THE IDEAL TEST TO PROVE UPPER TRACT OBSTRUCTION STILL ELUDES US

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Abstract
Urinary tract obstruction (UTO) is a relatively common problem. The obstruction to urinary flow may be acute or chronic, partial or complete, unilateral or bilateral, and may occur at any site in the urinary tract. The major causes of UTO vary with the age of the patient. From a practical standpoint, the diagnosis of urinary obstruction requires proof of increased resistance to urine flow. There are numerous tests available to the urologist for the diagnosis of obstruction. These include radiographic studies, such as plain film (KUB), intravenous urography (IVU) ultrasound, computed tomography, Lasix renogram, magnetic resonance (MR) urogram, Whitaker test and urinary biomarkers. Selection of a specific test depends on the acuity of obstruction and patient’s age and renal function. Consideration must also be made for cost of the test, reliability and feasibility of long term follow-up by repeated exams. The various tests differ substantially in their ability to provide both anatomical detail and physiological information. An ideal test should highlight on the anatomy of the urinary tract, the cause of obstruction, the level of obstruction, the effect of obstruction on the anatomy and function of the kidney proximal to the obstruction. It should be accurate, readily available, easy to perform and interpret, reproducible, objective, and cost-effective. Unfortunately none of the available tests satisfy all the criteria of the ideal test. Each of the tests used in the upper urinary tract evaluation has strengths and limitations that fit it for a specific role in diagnosis and management. Even though they provide overlapping information, they need to be used as complementary aid rather than as substitute. Although obstruction can be diagnosed qualitatively, there is still no absolutely reliable and universally accepted test to tell us which patients with mild obstruction need treatment and which do not.

Keywords: Urinary obstruction, Uropathy, Upper urinary tract, Imaging, Kidney, Ureter.

Introduction
Urinary tract obstruction (UTO) is a relatively common problem. The obstruction to urinary flow may be acute or chronic, partial or complete, unilateral or bilateral, and may occur at any site in the urinary tract. The major causes of UTO vary with the age of the patient. Anatomic abnormalities (stenosis at the ureterovesical or ureteropelvic junction) account for the majority of cases in children. In comparison, calculi are most common in young adults, while carcinoma, retroperitoneal or pelvic neoplasms, and calculi are the primary causes in older patients. Urinary obstruction results in a fall in the rate of urine removal from the urinary tract to levels below the rate of urine production, which upsets a sensitive, dynamic balance and impairs the process of urine formation. From a practical standpoint, the diagnosis of urinary obstruction requires proof of increased resistance to urine flow.¹

There are numerous tests available to the urologist for the diagnosis of obstruction. These include radiographic studies, such as plain film (KUB), intravenous urography (IVU) ultrasound, computed tomography, Lasix renogram, magnetic resonance (MR) urogram, Whitaker test and urinary biomarkers. Selection of a specific test depends on the acuity of obstruction and patient’s age and renal function.² Although obstruction can be diagnosed qualitatively, there is still no absolutely reliable and universally accepted test to tell us which patients with mild obstruction need treatment and which do not. Pregnant patients and those with contrast allergy require special provisions.² Consideration must also be made for cost of the test, reliability and feasibility of long term follow-up by repeated exams.
An ideal test should highlight on the anatomy of the urinary tract, the cause of obstruction, the level of obstruction, the effect of obstruction on the anatomy and function of the kidney proximal to the obstruction. It should be accurate, readily available, easy to perform and interpret, reproducible, objective, and cost-effective. Unfortunately none of the available tests satisfy all the criteria of the ideal test.

Pathophysiology

Urine is propelled from renal pelvis to the bladder by ureteral peristalsis. Renal pelvic pressure is normally 2-12 mmHg and varies with urine flow rate. With ureteral obstruction, raised pelvic pressure is transmitted to the tubules, eventually leading to the dilatation and atrophy of the tubules, cast formation, interstitial fibrosis and loss of glomeruli. Glomeruli are relatively better preserved than tubules, resulting in more derangement of medullary than cortical function after obstruction is relieved.

A defect in urinary acidification is the most common and sensitive indicator of tubular dysfunction in chronic obstructive nephropathy. Enzymuria and microproteinuria are also sensitive indicators of tubular damage. In cases with chronic partial obstruction, the degree of obstruction and the presence or absence of infection determine which kidneys will deteriorate with time. Partial obstruction often leads to greater pyelectasis than does complete obstruction for the same period. Pelvic capacity is determined by anatomy (intrarenal / extrarenal), compliance, and degree and duration of obstruction.

Diagnostic tests

Anatomical information has been central to the diagnosis of urinary obstruction, but under certain circumstances, reliance on the delineation of the urinary tract anatomy alone can be misleading. The absence of dilatation in early obstruction is well known. Also, obstruction is not the cause for all hydronephrosis. Therefore, the diagnostic process is best served by always correlating anatomy and function. The various tests differ substantially in their ability to provide both anatomical detail and physiological information. Each has strength and limitations fit for a specific role in the diagnosis and patient management.

Plain film (KUB)

A KUB film has limited role in evaluation of obstruction; though sufficient to diagnose ureteral stone. It is low cost with low radiation and can be done rapidly in urology clinic set up. However its sensitivity for stone visualization is about 50%. Stones larger than 5mm and with CT attenuation above 300HU are likely to be detected on plain radiography.

Ultrasound

Ultrasound is usually the first line investigation to evaluate patients for renal obstruction. It is inexpensive, noninvasive and portable. It is highly sensitive in detecting dilated systems and absence of hydronephrosis is generally a reliable sign of absence of obstruction. An exception is very early obstruction, as might occur in an acute obstructing stone. Nondilated or minimally dilated collecting systems have been reported in 4-5% of patients with obstructed renal failure (false-negative results). The price of setting of a low threshold for the diagnosis of mild hydronephrosis by sonography is loss of specificity. Findings indistinguishable from those of mild hydronephrosis (false-positive result) occur in 2-26% of kidneys shown to not be obstructed on urography.

The introduction of duplex and color Doppler ultrasound has expanded the role of ultrasound in suspected obstruction. A resistive index (RI) threshold of 0.70 and/or a 0.10 or greater interrenal difference (dRI) between the symptomatic and asymptomatic sides could differentiate between significantly obstructed and nonobstructed kidneys. The variation of the RI with age, state of hydration and the time interval between onset of obstruction and RI measurement limits its use. The use of non-steroidal anti-inflammatory drugs (NSAIDs) can also alter the renal vascular tone and thereby affect RI values. Berge et al. applied color Doppler of ureteral jets to diagnose acute obstruction in adults. Ureteral jets in normal subjects averaged 2.7 per minute.
periodic jet of urine effluxing from the ureteral orifice effectively rules out complete obstruction of the renal system.34, 35 A lengthy US examination may be required to fully assess the frequency and intensity of the ureteral jets.36, 37 Because of these technical limitations and because the findings in partial obstruction are inconsistent, evaluation of ureteral jets has limited usefulness. Nevertheless, in selected circumstances, such as pregnancy, in which radiation is to be avoided, looking for jets can be worth the effort.38, 39

Prenatal ultrasound is performed routinely and may pick up evidence of hydronephrosis in the developing fetus. In patients diagnosed with prenatal hydronephrosis, ultrasound should be repeated within several weeks of birth to evaluate for persistent hydronephrosis.40

**Intravenous urography (IVU)**

IVU plays an important role in the diagnosis of obstruction. It can assess anatomy and the function of the kidney. Acute obstruction is identified by (1) the presence of a delayed and often increased nephrogram, (2) delayed calyceal appearance time and transport of contrast material to the point of obstruction, and (3) variable dilatation of the collecting system and ureter.1 The level and cause of obstruction may be determined with the visualization of filling defects or stones in the renal pelvis or ureter, changes in renal contour and course of the ureters. Obstructions, which are not obvious initially, may, at times, be revealed after the administration of diuretic during IVU. This technique is generally reserved for suspected intermittent ureteropelvic junction (UPJ) obstruction.2

The IVU requires intravenous contrast and hence cannot be performed in a patient with decreased renal function. Nephrotoxicity of iodinated contrast is most likely in patients with chronic renal insufficiency especially if diabetes is also present.2 Patients with contrast allergy need to be premedicated prior to the procedure and non-ionic contrast media are to be used. IVU provides limited information on mural pathology and none on extramural pathology. In addition IVU requires significant amount of radiation exposure and may not be ideal for young children and pregnant women.17

**Retrograde urography**

With the improvement in IVU and other imaging technique, retrograde ureteropyelography is rarely needed for diagnosis. Retrograde studies find their greatest use in patients with persistent hematuria and a suboptimal IVU and in whom the intravenous administration of contrast media is contraindicated. Retrograde study can delineate the precise location and severity of obstruction when other studies fail to define the exact point or cause of obstruction. However, this is not a first-line study for patients with obstruction due to necessity of anesthesia.2 It is usually performed prior to definitive treatment or drainage of the obstructed system.

**Diuretic renogram**

Diuresis renography was first used by O’Reily in 1978.41 Presently, it is widely accepted as a useful test for investigation of the dilated urinary tract and to distinguish between obstructed and requires an operation, and a nonobstructed system in which urographic dilatation and stasis mimic obstruction but no genuine impedance to urine flow exists and a operation is not required.42 The technique provides dual information, consisting of quantitative data on individual renal function, and time-activity curves reflecting the urodynamics through the individual upper urinary tracts at normal and high urinary flow rates.42 Lasix is administered with the renal scan to verify delayed excretion and the presence of obstruction. The protocols used for this purpose include F+20, F-15, F+0, and combined F-15 and F+20. None of these protocols is recognized as a standard method for the time of diuretic administration.43 The renogram is non-invasive, easily repeatable and represents less radiation.

The diuretic renal scan, however, has a false-positive and indeterminate rate of 10-15%.44 This usually is due to variables such as the degree of dilatation of the pelvicalyceal system or ureter, the degree of bladder distension, the diuretic dose, and the state of hydration.45, 46 The renogram has other limitations too. In a kidney with impaired function or associated with an extremely large system the test may be invalid and the response to the diuretic often is in doubt in respect to the kidney in question and to the contralateral kidney.47 The diuretic response could be different according to whether the damage mainly is glomerular or tubular. In small children the
response of immature kidneys to diuretic is not known.\textsuperscript{47} With a renogram no information is achieved about compliance. Finally, diuretic renogram identifies the presence of obstruction but not the cause of obstruction; it provides very little anatomic information.\textsuperscript{17}

**Pressure flow studies (Whitaker test)**

The pressure flow study (Whitaker test) provides a precise but invasive measure of the presence or absence of obstruction in the dilated system.\textsuperscript{2} It provides a quantitative assessment of outflow resistance together with the opportunity to document any obstructive lesion on radiographs. Whitaker test is technically very demanding; it is easy to do the test badly and it is even easier to obtain spurious results.\textsuperscript{1} The main limitation of pressure-flow studies is that no information is provided on renal function. The studies are invasive in the sense of potential renal damage and the general anesthetic that often is needed in small children.\textsuperscript{47} They also provide less than perfect information about the compliance of the system. Lang et al have used videopelvimetric approach to examine the urodynamics of the upper urinary tract and by using different filling rates, they have tried to discriminate a compensated (stage I obstruction) from a decompensated (stage II obstruction) cavity system.\textsuperscript{48}

**Computed tomography**

In patients with urinary obstruction, CT scan is very useful in the following conditions: (1) screening patients with acute flank pain (‘colic’); (2) screening patients with azotemia who are strongly suspected to have an acute obstruction despite a negative sonogram; (3) establishing the etiology of ureteral obstruction when IVU, retrograde studies, ultrasound, or magnetic resonance urography have failed.\textsuperscript{1} Non-contrast CT compares favourably with IVU in diagnosing obstruction and shows more ureteral stones than the IVU. For detecting ureteral stones, CT is 94-100% sensitive and 96-99% specific.\textsuperscript{49,50,51} The secondary (indirect) CT signs of obstruction that are most likely to be present in patients with ureteral stones are ureteral dilatation (90%), pyelocaliectasis (83%), perinephric stranding (82%) and renal enlargement (71%).\textsuperscript{52} The combined presence of ureterectasis and perinephric standing has a positive predictive value of 99%, whereas their combined absence has a negative predictive value of 95%.\textsuperscript{53} Although non-contrast CT does not allow grading of the severity of obstruction, moderate or severe perinephric stranding or fluid generally indicate moderate or severe obstruction.\textsuperscript{54,55} The absence of more perinephric stranding does not, however, exclude severe obstruction. Non-obstructive ureteral stones account for 4-5% of all ureteral stones and lack the secondary signs of obstruction on CT.\textsuperscript{52,56} Indinavir sulfate calculi are of soft-tissue attenuation and are usually not visible on non-enhanced CT.\textsuperscript{57}

Contrast enhanced CT scans will further assess the function of a renal unit and more accurately detail the degree of hydroureteronephrosis. Also, it is particularly helpful in determining the etiology of occult ureteral obstruction, especially when intravenous or retrograde studies suggest extrinsic obstruction. If delayed contrast images are obtained, CT urography with 3-dimensional reconstruction can provide excellent visualization of the entire urinary tract.\textsuperscript{58,59}

**Magnetic resonance imaging**

Magnetic resonance imaging provides more detailed anatomy than nuclear renograms without the radiation exposure or the use of nephrotoxic contrast media. The most common MR urographic techniques for displaying the urinary tract can be divided into two categories: static-fluid MR urography and excretory MR urography.\textsuperscript{60} Static-fluid MR urography makes use of heavily T2-weighted sequences to image the urinary tract as a static collection of fluid, can be repeated sequentially (cine MR urography) to better demonstrate the ureters in their entirety and to confirm the presence of fixed stenoses, and is most successful in patients with dilated or obstructed collecting systems. Excretory MR urography is performed during the excretory phase of enhancement after the intravenous administration of gadolinium-based contrast material; thus, the patient must have sufficient renal function to allow the excretion and even distribution of the contrast material. Diuretic administration is an important adjunct to excretory MR urography, which can better demonstrate nondilated systems. Static-fluid and excretory MR urography can be combined with conventional MR imaging for comprehensive evaluation of the urinary tract.\textsuperscript{60}
With the implementation of rapid very heavily T2-weighted sequences such as RARE (rapid acquisition with relaxation enhancement)\textsuperscript{61, 62, 63}, the extremely fast HASTE (half-Fourier acquisition single-shot turbo spin-echo)\textsuperscript{64,65,66} or some variation thereof magnetic resonance urogram (MRU) of the dilated system can be obtained with short acquisition time (less than 20 seconds) and good to excellent image quality. MRU is especially helpful in pregnant women and patients with contrast allergy or renal failure.

MRU detects all cases of moderate to severe pyelocaliectasis and ureterectasis, but mild dilatation can be missed and parapelvic cysts can cause false-positive results.\textsuperscript{62,67} Unlike IVU, the level of obstruction is always shown by MRU regardless of renal function.\textsuperscript{65,67,68} For kidneys that function, MRU is poor compared to IVU for characterizing intraureteral obstructions, especially if they are small. MRU misses small stones (<4mm) altogether and fails to distinguish larger stones from tumor or blood clot unless conventional sequences are added. Extrinsic obstructive processes, such as pelvic or retroperitoneal tumors are usually visible on MRU, but complementary conventional spin-echo sequences should be added to fully characterize the abnormality.\textsuperscript{63,65} Like non-contrast CT scan, MRU finding of dilatation of the collecting system and ureter, accompanied by perinephric or periureteral fluid, provides compelling evidence of acute ureteral obstruction.\textsuperscript{64,69} MRU can distinguish symptomatic “physiologic” ureterohydronephrosis of pregnancy from “pathological” ureterohydronephrosis caused by obstructing stone.\textsuperscript{70}

Diuretic-enhanced excretory MRU(gadolinium-enhanced excretory MRU after low dosediuiretic injection) comes closest to matching conventional urography for demonstrating the morphology of the normal and abnormal urinary tract.\textsuperscript{71} Virtual endoscopy using MR urography data is feasible in patients with upper tract dilatations. It displays the renal pelvis, calices and ureter and, moreover, can show endoluminal changes caused by abnormalities.\textsuperscript{72}

A significant limitation of MRU is its inability to depict most intraureteral filling defects smaller than 4mm, including stones. MRU cannot distinguish between chronic obstruction and nonobstructive dilatation.\textsuperscript{69} Non-contrast MRU provides no information about function of the obstructed kidney, and calyceal detail is poor compared to that seen with IVU. Patients with cardiac pacemakers, brain aneurysm clips or prosthetic heart valves are not candidates for MR. High cost, the desirability of having a cooperative patient, and limited access to MR scanners are other disadvantages of MRU.

**Urinary biomarkers of congenital urinary obstruction**

Urinary biomarkers are a promising tool that could be used as a noninvasive assessment of congenital renal obstruction in children. Several cytokines, peptides, enzymes and microproteins are identified as major contributors to or ensuing from obstruction-induced renal fibrosis and apoptosis. The most important biomarkers were transforming growth factor-β\textsubscript{1} (TGFβ\textsubscript{1}), epidermal growth factor (EGF), endothelin-1 (ET-1), urinary tubular enzymes [N-acetyl-β-D-glucosaminidase (NAG), γ-glutamyl transferase (GGT) and alkaline phosphatase (ALP)], and microproteins [β\textsubscript{2}-microglobulin (β\textsubscript{2} M), microalbumin (M.Alb) and micrototal protein (M.TP)]. All biomarkers showed different degrees of success but the most promising markers were TGFβ\textsubscript{1}, ET-1 and a panel of tubular enzymes. These biomarkers showed sensitivity of 74.3% to 100%, specificity of 80% to 90% and overall accuracy of 81.5% to 94% in the diagnosis of congenital obstructive uropathy in children.\textsuperscript{73,74} Nevertheless, the currently available urinary biomarkers are not specific for obstructive uropathy. Increased urinary biomarkers were reported in other diseases such as IgA nephropathy, nephritic patients with membranous nephropathy, high-grade reflux, urinary tract infection, glomerulonephritis and in patients with diabetes mellitus.\textsuperscript{73}

**Role of Endoluminal sonography**

Catheter-based endoluminal sonography has been used for the evaluation of a wide range of genitourinary abnormalities. Two-dimensional images can depict embedded submucosal calculi, ureteral strictures and tumors. With volume rendering (3D) data, precise visualization of irregularly shaped structures, such as crossing vessels and septum, can be readily performed.\textsuperscript{75}

**Conclusion**

Each of the tests used in the upper urinary tract evaluation has strengths and limitations that fit it
for a specific role in diagnosis and management. Even though they provide overlapping information, they need to be used as complementary aid rather than as substitute. For most patients, noninvasive examination by IVU, ultrasound, CT, or nuclear medicine, alone or in combination, is sufficient to establish whether obstruction is present. MRI has a niche role in pregnant and certain other patients. Retrograde or antegrade pyelography is sometimes needed to pinpoint the level of obstruction, obtain material for bacteriological or cytological study, and if necessary, provide temporary drainage before definitive treatment. Urinary biomarkers appear to be promising noninvasive assessment of renal obstruction in children.

References


