therefore, we sought to determine the T1 relaxation times in RM, IM, and LVC and the T1 relaxation time difference between IM and RM (ΔT1 IM–RM) as well as IM and LVC (ΔT1 IM–LVC) over time after administration of Gd-DTPA and gadobutrol in order to determine the optimal imaging time point for cardiac LGE imaging with the two contrast agents based on the T1 relaxation times and to screen for systematic differences in post-contrast T1 relaxation times.

2. Methods

2.1. Population

The study was conducted as an intraindividual comparison of Gd-DTPA (Magnevist®, Bayer Healthcare, Berlin, Germany) and gadobutrol (Gadovist®, Bayer Healthcare, Berlin, Germany) for cardiac LGE imaging. Twelve patients with chronic myocardial infarction were included for T1 relaxation time measurements. Patients were examined on a 1.5 Tesla MR system (Siemens Magnetom Avanto) using a 32-channel phased array surface coil. All participants had glomerular filtration rates >60 ml/min/1.73 m^2 (estimated by the MDRD-formula). In two separate visits (2–30 days apart), patients received 0.2 mmol/kg Gd-DTPA and 0.15 mmol/kg gadobutrol in random order. Contrast agents were administered through a cubital vein catheter using an MRI-compatible infusion system (Spectrum Solaris®), followed by a 20 mL saline flush. Both the contrast agent and the saline flush were injected at a flow rate of 2 mL/s. The Federal Institute for Drugs and Medical Devices and the local ethics committee approved this single-center drug study. Informed written consent was obtained from all patients prior to enrolment in the study.

2.2. MR imaging

From 0 to 15 min after contrast agent administration, TI scout imaging (segmented inversion recovery TrueFISP, repetition time (TR) 23.49 ms, echo time (TE) 1.12 ms, flip angle 50, TI range 85–1000 ms, step size 25 ms) was performed approximately every 3 min. At 15 min, a segmented inversion recovery gradient echo (IR-GRE) sequence (2D T1-weighted fast low-angle shot (FLASH) 2D; TR 9.4 ms, TE 4.4 ms, flip angle 30, readout bandwidth 140 Hz/Px, matrix 256 × 197, in-plane resolution 1.6 mm × 1.3 mm, slice thickness 6 mm, slice gap 20%, adapted inversion time) was acquired for identifying sites of cardiac LGE. Thereafter, TI scout imaging was continued between 25 and 35 min.

2.3. Calculation of T1 relaxation times

Using dynamic regions of interest (ROI), an area of IM (infarct-type myocardial late enhancement localized on IR-GRE imaging), RM and LVC was encircled in all TI scout images and manually adjusted for regional wall movement during TI scout imaging (Fig. 1). T1 values were estimated by nonlinear regression of the signal intensities to the TI times using the following equation:

$$SI_{(TI)} = SI_0^* \left[1 - 2^* \exp\left(-\frac{TI}{T1}\right)\right]$$

As a measure of tissue contrast, differences between the T1 relaxation times of tissues were calculated (ΔT1 IM–RM and ΔT1 IM–LVC).

2.4. Statistical analysis

Continuous values are given as means with standard deviations (SD). To compare T1 relaxation times intraindividually, results were stratified into six groups based on the TI scout imaging time after contrast agent injection (0–3 min, 3–6 min, 6–9 min, 9–12 min, 12–15 min and 25–35 min). This resulted in a total of 65 valid intraindividual pairwise comparisons between both examinations, while seven pairs had to be excluded due to a missing TI scout in the corresponding time group. When more than one TI scout was acquired within any one of the six groups, the arithmetic mean of the T1 relaxation times was calculated. The mean T1 relaxation time for both contrast agents in all time groups and the mean intraindividual differences between contrast agents were calculated and compared using the Wilcoxon signed-rank test (two-sided p-values <0.05 were regarded as significant). All calculations were performed using a commercially available software package (SPSS Statistics 19, IBM, Armonk, NY, USA).

3. Results

3.1. T1 relaxation times in remote and infarcted myocardium and left ventricular cavity

The T1 relaxation times for RM, IM, and LVC at all time points are given in Table 1 and illustrated over time in Fig. 2. In RM, initial T1 relaxation times at 0–3 min were 225 ± 25 ms and 245 ± 40 ms in Gd-DTPA- and gadobutrol-enhanced images, respectively (Table 1). Thereafter, T1 times showed a steady increase with both contrast agents without any significant difference between the two contrast agents at any time point ($p > 0.05$; Table 1), indicating wash-out of the contrast agent from RM. Due to the circulating contrast agent, LVC showed T1 relaxation times of 115 ± 15 ms and 125 ± 15 ms for Gd-DTPA and gadobutrol, respectively, at 0–3 min. Likewise, T1 relaxation times of LVC showed a steady incline over time due to renal excretion. Significantly shorter T1 relaxation times were measured in LVC with Gd-DTPA compared to gadobutrol from 6 to 9 min onwards ($p < 0.01$; Table 1), indicating stronger enhancement of the LVC with use of Gd-DTPA from this time onwards.

IM showed T1 relaxation times of 160 ± 40 ms and 180 ±40 ms, respectively, in Gd-DTPA- and gadobutrol-enhanced images 0–3 min after administration (Table 1). T1 relaxation times of IM showed a steady incline over time and were lower than T1 relaxation times of RM at all times with both contrast agents, indicating "delayed" enhancement of IM beginning as early as 0–3 min after