Résumé
Étude scanographique multibarrette des voies excrétrices avec ou sans hyperdiurèse
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Matériels et méthodes. Étude prospective comparative des temps excrétores à 450 secondes chez 67 patients répartis en trois groupes : le premier sans furosémide (f = 0), le second avec 20 mg de furosémide (f = 20), le troisième avec 10 mg de furosémide (f = 10). Réalisation de reconstructions 3D en MIP. Sans connaissance du protocole utilisé, deux radiologues expérimentés ont analysé la qualité d’opacification de la VES divisée en 8 segments et la densité des VES au niveau des pyélon.

Résultats. L’injection de 20 mg de furosémide améliore significativement le taux d’opacification des VES : complète ou presque complète dans 82,6 % des examens, contre respectivement 43,5 % et 19 % pour les groupes f = 10 et f = 0. Les densités relevées sont 5 fois moins importantes dans les groupes f = 20 et f = 10 que dans celui f = 0.

Conclusion. Le furosémide trouve sa place dans le protocole d’uroscanner en améliorant la qualité de l’opacification des VES et le taux de remplissage. La diminution de la concentration du produit de contraste dans les VES distendues et entièrement visualisées permet de mieux analyser les anomalies de la lumière et de la paroi.

Mots-clés : Voies Urinaires, technique d’exploration, furosémide.

Abstract
Purpose. To optimize the MDCT urogram protocol for assessment of the upper tracts. To assess the value of furosemide injection.

Materials and Methods. Prospective study comparing excretory phase imaging at 450 seconds in 67 patients assigned to 3 groups: a group without furosemide (f=0), a group with 20 mg furosemide (f=20), and a group with 10 mg furosemide (f=10). 3D MIP images were generated. Two experienced radiologists blinded to protocol specifications analyzed the quality of opacification the upper tracts, divided in 8 segments and urine density at the renal pelvis.

Results. The injection of 20 mg of furosemide significantly improved the opacification of the upper tracts with complete or near complete opacification in 82.6% of cases compared to 43.5% and 19% for the F=10 and F=0 groups respectively. Density measurements were 5 times less for the F=20 and F=10 groups compared to the F=0 group.

Conclusion. Furosemide is useful for MDCT urography by improving upper tract opacification and filling; the reduced contrast concentration in the better distended and fully filled upper tracts improves evaluation of ureteral lumen and wall abnormalities.

Key words: Ureters. Imaging. Furosemide.


The availability of multi-detector CT (MDCT) with faster acquisitions and improved spatial resolution has had a significant impact on the field of urological imaging. The quality of renal parenchymal and upper tract imaging evaluation has markedly improved, making this examination mandatory in the work-up of renal and urothelial tumors (1-3), upper tract infections (4), urolithiasis (5, 6), and trauma (7-9), as well as pre-transplantation evaluation (10). Nowadays, the value of conventional “urography” is being reconsidered in multiple clinical settings, but is single excretory phase CT-urography adequate for evaluation of the upper tracts? The main pitfall of this newer technique is the frequent incomplete opacification of the ureters (11, 12). Several studies have been conducted to improve CT protocols: abdominal compression and prone position have not shown a significant improvement (12, 13); only hyperdiuresis has shown some efficacy with improved ureteral distension and opacification. This may be achieved by injection of a small dose of diuretics (14, 15), infusion of an isotonic saline solution (12, 13, 15), or by ingestion of water (16). Because we believed that furosemide injection would be more appropriate and reproducible, we have sought to assess its efficacy in the evaluation of the upper tracts using MDCT compared to a standard protocol without hyperdiuresis.

Materials and Methods

Patients
Prospective evaluation conducted from February to October 2005. A total of 67 patients were included (34 males/33 females; mean age of 51 (18-86) years). All patients were referred to CT for work-up of upper tract or renal pathology (CT-urogram), or evaluation of other GU pathology potentially involving the upper tracts (CT abdomen and pelvis with excretory phase): hematuria (n=8), renal stone (n=8), GU infection (n=4), renal
trauma (n=1), proteinuria (n=1), renal mass (n=2), staging (n=11) or follow-up (n=7) of urothelial tumors; work-up of hemopathy (n=16), chronic inflammatory syndrome (n=4), or sepsis (n=3). Exclusion criteria were the presence of obstruction and/or a serum creatinine level above 15 mg/l.

The patient population was randomized into 3 separate but similar and homogeneous groups: Group 1 or “control” group without use of furosemide (11 males/10 females; mean age=52 ± 19 years), Group 2 with injection of 20 mg of furosemide (11 males/12 females; mean age=50 ± 18 years) and Group 3 with injection of 10 mg (half dose) of furosemide (12 males/11 females; mean age=50±18 years). Five patients with single kidney were in the furosemide groups and one patient with single kidney was in group 1. One patient in the furosemide group had a Bricker type ureteral anastomosis. A single patient was excluded because of hydroureteronephrosis from a bladder tumor.

Protocol

The CT examinations were performed on a 40-detector row CT (Philips Brilliance 40, Philips Medical Systems, Best, Netherlands). Each CT examination included at least a noncontrast acquisition and an excretory phase contrast-material-enhanced acquisition (7 min 30 sec) covering the entire upper tracts. All acquisitions were performed with breath hold using the following parameters: 140 kV; automatic tube current modulation based on patient body habitus; gantry rotation time of 0.5 sec; 40x0.625 mm with pitch of 0.676 and increments of 0.8 mm; slice thickness of 1.5 mm; 512x512 matrix; mean acquisition time per series of 13 sec. All patients were injected with a weight-adjusted (400 mg/kg) volume of non-ionic iodinated contrast material (iohexol, Omnipaque 300®) using a power injector (Stellant, Medrad, USA) at a rate of 3 ml/sec. In addition, contrast volume guidelines were implemented: minimum of 90 ml iohexol for patients <70 kg, and maximum of 150 ml iohexol for patients >100 kg (table I).

Furosemide was hand-injected immediately prior to the administration of iodinated contrast material. The dose was adjusted depending on the group.

Data analysis

The excretory phase acquisitions were separated from the other images, de-identified by a resident (CC), and then sent to an independent workstation with real time MPR and MIP capabilities (Extended Brilliance Workspace). Images were reviewed by two experienced radiologists (LL, JD) blinded to patient group. From a total of 128 upper tracts (67 examinations), both radiologists independently evaluated the following items:

first, the degree of upper tract opacification along 8 segments: calices, pelvis, ureteropelvic junction, proximal ureter, lumbar ureter, ureter crossing the iliac vessels, pelvic ureter and ureterovesical junction (fig. 1). A score between 0 and 3 was recorded for each segment based on the degree of opacification: 0%=0/3, 1-49%=1/3, 50-99%=2/3, 100%=3/3. For junctions or crossing segments, only scores of 3 (visualized) or 0 (non-visualized) were recorded. Second, a density measurement was obtained over the renal pelvis for each upper tract from a 10 mm thick MIP image to assess the density of opacification (fig. 2).

Statistical analysis

A descriptive analysis of data was first performed for control and summary purposes (box-plots, means and standard deviation). Then, mean values for the different parameters were compared between all three groups using a variance

| Table I Iodine dose and contrast volume based on patient weight (Groups 1, 2 and 3). |
|---|---|---|
| Weight (kg) | mg Iodine | ml contrast |
| <70 | <28,000 | 90 |
| 70 | 28,000 | 93 |
| 75 | 30,000 | 100 |
| 80 | 32,000 | 107 |
| 85 | 34,000 | 113 |
| 90 | 36,000 | 120 |
| 95 | 38,000 | 127 |
| 100 | 40,000 | 133 |
| >100 | >40,000 | 150 |
analysis for non-parametric variables (based upon ranks). Comparison of paired mean values (post-hoc test) was performed with a Bonferroni correction. All statistical analyses were performed using the SAS V9.1 software (SAS Institute, Cary NC, USA).

**Results**

**Degree of opacification**

Results summarized in table II correspond to mean scores for each segment for each group. A significant difference (p < 0.05) between the 3 groups exists only for opacification of the distal segments: ureter crossing the iliac vessels, pelvic ureter and ureterovesical junction (table III). After injection of 20 mg of furosemide, opacification of all segments of the upper tracts with a score of 3/3 was noted in 52.2% of patients and opacification of all segments of the upper tracts with a score of 2/3 or 3/3 was noted in 82.6% of patients as opposed to 30.4% and 43.5% respectively after injection of 10 mg of furosemide and 0% and 19% respectively in patients without injection of furosemide.

**Density of opacification**

The mean renal pelvis density was 1310±398 HU for the group without furosemide, 265±90 HU for the group with 10 mg of furosemide and 255±77 HU for the group without furosemide (table III). No significant difference was noted between groups 2 and 3, but a significant difference was noted between these groups (2 and 3) and group 1. Bladder opacification was never homogeneous in group 1 patients, but it was homogeneous in 13 of 24 cases for group 2 patients and in 13 of 22 cases for group 3 patients.

**Discussion**

Over the recent years, CT urography has played an increasing role in the evaluation of the urinary tract. This is in part explained by technical advances allowing helical CT acquisitions over the entire urinary tract in a single breath hold. CT is a well-established imaging modality for characterization of renal masses, evaluation of urolithiasis, or congenital malformations (1, 4, 10, 17, 18). Opacification of the upper tracts, which frequently is incomplete, especially in the distal segments, remains a limitation on CT (11, 12). The main cause for this incomplete opacification is ureteral peristalsis, which is overcome by obtaining radiographs at different times on conventional urography. This technique is difficult to reproduce on CT because acquisitions must be limited to reduce radiation exposure (19). Some authors have explored other techniques to optimize opacification of the upper tracts.
tracts (table IV). Recently, the idea of induced hyperdiuresis was introduced.

The purpose of our study was to assess the value of furosemide induced hyperdiuresis on upper tract opacification at the excretory phase of CT urography, but also to assess the value of increasing the routinely prescribed dose of furosemide (10 mg) (14, 15, 20, 21).

Since iso-osmolar or nearly iso-osmolar iodinated contrast materials are routinely used in clinical practice, the injected volume has little impact on diuresis, but at similar diuresis, the iodine concentration will have an impact on upper tract opacification. Unlike other authors, we have injected all patients with a similar dose of iodine (400 mg/kg). In order to limit patient exposure, we have acquired a single helical series at the excretory phase using the automatic tube current modulation feature of our scanner. Based on a review of the literature, we have elected to acquire the excretory phase series at 450 seconds post injection: Caoili et al. have reported that a delay of 450 seconds was superior to a delay of 300 seconds for upper tract opacification (13). In a recent study by Kemper (21) where time delay for excretory phase acquisitions was patient-adjusted, the median time delay in 51 patients was 418 seconds (mean: 447±118 sec).

The concept of inducing hyperdiuresis for improved upper tract opacification was first introduced around 2000 (14). Several techniques can be used: intravenous infusion of 250 ml of normal saline (1, 12-14), oral ingestion of 1 liter of water (16), or intravenous injection of furosemide (14, 15, 20, 21) (table IV). Results of hyperhydration from infusion of NS are varied (1, 12, 13) and oral hyperhydration seems complicated to implement for patients referred for CT urogram (reproductibility, tolerance, poorly controlled efficacy). The use of diuretics has been evaluated by several studies, including those by Nolte Ernsting (14, 20) using furosemide (a potent short acting diuretic inhibiting sodium and chloride reabsorption mainly at the ascending loop of Henle) with a dose of 10 mg injected 3 to 5 minutes before administration of the iodinated contrast material. The only contraindications to its use are acute upper tract obstruction, dehydration, known hypersensitivity to sulfas, and hepatic encephalopathy. Complete upper tract opacification was noted in 95% of cases in a population of 16 (14). Two recent studies compared IV furosemide to IV administration of 250 ml of NS for upper tract opacification. Both groups of authors agreed that IV furosemide alone was necessary and sufficient to improve upper tract opacification.

Among other techniques to improve upper tract opacification on CT urogram (table I), we did not believe that it was worthwhile to use abdominal compression. The recent report by Caoili et al. (13) showed that abdominal compression did not significantly improve upper tract opacification, while it did improve distension. Prone acquisitions were not performed for similar reasons: lack of proven efficacy (12).

We have instead elected to evaluate the efficacy of furosemide on a larger patient population at the usual dose (10 mg) for Group 3, but also at a higher dose (20 mg – entire dose from a vial of Lasilix®) for Group 2.

Impact of hyperdiuresis

Furosemide provided improved upper tract opacification and distension in our patient population. Complete upper tract opacification was noted in 52.2% of patients after injection of 20 mg of furosemide versus 30.4% after 10 mg of furosemide and 0% of patients without furosemide. Opacification was complete or nearly complete (2/3 and 3/3) in more than 80% of series after 20 mg of furosemide versus 43.5% after 10 mg of furosemide and 19% without furosemide. Unlike Silverman et al. (15) we have not obtained measurements of the renal pelvis to assess the degree of upper tract distension. However, this was observed subjectively but unanimously by the reviewers.

The use of furosemide resulted in dilution of the excreted contrast in the upper tracts by a factor of nearly 5, from 1310 HU in Group 1, to 265 HU in Group 2 and 255 HU in Group 3.

Additional advantages related to the injection of furosemide are summarized in Tableau IV:

- probable increased sensitivity for detection of urothelial tumors from complete upper tract opacification and improved distension;
- reduction of streaking artifacts secondary to the high density of excreted contrast in the upper tracts that may prevent detection of small endoluminal lesions. Intravenous hyperhydration may also reduce these artifacts (13), but to a lesser extent than furosemide (14);
- intraluminal density better suited for evaluation of ureteral wall and lumen (lithiasis), decreasing the need for continuous window level and width adjustments. Because of furosemide, ureteral wall and lumen can be assessed using window settings similar to those required for renal parenchymal evaluation. This is a time saving feature at the time of image interpretation and it also facilitates detection of renal stones (fig. 4c);
- improved 3D reconstructions: the dynamic range of the upper tracts no longer overlaps that of bones, while being different than surrounding soft tissues, facilitating the generation of 3D images using automatic segmentation software (fig. 4);
- standardization and simplification of a CR urogram protocol: a 20 mg vial of furosemide is injected via the catheter placed

Tableau IV

<table>
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<th>CT urogram protocols and corresponding authors.</th>
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<tr>
<td><strong>Mechanical techniques</strong></td>
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<td><strong>Pharmacological techniques: hyperdiuresis</strong></td>
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<tr>
<td>Ingestion of 750 to 1000 ml of normal saline</td>
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<tr>
<td><strong>Miscellaneous techniques</strong></td>
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<tr>
<td>Multiple excretory phase acquisitions</td>
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<td>Increased delay to excretory phase scanning</td>
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for the iodinated contrast injection. No additional preparation or manipulation is required. Abdominal compression devices are no longer needed.

Limitations

Our results demonstrate that upper tract opacification is significantly more complete on CT urogram when using furosemide, but opacification remains incomplete in some cases.

Density measurements over the renal pelvis were inferior to 200 HU (about 160 HU) in 5 of 23 cases in Group 2. This low density was independent from the injected volume of contrast: mean injected volume of 104 ml in Group 3 and 95 ml in Group 2. Also, this effect was not increased in patients receiving a double dose of furosemide (20 mg): mean density of 255 HU for Group 2 and 265 HU for Group 3. This phenomenon does not appear related to the CT protocol but could relate to the hydration status of the individual patients: fasting or non-fasting, inpatient (IV fluids) or out-patient... Fasting prior to scanning has an impact on renal excretion, which may have an impact on upper tract opacification. Since iodinated contrast materials no longer cause nausea and vomiting, this requirement could potentially be changed. Patient renal function also has an impact on upper tract density.

Tableau V

Properties of furosemide and benefits on excretory phase CT urogram.

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<th>Properties of furosemide</th>
<th>Benefits on CT urogram</th>
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<tr>
<td>Distension of upper tracts</td>
<td>- improved distension and filling of pyelocaliceal structures, ureters and bladder, nearly completely opacified &gt; increased sensitivity for detection of urothelial tumors</td>
</tr>
<tr>
<td>Diluted contrast material with decreased endoluminal density</td>
<td>- reduced streaking artifacts (contrast concentration too high)</td>
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<tr>
<td>Homogeneous upper tract opacification</td>
<td>- facilitates image review with reduced need for continuous window settings adjustments</td>
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<tr>
<td>Simplification and standardization of CT urogram protocol</td>
<td>- facilitates detection of lithiases</td>
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<td></td>
<td>- time saving for technologist and patient</td>
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<td>- reduced time to excretory phase scanning at 420-480 sec (versus 600-720 after the first contrast bolus)</td>
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The density of excreted contrast through out the upper tracts was fairly homogeneous except for persistent increased density at the calices and bladder. This could be reduced by patient mobilization prior to excretory phase scanning.

Finally, furosemide was sometimes associated with heterogeneous nephrographic phase renal parenchymal enhancement (fig. 5), which did not interfere with image interpretation on excretory phase acquisitions. This heterogeneous appearance could be related to a differential recruitment of short and long nephrons.

Conclusion

Our results support the use of 20 mg of furosemide as part of the CT urogram protocol, prior to injection of iodinated contrast material, with excretory phase acquisition at 450 seconds. This protocol resulted in significantly more complete upper tract opacification compared to the standard protocol (without furosemide), reduced and more homogeneous upper tract attenuation (266 HU±91) facilitating ureteral wall and lumen evaluation, and improved 3D reconstructions. This standardized protocol is simple. The
need for fasting prior to CT urography remains unclear. Due to technical advances with MDCT and the effect of furosemide, it is now possible to replace standard intravenous urography by excretory phase MDCT urography, especially for the work-up of hematuria, granted that consideration is given to radiation exposure.

References