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Comparison of blood pool and extracellular gadolinium chelate for functional MR evaluation of vascular thoracic outlet syndrome☆

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ABSTRACT

Objective: To compare performance of single-injection blood pool agent (gadofosveset trisodium, BPA) against dual-injection extracellular contrast (gadopentetate dimeglumine, ECA) for MRA/MRV in assessment of suspected vascular TOS.
Materials and methods: Thirty-one patients referred for vascular TOS evaluation were assessed with BPA ($n = 18$) or ECA ($n = 13$) MRA/MRV in arm abduction and adduction. Images were retrospectively assessed for: image quality (1 = non-diagnostic, 5 = excellent), vessel contrast (1 = same signal as muscle, 4 = much brighter than muscle) and vascular pathology by two independent readers, with a separate experienced reader providing reference assessment of vascular pathology.
Results: Median image quality was diagnostic or better (score ≥ 3) for ECA and BPA at all time points, with BPA image quality superior at abduction late (BPA 4.5, ECA 4, $p = 0.042$) and ECA image quality superior at adduction-early (BPA 4.5; ECA 4.0, $p = 0.018$). High qualitative vessel contrast (mean score ≥ 3) was observed at all time points with both BPA and ECA, with superior BPA vessel contrast at abduction-late (BPA 3.97 ± 0.12; ECA 3.73 ± 0.26, $p = 0.007$) and ECA at adduction-early (BPA 3.42 ± 0.52; ECA 3.96 ± 0.14, $p < 0.001$). Readers readily identified arterial and venous pathology with BPA, similar to ECA examinations.
Conclusion: Single-injection BPA MRA/MRV for TOS evaluation demonstrated diagnostic image quality and high vessel contrast, similar to dual-injection ECA imaging, enabling identification of fixed and functional arterial and venous pathology.

1. Introduction

Thoracic outlet syndrome (TOS) refers to compression of neurovascular structures at the thoracic outlet. A vascular etiology accounts for less than 10% of cases [1], but can cause debilitating ischemia or congestion in arterial or venous TOS respectively, and potential complications of aneurysm or thromboemboli. Clinical diagnostic tests have not been found reliable [1], and imaging can identify and localize the site of compression, and demonstrate if these are structural or functional [2–4]. MR angiography (MRA) and equilibrium phase venography (MRV) have been described, with provocative imaging in both arm abduction and adduction, for the evaluation of functional compression of the subclavian vessels [3,5–8]. Contrast-enhanced 3D T1 weighted imaging provides large field of view imaging and reliable assessment of both arteries and veins [5,8]. Using a dual injection protocol, extracellular gadolinium chelate is administered into the non- or less-symptomatic arm, with acquisitions in arm abduction and adduction, to ensure good arterial and venous opacification in both positions. This leads to contrast doses of the order of 0.15–0.2 mmol/kg [5,7], greater than standard single dosage (0.1 mmol/kg) of extracellular agents.

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Recently, a blood-pool gadolinium chelate, gadofosveset trisodium (gadofosveset), was approved by the Food and Drug Administration for MR angiography in the United States [9] following multi-center phase 2 and phase 3 trials [10–14], and has been in use in Europe since 2005. No other blood pool contrast agents are currently approved and commercially available for MR angiography. Strong but reversible binding of gadofosveset to human serum albumin results in approximately five times greater T1 relaxivity of blood following contrast administration at 1.5 T compared to standard extracellular contrast agents [15,16], and prolonged arterial and venous enhancement, with an elimination half life of approximately 16 h [17]. This enables high quality venous imaging and gains in spatial resolution particularly during steady state imaging [7,18–22]. Additionally, higher T1 relaxivity results in a relatively lower standard dose for gadofosveset of 0.03 mmol/kg, suitable for MR angiography and venography.

Although use of gadofosveset has been anecdotally reported for MR evaluation of vascular TOS [23], its performance with a single administration has not been specifically compared against a standard two-injection protocol using an extracellular agent. The purpose of our study was to compare the image quality, vessel contrast and detection of vascular pathology of single-injection gadofosveset (blood pool agent, BPA) with dual-injection gadopentetate dimeglumine (extracellular contrast agent, ECA) functional MRA/MRV in patients presenting for evaluation of suspected vascular TOS.

2. Materials and methods

2.1. Patients

This was a retrospective Health Insurance Portability and Accountability Act compliant study approved by the Institutional Review Board, which waived informed consent. From April 2011, gadofosveset (Ablavar, Lantheus, North Billerica, MA) replaced gadopentetate dimeglumine (Magnevist, Bayer, Wayne, NJ) as the contrast agent used for MRA work-up of suspected vascular thoracic outlet syndrome at our institution. A total of 33 consecutive patients (21 female, mean age 36.5 years, range 18–77 years) were identified from the Radiology records that were scanned between September 2010 and March 2012. Two of the 33 patients were excluded, as they were scanned on a 3-T system. Of the final cohort, 18 patients (12 female, mean age 35.6 years) were scanned with BPA and 13 patients (9 female, mean age 39.4 years) were scanned with ECA. Indications for imaging were: known subclavian or upper extremity deep venous thrombosis ($n = 8$), isolated upper extremity pain ($n = 7$), pain and swelling ($n = 3$), pain and parasthesias ($n = 8$) and sensory disturbance alone ($n = 5$). 3/31 patients reported bilateral symptoms.

2.2. Imaging

Imaging was performed on a 1.5-T system (Avanto, Siemens, Erlangen, Germany) using two 6-element body phased-array coils anteriorly and a 24-element spine coil posteriorly, with individual elements automatically chosen by the system. According to the institutional clinical protocol, patients were first positioned with arms abducted bilaterally, as an initial provocative maneuver to identify position-related vascular compression, with arm abduction exacerbating vascular compression in true vascular TOS [24]. Following planning images and 2D time of flight images to evaluate direction of vertebral artery flow (not evaluated for this study), contrast-enhanced MR angiography was performed with a coronal 3D T1-weighted spoiled gradient echo sequence (FLASH), with one acquisition prior to contrast and two consecutive acquisitions following contrast, with injection via the non- or less-symptomatic arm. The non- or less-symptomatic arm was always used for contrast injection, as susceptibility artifacts from concentrated injected gadolinium in the veins may impact observed signal in adjacent arteries during the first pass [25]. The first post-contrast acquisition (abduction-early) was timed for peak arterial opacification using a bolus tracking approach. 0.03 mmol/kg BPA at a rate of 1 ml/s or 0.075 mmol/kg ECA at a rate of 2 ml/s was administered for the MRA, followed by a 20 ml saline flush. Volume interpolated breath hold imaging (VIBE) was performed 3 min following the contrast injection for venous assessment (abduction-late), according to our institutional protocol for MRV.

Table 1
Sequence parameters for FLASH (early phase) and VIBE (late phase) images.

Parameter	FLASH	VIBE
TR (ms)	3.0	3.6
TE (ms)	1.2	1.3
Flip angle (°)	25	12
Field of view (mm)	450 × 450	500 × 344
True voxel size (mm^3)	1.8 × 1.8 × 1.8	2.6 × 2.6 × 3.3
Base resolution	384 × 384	320 × 220
Slice resolution (%)	64	60
Phase resolution (%)	64	60
Orientation	Coronal	Axial
Parallel imaging factor (GRAPPA)	2	2
Bandwidth (Hz/pixel)	430	430
Number of measures in each arm position	1 pre-contrast, 2 post-contrast	1 post-contrast
Acquisition time per measure (s)	23	23

The patient was then repositioned with arms adducted and the identical imaging protocol performed. Imaging in the adduction position forms part of the evaluation for thoracic outlet syndrome, to determine if any vascular stenosis/compression present on the initial provocative abduction scan persists or resolves, indicating fixed versus functional abnormality, respectively. For patients receiving ECA, a second 0.075 mmol/kg injection was administered for repeat MRA (adduction-early) in arm adduction prior to repeat VIBE (adduction-late), for a total of 0.15 mmol/kg. However, for BPA patients, no second dose of contrast was administered in arm adduction, with imaging intervals between FLASH MRA and VIBE maintained. Sequence parameters for the FLASH and VIBE sequences are reported in Table 1. Total imaging time was recorded from the first localizer to the final adduction-late VIBE sequence.

2.3. Image analysis

Two readers (R1 (DCK), with 11 years, and R2 (ABR), with 4 years of experience with MR angiography) independently evaluated anonymized source images for both the symptomatic, non-injected, arm, and non- or less-symptomatic, injected arm using a standard PACS platform (iSite, Phillips, Best, The Netherlands). Parameters evaluated were image quality (1 = non-diagnostic, 2 = poor, 3 = satisfactory for diagnosis, 4 = good, 5 = excellent); arterial contrast at abduction-early and adduction-early (1 = same as muscle, 2 = slightly brighter than muscle, 3 = moderately brighter than muscle, 4 = much brighter than muscle); venous contrast at abduction-late and adduction-late, using the same 4-point scale relative to muscle; and arterial and venous pathology. Artifacts were recorded. For arterial pathology, stenosis was evaluated on a 5-point scale [4] (0 = no stenosis, 1 ≤ 50% stenosis, 2 = 50–69% stenosis, 3 = 70–99% stenosis, 4 = occluded), and readers were asked to record if post-stenotic dilatation (<50% increase in diameter of vessel compared to normal vessel), aneurysm (≥50% diameter increase), or thrombus were present. For venous pathology, stenosis was evaluated on a 4-point scale (0 = no stenosis, 1 ≤ 60% stenosis, 2 = 60–99% stenosis, 3 = occluded) based on a previously