Comparison of “Direct” and “Indirect”
Radionuclide Cystography

Geoff Bower, Frederick T. Lovegrove, Helen Geijsel, Agatha Van der Schaff, and George Guelfi

Departments of Nuclear Medicine, Princess Margaret Hospital for Children; and Sir Charles Gairdner Hospital, Perth, Western Australia

Thirty children were studied using both direct (catheter) and indirect techniques of radionuclide cystography. Of 54 ureters able to be compared, six showed vesicoureteric reflux (VUR) on the direct study but were read as negative on the indirect cystogram, and five showed no reflux on the direct cystogram but were read as positive for VUR on the indirect study. (Sensitivity of 68% and specificity of 86%). Regarding ureters read as true positives on indirect study, if that ureter has ever shown reflux at any time, or if it drained a scarred kidney specificity was improved to 97% without changing the sensitivity. Concerns about the validity of indirect cystogram results and the ease of assessment and low radiation dose from the direct cystogram has made direct cystography our preferred technique.


Vesicoureteric reflux (VUR) in children is an important condition often associated with urinary infection and at times renal scarring. The diagnosis of VUR has been made traditionally by x-ray cystography (MCUG) but also by radionuclide cystography. Since Winter first introduced catheter (“direct”) radionuclide cystography in 1959 (1), the technique has become quite widely adopted mainly in North American pediatric nuclear medicine departments (2,3). Many European and Australian centers, however, have preferred to avoid catheterization, using the “indirect” approach, first described by Dodge in 1963 (4,5). Before introducing the direct technique to our department’s protocol—at the request of physicians and to reduce patient radiation dose for VUR follow-up—we undertook a comparison of the two methods as originally suggested by Conway et al. some 10 yr ago (6).

MATERIALS AND METHODS

Thirty children, eight boys and 22 girls referred to the nuclear medicine department for assessment of renal and ureteric function as part of the follow-up of VUR, or recurrent urinary infection, were studied. Parents gave consent for urethral catheterization on each child and for the direct cystogram to be followed in the afternoon or on the next day by the technetium-99m diethyltriaminepentaacetic acid (Tc99mDTPA) renal scan and a delayed voiding cystogram. Catheterization and voiding direct cystogram were carried out in essentially the same manner as that detailed by Ulrich and Treves (2). Careful attention to urethral anesthesia was given for boys and sterile infant feeding tubes were used in most children. Voiding for all cooperative children was allowed in the upright sitting position, viewed posteri­rally with a restrainer belt across the chest and around the gamma camera. A bolus of Tc99m sulfur colloid (37 MBq) was then injected into the tubing at the commencement of bladder filling. Analog and digital acquisition was in 15-sec frames in 64 x 64 (word mode) matrix for 14 frames, followed by a 30-sec analog image when the bladder was full before catheter removal and voiding. Bladder filling occurred when patient discomfort was associated with bladder pressure exceeding hydrostatic pressure with the saline bottle at 100 cm above the bladder. Sixty 5-sec voiding frames were then collected and a 30-sec postvoid analog image obtained.

Analysis of the direct cystogram was by inspection of the analog images and computer processed digital images. Generally, several voiding frames were summed and an upper threshold used to improve image contrast, although when reflux occurred to the level of the upper ureter this was obvious, and was scored as...
FIGURE 1
Direct radionuclide cystogram analog image from 5-sec voiding frame showing right sided reflux to renal pelvis of scarred kidney in 10-yr-old girl with recurrent UTIs but normal x-ray cystogram.

FIGURE 2
Direct cystogram on 7-yr-old girl showing right-sided reflux to renal pelvis.

positive for VUR. Quantitation of VUR was not attempted.

Indirect cystogram was performed when ~80% of the i.v. administered $^{99m}$TcDTPA from renal study was in the bladder and the child expressed a strong desire to void. The study was then identical to that of the direct cystogram after the "filling phase." Analysis was by inspection of the analog images and time-activity curves from regions including each kidney and upper ureter as described by Ulrich and Treves (2) for their direct cystogram analysis. A playback buffer was produced in monochrome display with a fixed gray scale to allow for voided activity leaving the field of view of the camera with time, and two, nine-point smoothing processes were used on each frame. Questionable studies were reanalyzed using summed pairs of voiding frames. The indirect cystogram playback loops were read by three observers unaware of the patients' identity or other investigation results and a consensus score for each ureter as positive or negative for VUR was given.

Patient records were reviewed to determine previous x-ray examination results, and the $^{99m}$TcDTPA renal study was analyzed to assign relative and absolute glomerular filtration rate (GFR) for each kidney from single 20-min blood sample analysis and convolution/deconvolution of the renogram curves. X-ray cystograms had been performed in the department of radiology using a fixed protocol with limited fluoroscopy and 110 mm camera film. No attempt was made to re-x-ray children with VUR at the time of the nuclear medicine assessment.

RESULTS

Successful direct cystograms were obtained on all 30 children, ranging in age from 4 mo to 12 yr. Seventeen children (21 ureters) showed reflux during voiding and/or filling of the bladder. The first two patients (both male) complained of significant dysuria after catheterization using balloon catheters. No further difficulties were encountered with careful use of infant feeding tubes. All the ureters that showed VUR on direct cystogram had at some time had VUR shown on x-ray study or drained a scarred kidney without previous VUR having been demonstrated (two children) (Fig. 1). There were no studies with equivocal results. Twenty-seven children had successful indirect cystogram performed that could be analyzed fully. Two girls were unable to void within 15 min of initiating the study and one girl's data was lost from magnetic tape storage.

In general, there was good agreement between the results of direct and indirect studies for each ureter. Taking the direct cystogram as the "gold standard," the
indirect cystogram read abnormal in 13 of 19 “positive” cases (68% sensitivity) and normal in 30 of 35 “negative” cases (86% specificity). Ureters read positive for VUR on indirect study to be scored as true-positive results if (a) that ureter had either had VUR shown on direct cystogram or on x-ray cystogram in the past, or (b) if the kidney drained by it was scarred on IVU or had significantly (20% or greater) reduced glomerular filtration rate (GFR), produced a 68% sensitivity (17/25) and 97% specificity (28/29) for the indirect cystogram. The direct cystogram would then be assumed to have a 76% sensitivity. The period between x-ray and nuclear medicine assessment varied from 1 to 14 mo. Region of interest (ROI) data analysis was not helpful in detecting VUR into four ureters despite a positive reading on the playback data of the indirect cystogram. Seven ureters had significant peaks during voiding on the time-activity curves without any VUR scored on the playback analysis and without direct cystogram VUR or a scarred kidney. Patient movement during voiding was frequent, however, and was believed to have contributed to misleading time-activity curve results in some cases.

Although the indirect cystogram followed the direct cystogram temporally, the conditions of voiding were felt to be very similar between the two examinations. Discrepancies of results in an individual patient is well shown in Figs. 2 and 3. A girl with bilateral VUR shown on x-ray 1 yr before these studies had VUR shown only on the right side with direct radionuclide examination (Fig. 2), and probable VUR seen on the left hand side on the indirect voiding frames as shown, [Fig. 3(a) and (b)].

**DISCUSSION**

VUR is known to be a somewhat variable phenomenon with different conditions of hydration, bladder volume and pressure, and, therefore, examination technique. It might be expected that two different techniques attempting to diagnose VUR from two separate episodes of voiding would reveal some discrepancy in diagnostic results. We found a significantly different number of ureters read as showing VUR on indirect radionuclide cystogram from those positive for VUR on direct cystogram. Six out of 19 ureters positive for VUR on the direct study read negative on indirect study by both inspection of carefully displayed playback buffers and on (ROI) analysis. Five of the 35 ureters, negative on the direct cystogram were read as showing VUR on indirect analysis.

Allowing for this true discordance of results between the two methods, we have come to regard the direct study as giving more confidence about the exclusion of reflux. The result is more useful clinically with its images being more easily appreciated by the clinician and we have had no technical problems in a subsequent series of over 100 direct examinations in children. Confidence in the results has reduced the number of x-ray cystograms used in the follow-up of children with VUR. The indirect study is...
reserved for use in children who refuse catheterization and in whom the clinician is satisfied with a test result approximating the sensitivity and specificity shown in this study's population, (68% and 86%, respectively). This assessment of the indirect radionuclide cystogram would only be valid for such a relatively high VUR prevalence group as those studied here and may be quite different if applied to screening a post urinary tract infection (UTI) population. The large numbers of children found to have positive indirect studies for VUR but no other evidence of VUR, in some series may well represent an unacceptably high false-positive rate for this technique (5). The clinical importance of VUR diagnosed by direct radionuclide cystogram alone was stressed by Nasrallah et al. (3), and we found this in the two cases with scarred kidneys and VUR in our series. The same could not be said for most of the isolated positive indirect studies, which we feel are most likely false-positive results, in these patients.

ACKNOWLEDGMENTS

The authors are grateful to Ms. Cheryl Harwood and Mrs. Marina Bennett for secretarial assistance, and to the children for their cooperation during the study.

REFERENCES

Comparison of "Direct" and "Indirect" Radionuclide Cystography

Geoff Bower, Frederick T. Lovegrove, Helen Geijsel, Agatha Van der Schaff and George Guelfi


This article and updated information are available at:
http://jnm.snmjournals.org/content/26/5/465

Information about reproducing figures, tables, or other portions of this article can be found online at:
http://jnm.snmjournals.org/site/misc/permission.xhtml

Information about subscriptions to JNM can be found at:
http://jnm.snmjournals.org/site/subscriptions/online.xhtml