Gadopentetate Dimeglumine as an Intradicinal Contrast Agent

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Study Design. Magnetic resonance discography using gadolinium as an intradicinal contrast agent was investigated in a prospective study.

Objective. To evaluate the utility of magnetic resonance discography using gadolinium as an intradicinal contrast agent, as compared with the current standard of computed tomographic discography using intradicinal iodinated contrast agent.

Summary of Background Data. Magnetic resonance arthrography with gadolinium has been used to evaluate shoulder, elbow, wrist, hip, knee, and other joints. Gadolinium has not been used as an intradicinal contrast agent. The authors' preliminary results using gadolinium as an intradicinal contrast agent for magnetic resonance discography were reported previously. They report the results of their completed study.

Methods. For this study, 42 disc levels were studied in 13 patients. Water-soluble iodinated contrast and gadopentetate dimeglumine were injected at each disc level. After discography, anteroposterior and lateral radiographs, computed tomography scans, and T1-weighted magnetic resonance imaging were performed. Six physicians interpreted the results from each disc level in a blinded fashion. Interscan and interobserver interpretation variability was determined for magnetic resonance discography and computed tomographic discography using the Pearson correlation-coefficient (r) test.

Results. Interscan variability was highly correlated between computed tomographic discography and magnetic resonance discography when used to determine disc normality (r = 0.87), general degeneration (r = 0.87), annular fissure (r = 0.89), disc herniation (r = 0.92), and contrast leakage (r = 0.77). Interscan variability was assessed by the Pearson test, and all values of r for all the readers were noted to be statistically significant at P values less than 0.01. Interobserver variability was significantly correlated among the four more experienced readers (neuroradiologists and spine surgeons), but not among the spine fellows. Interobserver variability was also significantly correlated by computed tomographic (CT) and magnetic resonance imaging (MRI) discography for disc normality (CT r = 0.60; MRI r = 0.56), general degeneration (CT r = 0.76; MRI r = 0.71), annular fissure (CT r = 0.79; MRI r = 0.84), and disc herniation (CT r = 0.63; MRI r = 0.64). The readings for contrast leakage did not reach statistical significance for computed tomographic or magnetic resonance discography.

Conclusions. The high interscan and interobserver correlation rates obtained for magnetic resonance discography using gadolinium, as compared with the standard computed tomographic discography technique, indicate that magnetic resonance discography may be an acceptable substitute for the imaging of disc pathology. Magnetic resonance discography with gadolinium can be recommended for patients allergic to iodinated contrast agents and for patients who wish to limit their radiation exposure. [Key words: disc degeneration, discography, gadolinium, iodinated contrast media, magnetic resonance imaging] Spine 2002;27:839-843

Magnetic resonance (MR) arthrography can safely and effectively evaluate intraarticular anatomy and detect abnormalities. Joints evaluated include shoulders, elbows, wrists, thumbs, hips, knees, and ankles. In studies performed by Haje et al., gadolinium was considered the ideal contrast agent for MR arthrography. Gadolinium is a paramagnetic substance that produces a strong relaxation effect on adjacent hydrogen nuclei. A toxic heavy metal, gadolinium can form safe stable chelates such as gadopentetate dimeglumine that have been used safely as intravascular and intraarticular MR contrast agents. The current authors previously reported their preliminary results using gadopentetate dimeglumine as an intradicinal contrast agent for magnetic resonance imaging (MRI) discography. The current study was performed to clarify further whether MR discography using gadopentetate dimeglumine as an intradicinal agent is a suitable substitute for the current standard of computed tomographic (CT) discography using iodinated intradicinal contrast agents.

Methods

For this study, 42 discograms were performed in 13 patients. Discography was performed using a double-needle technique via a posterolateral approach. Both iodinated contrast agent (Conray 60 [Mallinckrodt, Inc., St. Louis, MO], meglumine iothalamate) and dilute gadopentetate dimeglumine (Magnavist [Berlex, Wayne, NJ], 3 mg/mL concentration) were injected at each level. The two contrast agents were mixed and injected together at the time of discography. After discography, anteroposterior and lateral radiographs, CT scans (contiguous 3-mm axial sections on a GE CTi Scanner [General Electric, Milwaukee, WI] with sagittal and coronal reformations), and MRI scans (GE Signa 1.5 T, T1-weighted FSE with fat suppression prepulse) were performed. Six physicians (2 neuroradiologists, 2 orthopedic spine surgeons, and 2 spine fellows) interpreted the images of each disc level in a blinded fashion. Interscan and interobserver interpretation variability was determined for CT discography and MRI discography using the Pearson correlation (r) test. The parameters evaluated for the current discography study were general degeneration, annular fissure, disc nor-
Table 1. Interscan Variability (r)

<table>
<thead>
<tr>
<th>Parameter Studied</th>
<th>Average</th>
<th>Range</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disc normality</td>
<td>0.87</td>
<td>0.67-1.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>General degeneration</td>
<td>0.87</td>
<td>0.75-0.97</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Annular fissure</td>
<td>0.89</td>
<td>0.76-0.98</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Disc herniation</td>
<td>0.92</td>
<td>0.80-1.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Contrast leakage</td>
<td>0.77</td>
<td>0.61-1.0</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Results

Table 1 presents the interscan variability results based on calculation of the Pearson correlation (r) coefficient. The interscan variability between CT discography and MRI discography correlated closely for all six readers in all the parameters evaluated. The average r among the six readers was 0.87 (range, 0.67-1) for disc normality, 0.87 (range, 0.75-0.97) for general degeneration, 0.89 (range, 0.76-0.98) for annular fissure, 0.92 (range, 0.80-1) for disc herniation, and 0.77 (range, 0.61-1) for contrast leakage. All values of r for all the readers were noted to be statistically significant at P values less than 0.01.

Table 2 presents the interobserver variability results as assessed by the Pearson test. Interobserver variability was correlated significantly among the four more experienced readers (neuroradiologists and spine surgeons), but not among the less experienced readers (spine fellows). The average r among the four readers was 0.60 (range, 0.40-0.82) for disc normality as assessed by CT discography and 0.56 (range, 0.36-0.88) as assessed by MRI discography, 0.76 (range, 0.64-0.89) for general degeneration as assessed by CT discography and 0.71 (range, 0.60-0.87) as assessed by MRI discography, and 0.79 (range, 0.73-0.86) for annular attenuation as assessed by CT discography, and lastly, 0.84 (range, 0.76-0.89) as assessed by MRI discography, 0.63 (range, 0.47-0.90) for disc herniation as assessed by CT discography and 0.64 (range, 0.45-0.90) as assessed by MRI discography. All r values for the preceding four parameters were noted to be statistically significant at P values less than 0.01, except for the parameter of disc normality as assessed by MRI (P < 0.02, statistically significant). The interobserver readings for contrast leakage did not reach statistical significance for either CT discography or MRI discography. For contrast leakage, the average r was 0.22 (range, -0.09-0.29) as assessed by CT discography and 0.41 (range, 0.26-0.54) as assessed by MRI discography.

Examples of MRI discogram as compared with CT discogram are shown in Figures 1 to 3. Figure 1A and 1B show axial images of a normal disc, respectively, on CT and MRI discograms. Figure 2A and 2B show images of a herniated disc. Figure 3A and 3B show sagittal images of multilevel degenerative disc disease, respectively, on CT and MRI discograms.

Discussion

The clinical value of discography continues to be controversial. Historically, various authors have reported that discography sensitively reflects the various stages of disc degeneration. The main criticism of dis-
cography lies in its level of accuracy. False positive rates up to 37\% have been reported in the literature. The specificity of discography can be improved by using stricter criteria to define a positive examination. Familiar and significant pain, along with degenerative morphology on discogram, constitutes the necessary criteria for a positive examination. The provocative aspect of discography with reproduction of exact or familiar pain is the most important part of the examination. Using such strict criteria, Walsh et al\(^\text{12}\) reported a false positive rate of 0\% and a specificity of 100\% for discography in a population of young asymptomatic volunteers.

Computed tomography scanning after discography has proved helpful because of the additional information obtained. The axial views provided by CT discography allow a classification of both disc degeneration and anular ruptures, as well as the identification of disc herniations and other pathology.\(^\text{11}\) Studies from the Texas Back Institute have shown that certain pathologic features (disc degeneration, anular disruption, and disc hernation) and personal or structural variables (age and lumbar level) affect the reporting of pain during discography.\(^\text{19,21-24}\) Other authors have disputed these findings, reporting that disc herniation and outer anular ruptures are the best predictors of pain reproduction.\(^\text{12,14}\) In their studies, disc degeneration, if not associated with outer anular rupture, was not a predictor of familiar pain. Despite the conflicting claims, there is general agreement that CT discography provides crucial information for the diagnosis and management of patients with discogenic back pain.\(^\text{24,19}\)

For physicians who use discography as a diagnostic aid, the current study offers an additional method for obtaining the same visual information as that acquired by CT discography. The data from this study demonstrate that MRI discography using gadolinium as an intradiscal agent can be effectively substituted for the current standard of CT discography using iodinated contrast material. The high interobserver correlation values...
values of \( r \) were obtained for disc herniation (0.92) and familiar pain on discography.\(^{50,54} \) Anular fissure (0.89), the two factors most predictive of high degree of interscan correlation. Very high correlation values for the MRI discography were very noteworthy because relatively inexperienced readers (spine fellows) were able to read the MRI and CT scans as high as the interscan correlation values, they did reach statistical significance. For each parameter studied, the correlation values for the MRI discography were very similar to the correlation values for the CT discography. This suggests that readers were as likely to agree or disagree with each other regardless of the visual medium (CT or MRI), that one medium was not necessarily any better than the other. The fact that the interscan correlations were very high, and higher than the interobserver correlations, supports the conclusion that MRI discography produces the same graphic anatomic information as CT discography.

In this study, iodinated contrast media (Conray) and gadopentetate dimeglumine (Magnevist) were mixed and injected together at the time of discography. Conray is not known to interact with gadolinium. The mixture of Conray with gadolinium does not adversely affect the MR images obtained as long as small amounts of Conray are used. When MR arthrography is performed, intraarticular needle placement often is confirmed by first injecting a small amount of iodinated contrast material. Gadolinium then is injected into the joint and the joint imaged. Kopka et al.\(^{11} \) mixed 10 mL of iodinated contrast material with gadolinium, injected the solution into shoulder joints, and noted no untoward effects on the MR images obtained. The addition of gadolinium to saline is unlikely to change the viscosity of the fluid. The concentration used (3 mg/mL) is equivalent to one drop of gadolinium in 10 mL of saline. The injection of a Conray and gadolinium mixture elicited concordant pain in a manner similar to the injection of any other agent of similar viscosity.

No studies investigating the effect of gadolinium on nucleus pulposus tissue have been published. Gadolinium has been widely used intravascularly and is safe for intraarticular use.\(^{7} \) The composition of nucleus pulposus, with its high Type 2 collagen and proteoglycan content, most closely resembles articular cartilage. Given its safety in intraarticular use, its safety for intradiscal use can be surmised. However, the long-term effect of gadolinium (even in the very small concentration used) on an avascular tissue such as the disc is not known. Since 1997, the authors have used gadolinium in their patients allergic to iodinated contrast agents, noting no adverse effects. More research in this area is needed.

Allergic reactions to iodinated contrast agents are a potential complication of discography. Older, ionic iodinated contrast agents (e.g., Conray) have been reported to cause adverse reactions in approximately 10% to 15% of patients.\(^{4} \) Newer nonionic iodinated contrast agents (e.g., Omnipaque) have lower osmolality, and are thought to reduce the incidence of adverse reactions. Katayama et al.\(^{10} \) reported on 169,284 patients injected with either iodonic or nonionic contrast agents. The incidence of total adverse drug reactions (ADRs) was 12.66% in the ionic contrast media group, as compared with 3.13% in the nonionic contrast media group. The incidence of severe ADRs (dyspnea, sudden hypotension, cardiac arrest, or loss of consciousness) was reported to be 0.22% (ionic contrast) and 0.04% (nonionic contrast). One death was reported in each of the two groups.\(^{10} \)

In patients with a history of asthma or bronchospasm, previous adverse reaction, or allergy to iodides or other foods, the rate of adverse reaction to contrast media is increased 5- to 10-fold.\(^{5} \) Other known risk factors are diabetes, inadequate hydration, and cardiac, renal, or hematologic diseases.\(^{7} \) Premedication with steroids and antihistamine is advised for patients with known risk factors. No large studies on the rate of ADRs in patients with known risk factors who received steroid/antihistamine premedication before contrast media injection have been published. Such data would be extremely helpful.

The frequency of adverse reactions to gadolinium is lower than the frequency of such reactions to iodinated contrast media. Murphy et al.\(^{15} \) reported on 21,000 patients for whom gadolinium contrast media were administered. The incidence of total ADRs was 0.138% whereas the incidence of severe ADRs was 0.01% when gadopentetate dimeglumine was used. In a survey encompassing 108 centers and 687,255 patients receiving gadopentetate dimeglumine, an overall ADR incidence of 0.06% and a severe ADR incidence of 0.0014% were reported.\(^{16} \) Although safer than iodinated contrast agents, gadolinium can cause severe life-threatening reactions. As with iodinated contrast media, mortality has been reported with the use of gadolinium contrast agents.\(^{9} \)

At the authors' institution, the hospital charge for a lumbar MRI is $1328. The hospital charge for a lumbar CT scan also is $1328, plus an additional $765 for sagittal and coronal reformation. The charge for a limited lumbar CT scan, a few slices at one or two disc levels, is $1063. Excluding other costs associated with the procedure, the cost of a lumbar MRI represents a 25% increase over the cost of a limited lumbar CT scan. This is a mild premium given the safety of a lumbar MRI and potential savings from fewer patient adverse reactions.

Another potential advantage of MRI discography over CT discography is the reduced radiation exposure. Magnetic resonance imaging does not expose the patient to any radiation. The amount of radiation with CT imaging varies depending on whether a limited or full lumbar CT is performed. In middle-age and elderly patients,
radiation exposure will be of less concern. In younger patients, radiation exposure should be minimized.

One shortcoming of gadolinium is its inability to be visualized fluoroscopically during intradiscal needle placement. During MR arthrography, needle placement is confirmed by a small amount of injected iodinated contrast agent. For patients with a true iodine allergy, this option is not possible. Accurate needle placement under biplane fluoroscopy is critical before intradiscal injection with gadolinium contrast media.

In summary, the utility and value of discograms continue to be controversial. For those who find CT discography helpful in diagnosing and treating discogenic low back pain, MRI discography may prove to be a suitable substitute. The current data show that high interscan correlation rates were obtained for MRI discography using gadolinium as an intradiscal contrast agent, as compared with CT discography using iodinated contrast media. Gadolinium contrast agents are safer and cause fewer adverse reactions than iodinated contrast agents. The cost of MRI discography, as compared with CT discography, is only mildly higher. Patients are exposed to less radiation with MRI discography than with CT discography. According to the findings, MRI discography may be recommended for patients with true iodine allergy. The excellent visual information obtained, along with the pain provocation response, may prove helpful in the diagnosis and treatment of discogenic low back pain.

**Key Points**
- As shown in this study, MRI discography using gadolinium as an intradiscal contrast agent is a suitable substitute for CT discography using iodinated contrast media.
- Gadolinium contrast agents are safer and cause fewer adverse reactions than iodinated contrast agents.
- Patient exposure to radiation is significantly less with MRI discography than with CT discography.

**References**