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ORIGINAL ARTICLE

Comparison of gadofosveset (Vasovist®) with gadobenate dimeglumine (Multihance®)-enhanced MR angiography for high-grade carotid artery stenosis

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Magnetic resonance imaging;
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Summary
Objective: To prove superiority of blood pool contrast agent gadofosveset over conventional contrast agent gadobenate dimeglumine for assessment of stenotic internal carotid artery (ICA).
Methods: Eleven patients with high-grade ICA stenosis (≥ 75%), confirmed by duplex sonography, underwent MR angiography (MRA) with gadofosveset and gadobenate dimeglumine.
Results: Agreement in stenosis grade was reached in 7 of 10 stenotic ICAs. In two ICAs, gadobenate dimeglumine led to underestimation of stenosis grade. There was a significant difference in signal intensity (pre-/post-stenotic segments), showing higher values for gadofosveset ($P < 0.01$; $P < 0.05$). Impression of contrast intensity with gadofosveset was better in 8 ICAs and only in 1 ICA with gadobenate dimeglumine ($P < 0.05$).
Conclusion: Gadofosveset-enhanced MR angiography may be superior for assessment of high-grade ICA stenosis compared with gadobenate dimeglumine MR angiography.

Introduction

Carotid artery disease is one of the most common reasons for a stroke. Stenoses of the carotid arteries are responsible for approximately 20% of all stroke events. The early

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detection of ischemic areas has been improved since 3-T optimized diffusion-weighted magnetic resonance imaging (MRI) with use of high b-values is available [1,2]. By use of multimodality imaging, both acute hemorrhage as well as far-reaching morphologic and pathophysiologic information of brain tissue can be gained within an acceptable timeframe [3]. However, the main goal is to prevent potential patients to suffer a stroke. Several large studies (NASCET, ECST) revealed for patients with a symptomatic or asymptomatic high-grade stenosis (> 70%) of the internal carotid artery (ICA) a significant reduction of the risk for an ischemic event by carotid endarterectomy (CEA) [4—7]. Preprocedural planning before CEA requires a reliable imaging tool for the assessment of the stenosis degree. Contrast-enhanced (CE) magnetic resonance angiography (MRA) using a T1 shortening contrast agent has been well established as an alternative to conventional catheter-based angiography in diagnostics of vascular diseases [8—11]. The accuracy of gadolinium-enhanced MRA for characterizing the degree of carotid stenosis is high and MRA based grading of stenosis agrees with findings of digital subtraction angiography in 92—94% [12]. In opposite to non-contrast-enhanced MRA, CE MRA displays certain advantages, it is independent of the blood flow, enables a fast acquisition of angiograms in a short scan time, offers high anatomical coverage and better contrast of vascular structures [13,14]. With high-field MRA, even small arteries like the artery of Adamkievicz can precisely be detected and evaluated. This implicates that the middle sized vertebral arteries can clearly be evaluated with MRA what may be essential for the vascular surgeon. Moreover, important preoperative findings, e.g. arteriovenous malformations and dural fistulas can simply be detected with MRA [15].

A potential drawback of CE MRA is related to the short plasma half-life of extracellular gadobenate dimeglumine-based contrast agents in the order of 100 seconds, providing only a short time window with optimal vascular contrast [16]. Therefore, only first-pass (FP) image acquisition is possible with CE MRA using extracellular contrast agents restricting the potential spatial resolution. Improvement of spatial resolution and thereby image quality could be obtained if a prolonged imaging window with optimal vascular contrast was available. Intravascular blood pool contrast agents binding reversibly to serum albumine are a promising approach to overcome this drawback [17—20]. Gadofosveset is the first intravascular contrast agent approved for MRA use in the European Union and is characterized by a long lasting presence in the intravascular space up to 60 minutes due to its high affinity to albumine, providing significantly higher T1 and T2 relaxivities and extended intravascular enhancement compared to existing extracellular magnetic resonance contrast agents [21]. Gadofosveset is commercially available as Vasovist®. By using blood pool agents like gadofosveset, the time window for the acquisition of angiograms with high vascular contrast can be widened up to 60 minutes permitting steady-state (SS) MRA with high-spatial resolution [21]. Therefore, administration of gadofosveset might be an appropriate strategy to optimize diagnostic quality of CE MRA particularly in cases of high-grade stenosis of the ICA.

Although several studies exist about the use of gadofosveset in different areas of the vascular system [22—24], there is only limited evidence about the performance of the agent in imaging of the cervical vessels [25—27].

The aim of this study was to evaluate the diagnostic accuracy of gadofosveset-enhanced MRA and the potential benefit originating from steady-state imaging in the assessment of a high-grade carotid artery stenosis in comparison with conventional CE MRA performed with the high-relaxivity contrast agent gadobenate dimeglumine.

Material and methods

Study design

This single center study was approved by the local ethics committee and was conducted according to Good Clinical Practice. All patients gave written informed consent. Table 1 summarizes baseline demographics and clinical data. With the exception of the patient 04-002, who developed a high-grade stenosis of the ICA due to traumatic dissection, all patients had atherosclerosis as underlying etiology.

The study was a phase IIIb study designed to show the superiority of gadofosveset over gadobenate dimeglumine regarding the visibility of cervical vessels. In this study, gadofosveset and gadobenate dimeglumine were investigated with an intraindividual cross-over comparison. Inclusion criteria were at least one high-grade stenosis of the carotid artery (> 75%) confirmed by ultrasound of local diameter reduction according to ECST-criteria [4]. All patients were assigned for carotid endarterectomy and referred to us by the department of vascular surgery. Exclusion criteria were pregnancy, reduced kidney function (GFR < 60 mL/min), general MR contraindications (pacemaker, magnetic clips, severe claustrophobia), and history of anaphylactic or anaphylactoid reaction to any drugs or contrast agents.

In all subjects, gadobenate dimeglumine (MultiHance®, Bracco Imaging SpA—Via EgidioFolli, 50, 20134 Milano, Italy) was injected first. Gadofosveset-enhanced MRA (Vasovist®, Bayer Schering Pharma AG, Berlin/Germany) followed at a time interval of at least 48 hours to guarantee a complete excretion of gadobenate dimeglumine.

Primary target variable was defined as the subjective overall (per patient) superiority for SS-MRA vs. FP-MRA regarding visibility of vessel segments using a visual analog 19-point scale from −9 to 9 with 0 = both procedures are equal. Secondary target variables included the assessment of the degree of stenosis (< 75%, 75% to < 90%, 90—99%, 100%), the length of stenosis, signal intensity of pre- and post-stenotic segments of the ICA as well as the diagnostic confidence and impression of contrast intensity in a 4-point scale (very confident, confident, not confident, not confident at all).

MR imaging

MRI was performed using a 1.5 Tesla MR unit (Magnetom Avanto; Siemens Medical Solutions, Erlangen, Germany). Patients were placed in the supine position. For signal acquisition a head-neck array coil was used. MRI study protocol was standardized and included morphological imaging in addition to CE MRA.