3D Excretory MR Urography: Improved Image Quality With Intravenous Saline and Diuretic Administration

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Purpose: To assess the effect of diuretic administration on the image quality of excretory magnetic resonance urography (MRU) obtained following intravenous hydration, and to determine whether intravenous hydration alone is sufficient to produce diagnostic quality studies of nondilated upper tracts.

Materials and Methods: A total of 22 patients with nondilated upper tracts were evaluated with contrast-enhanced MRU. All patients received 250 mL of saline intravenously immediately prior to the examination. A total of 11 patients received 10–20 mg furosemide in addition to saline. Imaging was performed with a three-dimensional (3D) and two-dimensional (2D) breathhold spoiled gradient-echo sequences. Excretory MRU images were acquired five minutes after the administration of 0.1 mmol/kg gadolinium and were independently reviewed by two radiologists, who were blinded to the MRU technique. Readers evaluated the calyces, renal pelvis, and ureters qualitatively for degree of opacification, distention, and artifacts on a four-point scale. Statistical analysis was performed using a permutation test.

Results: There was no significant disagreement between the two readers (P = 0.14). Furosemide resulted in significant improvement in calyceal and renal pelvis distention (P < 0.005), and significant artifact reduction in all upper tract segments (P < 0.001) compared to the effect of saline alone.

Conclusion: Intravenous furosemide significantly improves the image quality of excretory MRU studies obtained following intravenous hydration. Intravenous saline alone is insufficient to produce diagnostic quality studies of the non-dilated upper tracts.


MR UROGRAPHY (MRU) permits evaluation of the urinary tract without the exposure to ionizing radiation and iodinated contrast medium. Two imaging strategies have been developed for MRU: nonenhanced MRU, which is performed using heavily T2-weighted (T2-W) sequences; and contrast-enhanced MRU (CE-MRU), which is performed with fast T1-weighted (T1-W) pulse sequences following intravenous gadolinium administration (1–14).

Excretory CE-MRU is the technique most commonly used to evaluate the nondilated collecting system (10–14). After excretion of intravenous gadolinium chelates by the kidneys, fluid within the upper tracts becomes visible on T1-W sequences, allowing for their assessment. The rapid pulse sequences used for imaging significantly reduce motion artifacts, enable evaluation of the renal parenchyma, and provide at least gross renal functional information (10–15).

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Since low-dose (5–20 mg) intravenous furosemide administration has been recommended for excretory CE-MRU to improve visualization of the nondilated upper tracts (10–12,14), it is conceivable that intravenous fluid administration alone may have the same effect, obviating the need to administer an intravenous drug
with its potential, albeit low, side effects. The objective of our study is to compare the image quality of excretory MRU studies obtained following intravenous hydration without and with intravenous furosemide, and to determine whether intravenous hydration alone is sufficient to obtain a diagnostic quality examination of the non-dilated upper tracts.

MATERIALS AND METHODS

Patient Population

A total of 44 consecutive CE-MRU studies were performed between August 2001 and May 2002. Initially, MRU studies performed at our institution were done with intravenous fluid only and without furosemide (N = 21) in an attempt to avoid intravenous drug administration. However, due to artifacts seen on some studies, we began using intravenous furosemide routinely for all patients undergoing CE-MRU (N = 23), except those with markedly dilated upper tracts. The upper tracts represent the intrarenal collecting system (calyces and renal pelvis) and ureters.

All 44 MRU studies were retrospectively reviewed to identify patients with nondilated upper tracts. The upper tracts were characterized as nondilated if the calyces were not visualized on the coronal T2-W SSFSE localizer sequence, or they were seen as a thin line of hyperintense signal intensity. Renal pelvis dilatation without calyceal dilatation was considered normal and related to an extrarenal pelvis. A total of 22 patients, including five women and 17 men, were identified and constituted our study population. These patients were referred for conventional MR imaging and CE-MRU to evaluate for known or suspected genitourinary tract pathology including known renal cell carcinoma (RCC) (N = 6) and transitional cell carcinoma (TCC) (N = 5), suspected renal mass (N = 5), hematuria (N = 4), flank pain (N = 1), and congenital anomaly (N = 1). The mean patient age was 50 years (range = 37–94 years). Six patients had undergone unilateral nephrectomy (N = 4) and nephroureterectomy (N = 2) for RCC and TCC, respectively. Serum creatinine levels ranged between 0.6 and 2.2 mg/100 mL. Institutional review board approval was sought and obtained for this retrospective study and the need for a consent form was waived.

All 22 patients with nondilated upper tracts were classified in two groups: Group A (N = 11) included those who received 250 mL saline only prior to starting the MR study (mean age = 53.9 years, range = 37–81 years, mean creatinine level = 1.62 mg/100 mL, range = 0.6–2.2 mg/100 mL); Group B (N = 11) included those patients who, in addition to 250 mL saline, received intravenous furosemide immediately prior to intravenous gadolinium administration (mean age = 67 years, range = 37–93 years, mean creatinine level = 1.35 mg/100 mL, range = 0.9–2.1 mg/100 mL). There was no statistically significant difference between the creatinine levels in the two groups (P = 0.23; unpaired t-test). Saline was given as a bolus injection immediately prior to laying the patient on the scanning table. The dose of furosemide varied according to the serum creatinine level and was increased with increasing serum creatinine level as follows: 10 mg for patients with serum creatinine levels below 1.5 mg/100 mL; 15 mg for patients with levels between 1.5–2 mg/100 mL; and 20 mg for patients with levels over 2 mg/100 mL. Furosemide was given as a slow intravenous injection over one minute immediately prior to injecting the intravenous gadolinium to achieve the maximum diuretic effect, which helps expand the intrarenal collecting system, and minimize possible washout of excreted gadolinium due to increased diuresis (10).

MR Imaging

All 22 conventional MRI/MRU studies were performed on a 1.5-T scanner (General Electric Medical Systems, Milwaukee, WI, USA) using a four-element torso phased-array coil. The imaging sequences used were as follows:

1. Coronal and axial T2-W SSFSE localizers (TR > 1000 msec, TE 90 msec, number of excitations [NEX] = 0.5, slice thickness/intersectional gap = 8 mm/2 mm, matrix size = 256 × 128–160 [frequency × phase]).

2. Axial T1-W breathhold dual-echo spoiled gradient echo (SPGR) through kidneys (TR = 155 msec, TE = 2.3 msec/4.6 msec [out-of-phase/in-phase], flip angle = 70°, NEX = 1, slice thickness/gap = 6 mm/0 mm, matrix size = 256 × 160 [frequency × phase]). This sequence is used to detect and characterize renal and adrenal lesions.

3. Axial T2-W fat-suppressed fast spin-echo (FSE) through the liver and kidneys (TR = 3650–4600 msec, TE = 96–98 msec, NEX = 2–4, slice thickness/gap = 6 mm/0 mm, matrix size = 256 × 224–256 [frequency × phase], echo train length = 8–12, respiratory triggering). This sequence is used predominantly to detect and characterize hepatic, renal, and adrenal lesions, and to identify enlarged lymph nodes.

4. Coronal T1-W breathhold three-dimensional SPGR (3D SPGR) (TR = 6.8–7.5 msec, TE = 1.4–2.2 msec, flip angle = 12°, NEX = 0.5, section thickness = 2.6–3.6 mm, matrix size = 256–320 × 160–256 [frequency × phase], frequency selective fat saturation, phase-encoding direction = right-left, scan time = 24–29 seconds) through kidneys and bladder before and following gadolinium administration in the cortical (30 seconds) and nephrographic (one minute) phases of enhancement (16). These images are used to evaluate the renal arteries and veins, renal parenchyma, and assess for the presence of early enhancing TCC in the upper tracts and bladder. Coronal imaging was repeated in the excretory phase at five minutes following gadolinium administration using the same sequence with the same parameters except for the flip angle, which was increased to 35° to suppress the background signal from abdominal organs and emphasize the gadolinium-enhanced urine in the upper tracts. The excretory phase images are used to evaluate the morphology of the contrast column in the upper tracts, and detect filling defects (usually TCC that
distort this column. Scanning of each of these phases (pre-gadolinium, cortical, nephrographic, and excretory) was performed during 24–29-second breathholding.

5. Axial excretory phase T1-W SPGR from the top of the kidneys to below the bladder at approximately seven to eight minutes following gadolinium administration (TR = 190–215 msec, TE = 1.3 msec, flip angle = 70°, NEX = 1, slice thickness/gap = 5 mm/0 mm, matrix size = 512 × 160 [frequency × phase], frequency selective fat saturation, 20 slices, 24 seconds). Up to four separate acquisitions were acquired to cover the entire urinary tract. Each of these acquisitions was performed in a 24-second breathhold. These images are used to evaluate the wall of the upper tracts and bladder, identify intraluminal masses that will distort and displace the contrast enhanced urine, assess the other abdominal and pelvic organs, and detect enlarged lymph nodes and bone lesions. These images provide higher in-plane resolution compared to the axial reformatted images of the excretory MRU images, which have limited spatial resolution due to constraints imposed by scan time limitations; higher resolution increases the scan time beyond the patient’s ability to suspend respiration.

The total table time was 45 minutes. Gadolinium (Magnevist; Berlex Wayne, NJ, USA or Omniscan; Amersham Health, Princeton, NJ, USA) was administered at a dose of 0.1 mmol/kg (maximum 20 mL) through a 20–24-gauge cannula placed in the antecubital fossa at a rate of 2 mL/second using a power injector (Spectris, Medrad, Pittsburgh, PA, USA). The arterial/corticomedullary phase acquisition was timed using the automated contrast-bolus detection technique (Smart Prep; General Electric Medical Systems).

Image Analysis

The coronal (last phase of sequence #4) and axial (sequence #5) excretory phase images of the CE-MRU studies were independently reviewed by two expert MR radiologists (H.K.H., R.C.C.) with seven and eight years of experience in abdominal MR imaging, respectively. Reviewers evaluated both the source and maximum intensity projection (MIP) images. The readers were blinded to the MRU technique (i.e., with or without furosemide). The readings were done in two sessions and in each session; each reader was given a random combination of cases performed with either technique. The coronal images were interactively reviewed and reformatted in multiple planes on a workstation (Advantage Workstation, version 4.0; General Electric Medical Systems). The multiplanar image reformats were generated using an MIP algorithm. We did not use subtraction techniques when evaluating these images.

The upper tracts were divided into five segments: calyces, renal pelvis, proximal ureter (to the level of the lower pole of the kidney), middle ureter (between the lower pole of the kidney and iliac crest), and distal ureter (from iliac crest to bladder). Readers evaluated each of the upper tract segments subjectively for the following: 1) degree of opacification (defined as the presence of contrast within the segment); 2) distention (assessed qualitatively according to the reader’s ability to adequately visualize the internal details of the segment); and 3) the presence of susceptibility and truncation artifacts. These features were evaluated on a four-point scale as follows: for opacification and distention (1 = poor, 2 = fair, 3 = adequate, 4 = excellent); for the presence of artifacts (1 = none, 2 = mild, 3 = moderate, 4 = severe artifacts).

Statistical Analysis

Each observer independently scored each segment for opacification, distention and susceptibility artifact. Interobserver disagreement in grading was determined by a permutation test (17). The difference between each observer’s scores (indexed by segment with and without furosemide) was calculated and observer labels were permuted 10,000 times. There was no significant difference between observer ratings and their ratings were therefore averaged. Thus, to determine the effect of furosemide on upper tract opacification, distention, and presence of artifacts, a two-sample permutation test with 10,000 permutations was performed on each segment. Each test was performed by computing the average score, for example, of the distention of the calyx over both observers with and without furosemide. Control/furosemide labels were permuted and the difference between average scores with and without furosemide was assessed for significance. If the observed difference in the average was more extreme than 9950 of the 10,000 permutations, then the observed difference was significant. That is, a $P$-value of less than 0.005 was considered to be significant. Reducing the significance level by a factor of 10 (from the standard 0.05) adjusts for the multiple testing that was performed. Permutation tests were used to test hypotheses in this study as a nonparametric alternative to analysis of variance methods.

RESULTS

A total of 38 nondilated upper tracts (190 segments) in 22 patients were evaluated including 20 upper tracts (100 segments) in Group A (saline) and 18 upper tracts (90 segments) in Group B (saline and furosemide). To assess for a statistically significant difference in the interpretation of the two observers, the average difference of all grades between observers 1 and 2 was calculated and a permutation test with 10,000 permutations performed. The average difference was $-0.06$ with $P$-value of 0.14, indicating that there is no statistically significant disagreement in grading between the two readers.

With regard to opacification, there were no statistically significant differences in the opacification of any of the upper tract segments between Group A patients, who received saline only, and Group B patients, who received saline and furosemide (Fig. 1a, b; Table 1). No nonopacified segments were seen in either group. For reviewer 1, opacification was incomplete (i.e., less than excellent) in 18 of 20 (90%) patients in Group A and 16
of 18 (88.9%) patients in Group B, with the proximal one-third of the ureter being the most common segment to have less than excellent opacification in both groups. For reviewer 2, opacification was incomplete in 19 of 20 (95%) patients in Group A with calyces being the most common segment to have less than excellent opacification, and in 14 of 18 (77%) patients in Group B with the proximal one-third of the ureter being the most common segment to have less than excellent opacification.

Furosemide, however, significantly improved the degree of calyceal and renal pelvis distention with \( P \)-values less than 0.005 for both segments (Fig. 2a, b). It had no significant effect on ureteric distention (Table 2). Furosemide significantly reduced susceptibility and truncation artifacts throughout the upper tracts with \( P \)-values below 0.001 for all segments (Fig. 3a–c; Table 3). Opacification appeared more homogeneous in Group B patients compared with Group A. This is likely due to a combination of improved distention and reduced artifacts. Ghosting artifact related to ureteric peristalsis was not observed.

**MRU Findings**

The excretory MRU was interpreted as normal in 19 patients and abnormal in three patients. The normal studies were confirmed at surgery, ureteroscopy, and follow-up. The three abnormal studies included a patient with von Hippel Lindau disease who was being followed after radiofrequency ablation of RCC in both

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*No significant effect on upper tract opacification was seen after Furosemide. Significant \( P \)-value is <0.005.

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†Furosemide significantly (\( P \)-value <0.005) improved calyceal and renal pelvis distention but had no significant effect on ureteric distention.
kidneys. The excretory MRU done with saline only demonstrated contrast extravasation into the perinephric space. The second patient had an anastomotic stricture of the distal right ureter following cystectomy and ileal loop conduit reconstruction for bladder TCC and had undergone balloon dilatation of stricture. The MRU done with furosemide and saline showed minimal residual narrowing of the ureter at its junction with the ileal conduit without signs of obstruction. The third patient was 18 years old and had history surgery at the age of five years for ureteropelvic junction (UPJ) obstruction. The excretory MRU done with furosemide and saline showed moderate dilatation of the renal pelvis with UPJ narrowing but no calyceal dilatation or other sign of obstruction and was considered a satisfactory postoperative appearance (Fig. 4a, b). Eight patients were evaluated for the presence of TCC (primary hematuria, N = 3; follow-up TCC, N = 5) and none was found to have TCC as confirmed by cystoscopy/ureteroscopy (N = 5), cystoscopy/ureteroscopy and biopsy (N = 1), clinical follow-up for one year (N = 1), and conventional intravenous urography (IVU) (N = 1)

**DISCUSSION**

Excretory contrast-enhanced MRU has been used to determine the level of obstruction in mild or moderately dilated systems, to evaluate urinary tract anomalies, and assess tumor morphology (12–14). 3D excretory MRU uses similar imaging parameters as MR angiography (18) to enhance the appearance of gadolinium-enhanced urine and suppress signal from background soft tissue. Excretory MRU utilizes the same principle of contrast excretion as conventional IVU and its feasibility is determined by the ability of the kidneys to excrete the intravenously administered gadolinium. A technically adequate excretory MRU study is expected to result in opacification and adequate distention of the upper tracts without artifacts to enable the identification of filling defects and the evaluation of ureteral wall abnormalities.

Similar to conventional urography, the production of a sufficient volume of urine is necessary for the technical success of excretory MRU. The use of a standard dose of gadolinium chelate in combination with intravenous hydration and low dose furosemide (5–10 mg) results in a good urographic effect in patients with serum creatinine levels up to 2 mg/100 mL (12). However, in patients with impaired renal function, an increased dose of furosemide is required to produce the same effect (10). The main advantage of CE-MRU is that it can be performed in patients with impaired renal function, who cannot tolerate iodinated contrast medium for IVU or computed tomography (CT) urography studies. Low-dose gadolinium (up to 0.1 mmol/kg body weight) is not nephrotoxic in patients with impaired renal function (19,20), but safety issues with higher doses are controversial (21,22). Only two of our patients, one from Group A and one from Group B, had creatinine levels slightly above 2 mg/100 mL. The patient from Group A (without Lasix [furosemide]) had good opacification, adequate distention, and moderate artifacts compared to
good opacification, good distention, and no artifacts for the patient from Group B (with Lasix).

Gadolinium-chelates are hydrophilic low molecular weight contrast agents that are excreted by the kidneys through glomerular filtration (23,24). They induce shortening of T1 and T2 (or T2*) relaxation time. In low concentrations, i.e., at the clinically used dose of 0.1 mmol/kg, the T1 shortening effect predominates over the T2 (or T2*) shortening effect, resulting in an increase in the signal intensity of urine on T1-W imaging. Conversely, at higher concentrations, the T2 (or T2*) shortening effect predominates, resulting in a decrease in the signal intensity of urine on T1-W imaging (25). The T2* effect refers to signal decay that occurs due to the combination of tissue T2 value and the contribution from field inhomogeneities. The latter is exaggerated by the susceptibility effect of concentrated gadolinium. Since normal kidneys are able to concentrate the excreted gadolinium by a factor of 50–100 (26), T2* effect of concentrated gadolinium can result in dark signal in the collecting system on excretory MRU studies. Concentrated gadolinium also creates local magnetic field inhomogeneities, resulting in susceptibility artifacts and producing zones of signal loss (27). On excretory MRU images, this artifact can be seen as dark and bright lines around the collecting system. Highly concentrated gadolinium in the upper tract also results in high contrast interfaces between the gadolinium-filled ureter and the dark signal from retroperitoneal fat, which is suppressed by a frequency-selective fat-saturation pulse. This will result in truncation artifacts when low spatial resolution matrices are used, due to undersampling of data (27). On excretory MRU images, truncation artifacts appear as a series of alternating bands of low and high signal intensity along the phase encoding axis of the image, parallel to the course of the ureters. Conspicuity of truncation artifact can be reduced either by using a higher resolution imaging matrix or decreasing the contrast at the interface. Since it is not practically possible to increase the resolution of the image beyond a certain limit dictated by the patient’s ability to breathhold, the only alternative solution is to decrease the contrast interface, which can be accomplished by diluting the urine within the upper tracts.

Furosemide is a powerful loop diuretic (28). Its effect starts immediately after the first pass through the kidneys, causing rapid water retention in the tubules (29). This will increase the fluid in the collecting system, which helps to dilute the excreted gadolinium and homogenize its distribution (13), resulting in decreased T2* effects, susceptibility, and truncation artifacts.

Several techniques have been used to overcome T2* effect of concentrated gadolinium in excretory CE-MRU examinations (14,15,30,31) such as the use of oral saline, low dose diuretic, or low dose gadolinium. Szopinski et al (30), in a study of 91 patients, used a very low dose of Gd-DTPA (0.01 mmol/kg) and had the patients drink 1 liter of water. A very low dose of gadolinium without furosemide can be effective in preventing T2*, but may fail to demonstrate enhancing pathology because of the inadequate dose of gadolinium. Hughes et al (31) compared low-dose (total of 2 mL) and high-dose (0.4 mL/kg) gadolinium-enhanced excretory 3D MRU for visualization of the calyces, renal pelvis, and ureters and found that the low gadolinium-dose technique allowed better visualization of calyces and pelvis. This was attributed to the T2* effect of highly concentrated gadolinium. No statistically significant difference between the two techniques was detected with regard to visualization of the ureters.

Farres et al (14), in a study of 38 patients, compared visualization of the calyces, pelvis, and ureters in examinations performed with (N = 13) and without (N = 25) 20 mg of intravenous furosemide without intravenous or oral fluid. The authors found improved visualization of calyces and ureters with furosemide. Likewise, Nolte-Ernsting et al (10,11,13) reported a positive effect of furosemide on the quality of excretory CE-MRU. These authors stated that furosemide initially induces an increase in urine volume resulting in mild distention of the urinary tract, then there is the dilutional effect on the excreted gadolinium and the increased urine flow, which leads to rapid and uniform distribution of gadolinium. Our results are similar to those reported by Nolte-Ernsting et al (10,11,13), except that we did not find a positive effect of furosemide on the degree of ureteric distention. This may be attributable to the additional use of intravenous saline in our patients, which may enhance the “dilution” and “distribution” effect of furosemide. However, our results suggest that intravenous saline alone is not sufficient for optimal distention of the intrarenal collecting system and reduction of artifacts, and that furosemide, in addition to hydration, is essential for adequate distention of the intrarenal collecting system.

Furosemide is a sulfonamide derivative that may have cross-reactivity in patients with sensitivity to other sulfonamides (i.e., sulfonamide antimicrobials, carbonic anhydrase inhibitors, sulfonylureas, and thiazide diuretics) (28,32). No allergic reaction to furosemide was reported by any of our patients.

We acknowledge several limitations to our study. We had no internal control for our patients as we did not perform a direct comparison of the two techniques in the same patient. We also did not evaluate the effect of furosemide alone without saline on the quality of excretory MRU. The variable hydration status and serum creatinine levels in our patients may have had an impact on the amount of urine produced and gadolinium excreted by the kidneys, which in turn affected the resultant image. We attempted to minimize these effects by giving intravenous saline and increasing the dose of furosemide in patients with higher creatinine levels. Additionally, we only evaluated the nondilated upper tracts, which we consider the most difficult to adequately distend. It is therefore possible that intravenous hydration alone is sufficient to distend the mildly or moderately dilated upper tract and produce a technically adequate study. Moreover, we did not attempt to determine the effect of improved upper tract distention on the detection of urinary tract pathology. Last, our sample size is relatively small and we did not do a randomized patient selection.

In conclusion, intravenous furosemide administration for gadolinium-enhanced excretory MRU studies
results in rapid and uniform distribution of the excreted gadolinium and helps to minimize T2* susceptibility, and truncation artifacts throughout the upper tracts. Furosemide administration improves calyceal and renal pelvis distention, which improves image quality. Intravenous saline alone is not sufficient to produce diagnostic quality MRU studies of the nondilated upper tracts. We now routinely administer furosemide, in addition to intravenous saline, to all our patients with nondilated collecting systems undergoing MRU examination.

ACKNOWLEDGMENT

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REFERENCES