Gadobenate Dimeglumine for Contrast-Enhanced MR Angiography of the Carotid, Renal, and Peripheral Arteries: Overview of Phase III Clinical Trials

G. Soulez[1], S. Thurnher[2], N. Anzalone[3], and G. Pirovano[4]

[1]Radiology, University of Montreal, Montreal, Quebec, Canada, [2]Radiology, University of Vienna, Vienna, Austria, [3]Radiology, San Raffaele Hospital, Milan, Italy, [4]WW Medical Affairs, Bracco Diagnostics Inc., Princeton, NJ, United States

Purpose

To review information from the Phase III clinical program to assess the safety and efficacy of 0.1 mmol/kg gadobenate dimeglumine (Gd-BOPTA; MultiHance®) for contrast-enhanced MR angiography (CE-MRA) of occlusive disease of the carotid, renal, and peripheral arteries using digital subtraction angiography (DSA) as a reference standard.

Methods

Carotid Arteries[1]

Patients with suspected coronary artery disease (N=248) underwent MRA and DSA within 2 weeks. MRA (1.5T; from the aortic arch to the carotid siphons) comprised an unenhanced 2D-TOF sequence and a contrast-enhanced (Gd-BOPTA; 0.1 mmol/kg at 2 ml/sec) 3D spoiled GRE sequence. Images were evaluated by 4 experienced blinded readers. Analyses included determination of: technical adequacy of MRA; sensitivity, specificity, and accuracy for detection of significant (≥60%) stenosis for MRA and DSA; and determination of inter-reader agreement. A complete safety assessment was performed.

Renal Arteries[2]

Patients (N=293) underwent CE-MRA using 3D spoiled GRE acquisitions after administration of 0.1 mmol/kg Gd-BOPTA at 2 mL/sec. DSA was performed in 268 (91.5%) subjects. CE-MRA images were evaluated by 3 independent, blinded reviewers. Statistical analyses included determination of: sensitivity, specificity, and accuracy of CE-MRA for detection of significant (≥51% vessel lumen narrowing) steno-occlusive disease at the segment and patient level using DSA as reference standard; positive and negative predictive values and positive and negative likelihood ratios; and inter-observer agreement. A full safety evaluation was performed.

Peripheral Arteries[3]

MRA and DSA were performed for the iliofemoral arteries in 272 subjects and the calf arteries in 241 subjects. MRA was performed before (2D-TOF and 3D spoiled GRE acquisitions) and after (spoiled GRE acquisitions only) administration of 0.1 mmol/kg Gd-BOPTA at 1-2 mL/sec. Images were evaluated on-site and by 4 blinded reviewers. Comparative diagnostic performance for the detection of significant (≥51% vessel lumen narrowing) disease was evaluated, inter-observer agreement was assessed, and the technical failure rates of the 2 techniques were compared.

Results

Carotid Arteries[1]

DSA revealed 196 vessels with significant stenoses and 108 vessels with occlusions. Significantly ($p<0.001$; all readers) more technically-inadequate images were noted for 2D-TOF than for CE-MRA. All readers noted significant ($p<0.001$) increases in specificity and overall accuracy on CE-MRA compared to 2D-TOF MRA. Better 3-reader agreement was noted for CE-MRA (84.7% agreement; $\kappa=0.64$) than for 2D-TOF (77.1% agreement; $\kappa=0.61$, $p<0.0001$). Just 5.2% of patients experienced a mild or moderate AE that was possibly or probably related to injection of Gd-BOPTA.

Renal Arteries[2]

Of 268 subjects evaluated with both MRA and DSA, 178 had significant steno-occlusive disease of the renal arteries on DSA. The sensitivity, specificity, and accuracy of CE-MRA for detection of ≥51% stenosis/occlusion ranged between 60%–84%, 89%–95%, and 80%–87%, respectively, at the segment level. Similar values were obtained for predictive values and for patient-level analyses. Very few CE-MRA examinations (2–3%) were technically inadequate. Inter-observer agreement for the detection of significant steno-occlusive disease was good (87.9% agreement; $\kappa=0.69$) and no safety concerns were noted.

Peripheral Arteries[3]

DSA confirmed significant disease (597 stenoses, 386 occlusions) in 983 iliofemoral segments. The sensitivity (54%-80.9%), specificity (89.7%-95.3%), and accuracy (85%-87.5%) of CE-MRA for the detection of significant iliofemoral disease was significantly ($p<0.001$, all readers) better than that of TOF MRA (33.2%-62.8%, 74.3%-88.9% and 68%-77.3%, respectively). Similar diagnostic performance was obtained for the calf arteries. The technical failure rate with CE-MRA (2.5%-3.4%) was similar to that of DSA (1.4%) and significantly ($p<0.001$) lower than with TOF MRA (6.2%-18%). Significantly better reproducibility ($p<0.001$) was obtained with CE-MRA (82% vs 65.2% agreement; $\kappa=0.66$ vs $\kappa=0.47$).

Conclusion

CE-MRA with 0.1 mmol/kg bodyweight Gd-BOPTA is accurate and safe, and provides better agreement with DSA than 2D-TOF MRA for evaluation of the carotid, renal, and peripheral arteries.[1-4]

References

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