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UROGENITAL

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What is left of i.v. urography?

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Abstract Since its introduction into clinical practice in the early 1930s, intravenous urography (IVU) was the primary imaging technique for the investigation of urinary system disorders for many years, until the advent of digital cross-sectional-imaging techniques gradually started to undermine many of its indications. Intravenous urography has been superseded for some indications such as renovascular arterial hypertension, prostatic dysuria, renal failure, palpable abdominal masses and recurrent urinary tract infection in women. Intravenous urography has been reduced, in the sense that it is no longer a primary examination, for other clinical indications such as renal colic, renal trauma, uroseptic fever, asymptomatic haematuria, medical haematuria, obstructive uropathies and follow-up of various disorders. Intravenous urography is indicated and often mandatory in congenital anomalies of the urinary tract, prior to endourological procedures, possible fistulas, renal transplantation, tuberculosis and ureteral pathology. In conclusion, IVU is still the examination of choice where there is a need to visualize the entire urinary system and to evaluate the state of the papillae and calyces. Computed tomography urography and MR urography are the imaging modalities ready in the near future to replace IVU.

Key words Intravenous urography · CT urography · MR urography · Imaging of urinary tract

Introduction

Since its introduction into clinical practice in the early 1930s, intravenous urography (IVU) was the primary imaging technique for the investigation of urinary system disorders for many years, until the advent of digital cross-sectional-imaging methods gradually started to undermine many of its indications.

In 1975 an estimated 10,000,000 urograms were obtained annually in the United States. Just 20 years later, in 1995, the number of IVUs had dropped to approximately 600,000 per year [1]. As early as 1985, Pollack and Banner [2], two of the world's leading uroradiologists, illustrating the "Current status of excretory urography" added to his title "A premature epitaph?", and concluded their paper stating, "It appears safe to say that IVU will be with us for many years to come. Indeed, it seems fair to add that the practice of urology and uroradiology would be very difficult without it". Since that time, however, the enormous technological advances of CT and MR imaging have had an exceptional impact on the study of the urinary system, including parenchymas, urinary tract and vessels. At the end of 1999 Amis [3] entitled his editorial "Epitaph for the urogram" where he stated that, "The remaining major indication for excretory urography is hematuria", and he went on to conclude that, "In the near future, excretory urography will be replaced ... by CT urography to evaluate for hematuria and other genitourinary conditions". In Amis's opinion, therefore, urography is agonising.

Table 1

Clinical requests	IVU 1999 No. of inpatients: 187	US 1999 No. of inpatients: 617
Renal colic	22	109
Lithiasis	22	9
Haematuria	71	126
Bladder tumour surveillance	29	15
Uroseptic fever	9	31
Hydronephrosis	11	20
Post-surgical check	11	12
Dysuria/prostatism	4	121
Various	3	56
Prostatic tumour		29
Renal tumour		14
Acute renal failure		36
Chronic renal failure		30
Medical nephopathies		9

In the past decade several authors have discussed the role of the IVU after appearance of the cross-sectional-imaging techniques [4, 5, 6, 7, 8, 9, 10, 11, 12].

In this paper the present author illustrates "what is left of intravenous urography" by first looking at the clinical indications and then considering some pathological conditions.

This paper starts by providing the figures relating to the activity of our department. In the past 10 years we have gone from the 1810 IVUs performed in 1989 to 484 in 1999, so the reduction has been dramatic, i.e. approximately 73%.

There is no doubt that one of the main causes of this reduction has been ultrasonography (US), as is seen in Table 1, which shows the number of exams performed on inpatients studied using the two techniques in 1999 for three of the most common clinical indications: renal colic; haematuria; and uroseptic fever. The more frequent use of US is dramatic for renal colic, very evident for haematuria and evident for uroseptic fever. For dysuria and prostatism the indication has been almost cancelled in favour of US, as is seen from the list of examinations ordered.

Based on a review of our case series and the international literature on the topic, we have traced the current role of excretory urography: IVU has been superseded for some indications, and reduced – in the sense that it is no longer a primary examination – for others, whereas it is still the investigation of choice in some specific clinical situations.

IVU: superseded roles

This section briefly considers the clinical indications for which urography has been supplanted by other imaging techniques.

Renovascular arterial hypertension

In the past, minute-sequence IVU was considered the best test-screening method for renovascular hypertension based on the following criteria: size differences between the two kidneys; delayed excretion; and pyelic hyperconcentration on the side corresponding to the renal artery stenosis.

This indication has been superseded due to the high number of false negatives ranging from 22 to 58% [2], and to the introduction of new modalities capable of a high degree of accuracy [12a] in identifying directly the existence of renal artery stenosis, such as Tc-99m DTPA scintigraphy, Tc-99m MAG 3 and Captopril, echo colour Doppler, helical CT, angio-MR imaging and intra-arterial digital arteriography.

The problem, however, is not only one of ascertaining the existence of renal artery stenosis, but also of establishing whether it is responsible for the state of hypertension. Of the various techniques, MR imaging with Captopril seems capable of ascertaining both the stenosis and its functional impact [13].

Prostatic dysuria

Ultrasound has completely replaced IVU, which in any case always had a modest role as it could only visualize the imprint on the bladder and the upward displacement of the distal ureters caused by the gland enlargement and, in obstructive forms, the existence of hydroureteronephrosis.

Presently, intracavitary US can accurately determine the gland's morphology and structural alterations, as well as the possible presence of hydronephrosis. In addition, it can guide the biopsy in cases of suspected tumour. If the biopsy is positive, MR imaging is used to stage the tumour and guide therapeutic, surgical or medical decisions.

Renal failure

In renal failure, IVU has been superseded by a variety of other techniques which all serve different purposes. There are various causes of the renal failure. The main imaging problem in renal failure is that of establishing, particularly in the acute phase, whether the failure is obstructive or non-obstructive, surgical or medical.

Presently, dilatation of the urinary tract is established by US and MR urography, with IVU being limited to special cases to avoid contrast-medium nephrotoxicity on an injured kidney, although presently this risk is greatly reduced.

The role of US is to document the urinary tract dilatation, its level and sometimes its cause, especially if the

dilatation is of prostatic origin. The cause may, however, be better defined by MR urography using both urinary tract and parenchymal sequences.

If the renal failure is of a medical nature, a combination of US and Doppler is used for identifying renal volume and echo pattern, aspects which may be more useful for monitoring the nephropathy during medical treatment than for diagnosing its nature. Evaluation of the resistive index, on the other hand, may be useful for differentiating renal from pre-renal failure.

Functional MRI may have a role in differentiating vascular from interstitial nephropathies based on the different patterns followed by the curves expressing the cortical and medullary peaks [14].

A functional evaluation may also be obtained by scintigraphy using both Tc-99m DTPA with glomerular excretion and Hippuran I-131 with tubular excretion. The diagnostic pathway depends on the team's work environment and experience.

There are no differences in approach between acute and chronic renal failure. Intravenous urography has therefore lost its role in evaluating patients with renal failure, except for rare cases of chronic renal failure, as in cases of bilateral tubercolosis.

Palpable abdominal masses

In both, adults and children, this clinical finding is first investigated by US and then followed by CT and, if necessary, by MRI. Both CT and MRI are better for defining the origin of the mass and its relation to the surrounding anatomical structures for pre-operative purposes.

If required by the surgeon, a urinary tract road map, in particular of the ureters, can be obtained by performing a urogram at the end of the CT examination.

Recurrent urinary tract infection in women

Intravenous urography has traditionally been used to investigate the recurrent urinary tract infection in women in the hope of identifying a correctable congenital pathology or reflux nephropathy.

First of all, renal lesions generally occur in early life and additional infections in the adult do not cause additional damage. Moreover, we have to consider the minimal yield of IVU in such settings: from the 1.4% obtained by Newhouse et al. [15] in 1000 women investigated to the slightly higher, but still low, percentages found in smaller study groups [12, 16, 17]. Intravenous urography is therefore to be considered a modality which is ineffective, expensive and high in radiation exposure.

IVU: reduced roles

Renal colic

In very recent years, many centres have turned to helical CT to diagnose patients with renal colic [18], as this examination has been found to be superior to IVU in detecting the presence of the stone, as well as its size and location, which are crucial elements for deciding therapy.

Besides these direct signs, unenhanced helical CT (UHCT) is based on indirect signs such as pyelo-ureteral dilatation, perinephric and periureteral strandings, renal enlargement, renal sinus fat blurring and rim sign [19, 20].

There is no doubt that the data reported in the recent literature argue in favour of UHCT vs IVU for numerous reasons:

1. Unenhanced helical CT detects almost all urinary stones, whereas IVU fails in 31–48% of cases depending on the authors [21, 22, 23, 24].
2. It identifies renal microcalculi not detectable by plain film and therefore stone-related diathesis.
3. It identifies alternative urinary conditions not always detectable by IVU, such as acute pyelonephritis or subcapsular renal haemorrhage.
4. It recognizes a wide variety of alternative or associated extraurinary conditions which may involve the intestinal tract (e.g. small bowel obstruction, Crohn's disease, diverticulitis, appendicitis, colitis, volvulus intussusception), liver and biliary tree, pancreas, vascular system and adnexa (ovarian mass, haemorrhagic cyst, hydrosalpynx, endometriosis). The incidence of these extraurinary conditions varies according to authors from 2.3 to 15.6%: this difference is due to different attitude of the referral in requesting the UHCT [25, 21, 26].
5. According to our economical analysis, the exam is slightly cheaper. In addition, it entails less discomfort for the patient in that it does not require bowel cleaning and contrast medium, with very few exceptions, and the examination time is much shorter.
6. The radiation dose with UHCT is only a little higher when correct parameters are used.

Nevertheless, IVU is indicated after UHCT in the following cases:

1. When the urologist requests a map of the urinary tract for percutaneous or endoureteral or surgical procedures
2. When a urothelial tumour is suspected, given the need to explore the entire urinary tract

3. When the colic arises in a diabetic patient in whom no stone was detected and papillary necrosis is suspected

Helical CT may be not available. In this case plain film (KUB) and US can be the initial protocol. In our experience, this approach can solve 70% of the cases [27]. Whatever the percentage of accuracy, in unsolved cases IVU is indicated:

1. When US evidences hydronephrosis in the absence of a stone at the KUB (possible ultrasound false positives)
2. When the stone is suspected at the KUB in the absence of evidence of stone or hydronephrosis at US (possible KUB false positives)
3. When the colic recurs with negative KUB and US
4. To precisely define the anatomy of the urinary tract before interventional surgical therapy

In conclusion, IVU should not be the method of first choice in investigating patients with renal colic. The present approach to the patient with renal colic considers helical CT or KUB and US followed by helical CT, or when not available IVU, in unsolved cases.

Renal trauma

It is well known that the effects of trauma on the kidney may be mild (contusion, parenchymal and/or subcapsular haematoma, calyceal laceration), severe (fracture of the parenchyma or urinary tract) or very severe (fracture with kidney shattering, rupture of the renal artery with haemorrhage).

Most urologists tend to intervene only in very severe traumas and to adopt a "watchful waiting" approach in other cases, which heal spontaneously most of the time.

In cases of very severe trauma with shock, helical CT is the examination of choice because it allows evaluation of the entire abdomen. In other cases, IVU with nephrotomography should be sufficient. However, since evaluation of the lesions is not as accurate as with helical CT, the latter is preferred in many centres [28, 29] especially when medico-legal issues are involved.

If US is positive at the time of the trauma, in cases of "watchful waiting" US can be used to monitor regression of the lesion, because it spares the patients the ionizing radiations delivered by IVU and CT.

Uroseptic fever

Pyelonephritis and its complications are diagnosed clinically and by means of laboratory investigations. Imaging modalities are indicated for establishing the extent of the damage (localised or diffuse pyelonephritis, abscess, extent of the extrarenal process) in:

1. Patients with predisposing factors (stones, urinary tract obstruction, neurogenic bladder, vesicoureteral reflux, surgical complications, diabetes, immunodeficiency)
2. Patients not responding to antibiotic therapy
3. Women with relapsing uroseptic infections, to identify the lesion and its extension and to document the efficacy of medical therapy

The low sensitivity [30] and specificity of IVU has made it loose its role of primary investigation to US and CT [31]. In children the first approach can be based on scintigraphy with Tc-99m DMSA which has a very high sensitivity, despite the fact that it is unable to characterise the anatomo-pathological features of the lesion or determine its extrarenal extension.

Ultrasound has a good sensitivity for renal lesions, but less for extrarenal extension, which makes it good as an initial investigation, an examination to follow up medical therapy and as a guide for possible drainage.

The excellent sensitivity and diagnostic accuracy of CT make its role central.

Intravenous urography maintains its indications in uroseptic fever in cases of stones, diabetes and urinary tract obstruction. It is noted that a urogram can be acquired after contrast-enhanced CT, so that IVU can be avoided.

Asymptomatic haematuria

Haematuria associated with other symptoms is approached in the same way as colic, renal trauma and uroseptic fever, all clinical situations in which the role of IVU has been reduced, as has been stated.

Haematuria without other symptoms may present as microhaematuria or gross haematuria. The extent of haematuria gives no indication as to the severity of the lesion, so that the patients, including those with microhaematuria, should be thoroughly investigated bearing in mind that approximately 20% of patients over 45 years with microhaematuria have significant lesions of the urinary system, as compared with only 2% of those under the age of 45 years [32, 33].

Microhaematuria must be investigated even with three red blood cells per high-power field, as there is no threshold under which urothelial cancer can be safely ruled out [34]. The investigations to be considered are urine microscopy, urine cytology, IVU, US and flexible cystoscopy.

In the literature different approaches have been described in patients over 45 years. Kadra et al. [34] found significant disease in 18.7% of 982 patients with micro-

scopic haematuria, which indicates that thorough evaluation is indicated for all.

After examining 1930 patients with micro- and macro-hematuria, the same Authors concluded that both US and IVU are necessary, followed by cystoscopy. This approach allowed detection of 100% of tumours affecting the urinary system. This view is shared by Murakami et al. [35].

Which of the two examinations should be given priority?

According to Webb [36], the fact that US has greater sensitivity than IVU in detecting bladder tumours should not be used as a reason to choose US as the first imaging method of choice. The device should be based on the best method to detect upper tract pathology. Webb [36] therefore concludes that IVU should be used first, based principally on the fact that it is the best "catch all" method for the upper tracts. If the urogram and cystoscopy are negative, the patient should then have renal US to check for renal masses not shown at urography.

Other authors do not share this view. They believe US and cystoscopy to be the best first approach [8, 37, 38, 39]. Yip et al. [39] routinely combine US with KUB with the aim of detecting the presence of stones. Intravenous urography is planned when necessary.

The present author agrees with this approach. Firstly, IVU becomes redundant when US and KUB disclose renal masses [8] or asymptomatic stones.

Bladder tumours, one of the most common causes of asymptomatic haematuria, can be accurately diagnosed by a combination of US and cystoscopy [37, 39], whereas the sensitivity of cystography during IVU cannot approach that of cystoscopy, which is now commonly conducted using the flexible technique on an outpatient basis [40]. In these cases IVU is subsequently and eventually performed to detect synchronous tumours of the upper urinary tract.

On the other hand, over 60% of haematurias, according to Kadra et al. [34], and over 50% according to our case series, are found to be negative at both examinations, which means that IVU is redundant: what may be missed in these patients is only an early mucosal cancer of the upper urinary tract, but this is a very rare occurrence that does not justify the use of IVU in all patients. Herranz-Amo et al. [41] reported an incidence of upper tract urothelial tumours of 1.1% on 793 patients with primary tumour of the bladder: they discovered 9 cases, although IVU only diagnosed 6 cases (0.7%). Herranz-Amo et al. [41] therefore conclude excluding IVU routinely performed in the diagnostic work-up of patients with primary transitional cell tumour of the bladder and supporting IVU only in patients who are candidates for radical cystectomy.

In addition, Booth and Kellett [42] using a combination of IVU, cystoscopy and cytology established a diagnosis in 58% of 203 patients with urothelial carcinoma located in the pelvicalyceal system or in the ureter.

Intravenous urography therefore may be considered complementary to US, KUB and cystoscopy.

As regards microhaematuria in patients under the age of 45 years, the present author only recommends IVU in patients with positive urine cytology for tumoral cells, as transitional cell carcinoma (TCC) is extremely rare at this age.

Medical haematuria

Medical haematuria is characterised by the presence of cylindruria, proteinuria and dysmorphic red blood cells in the urine. Whereas US is indicated in the haematuria accompanying diffuse nephropathies because it can document morphology, structure and resistive index for the follow-up, IVU should be considered in the haematuria – especially if relapsing – that accompanies dysmetabolic nephropathies (diabetes, gout) and in the haematuria accompanying tuberculosis, particularly in the presence of a lung process. In these cases the initial lesions are papillary and can therefore only be detected by IVU.

Obstructive uropathies

Until a few years ago acute and chronic obstructive uropathies were investigated by IVU which allowed determination of dilatation of the urinary tract, the level of obstruction and often the causes, if these were intrinsic.

Presently, however, US, CT and MRI are capable of detecting the presence of both acute and chronic obstructive uropathies; of these, US has become fundamental because it represents a cost-effective procedure to establish obstruction [43]. This examination may be sufficient in the acute forms if it documents the existence of a stone or a voluminous hypertrophic prostate.

In other cases, in both acute and chronic forms, the US examination should be followed by CT and MRI: MR urography has the advantage [44, 45, 46, 47, 48] of providing more precise images of both the dilatated urinary tract and the cause of the obstruction, particularly if its origin is extra-urinary. As the kidney is often non-visualized in obstructive uropathy or, when uropathy is bilateral, in a state of insufficiency, IVU has only limited indications presently, such as unavailability of high-tech imaging.

Follow-up of various disorders

One of the roles of IVU was to follow the progression or regression of a variety of disorders. This role has been

greatly reduced. Intravenous urography can be performed *after* cystectomy for TCC, although the usefulness of this procedure is controversial. Once the bladder tumour has been identified and treated, it remains to be decided whether to follow up the patient by IVU to detect relapses or new localizations.

As stated previously, the issue is controversial, some authors being in favour [49, 50] of the procedure and others against it [51, 52, 53, 54]. Holmang et al. [54] found the incidence of subsequent carcinomas of the renal pelvis and ureter in their cohort to be 2.4 %, which is equal to the average of nine reports comprising 2580 patients [49]. Given this low incidence, the approach is not cost-effective and IVU is not justified [51]. In addition, the results obtained by Holmang et al. [54] and validated by others indicate that tumours of the upper urinary tract after cystectomy are rarely diagnosed as a result of IVU screening, and that they are high-grade tumours (grade III) with short survival after diagnosis. Prognosis does not appear to be significantly improved for tumours identified as a result of IVU screening.

The most convincing view, in our opinion, is that expressed by Booth and Kellett [42], Skinner et al. [55] and Zingg and Wallace [56] who recommend post-cystectomy IVU follow-up of patients at risk, which is those with recurrent bladder TCC, high-grade, high-stage bladder TCC, known analgesic abusers, those employed in dye manufacturing or other chemical industries, those with bladder tumours and vesicoureteral reflux, or those exposed to other known urothelial carcinogens such as cyclophosphamide.

Another possible reason for follow-up after cystectomy is the finding of ureteral stenosis at the opening into the neo-bladder. Annual follow-ups by IVU are debatable: in Stein et al.'s [57] series IVU failed to detect any of the cases diagnosed incidentally, as the cases with stenosis of the afferent antireflux valve in the Kock pouch continent urinary diversion were all symptomatic. Nevertheless, US can replace IVU in detection of hydronephrosis; the same applies to the detection of stenosis which may occur after transurethral resection over or close to an orifice [58].

One surviving indication for IVU follow-up is renal tuberculosis undergoing medical treatment, although its use has become less common. Ultrasound allows evaluation of the regression of both parenchymal cavities and hydronephrosis related to ureteral stenosis. Similarly, regression of hydroureteronephrosis related to a medically treated stone can also be followed by US.

Ultrasound has come to replace IVU in the follow-up of a polycystic kidney, as it allows evaluation of the progression of the cysts and any complications, such as haemorrhage and infection. Likewise, simple cysts can also be monitored by US.

Weak points of IVU

To conclude this section on the clinical situations in which the role of IVU has been superseded or reduced, the following weak points of IVU are summarized:

1. Use of ionizing radiations and contrast media
2. High cost of investigation compared with US
3. Accuracy depends on renal function
4. Poor functional information limited to visualized or poorly visualized or non-visualized kidney
5. Inability to recognise numerous renal lesions, such as, for example, some small renal tumours, minor traumatic lesions, non-extensive pyelonephritis.
6. Rare characterization of renal masses

IVU: mandatory role

Strong points of IVU

Intravenous urography has numerous strong points such as:

1. Immediate visualization of the entire urinary system, parenchyma and urinary tract, with the possibility of identifying their inter-relations, such as those between calyx and renal papilla
2. Detailed evaluation of calyces and ureter which allows diagnosis of even the smallest lesions at the initial stage, as previously described

Then IVU is indicated and often mandatory in certain conditions, which are:

Congenital anomalies of the urinary tract

Intravenous urography is the only investigation that gives a panoramic view of the various anomalies of the urinary system, such as, for example, pyelo-ureteral duplication, various forms of ectopia and abnormal ureteral opening. The recognition of such abnormalities is important both for identifying complex body malformations and understanding certain local disorders such as pyelo-ureteral duplication.

Prior to endourological procedures

According to Pollack and Banner [2], before engaging in urological intervention in the renal collecting system or ureter, it is necessary to have a precise knowledge of the anatomy of these structures. This has been documented by Gupta et al. [59] who stressed the need to establish a relationship between lower calyx, pelvis and

ureter before deciding the best approach to stone disease.

Possible fistulas

The fistulas may be either iatrogenic or occurring after targeted intervention on the urinary system. Drip-infusion IVU is able to demonstrate the presence of fistulas between the urinary system – especially the ureter – and adjacent anatomic structures, such as intestine, vagina and pelvis.

Renal transplantation

Intravenous urography is a useful technique for screening potential renal donors for unsuspected renal or ureteral disease that makes them ineligible for kidney donation. It is also useful after transplantation when extravasion is suspected.

Tuberculosis

Since tuberculosis may affect the entire urinary system, IVU is useful for determining the precise location of the disease and guiding the most appropriate therapy; however, it is always advisable to integrate IVU with cross-sectional modalities.

Ureteral pathology

Intravenous urography is the only investigation capable of documenting with excellent spatial resolution even the most subtle alterations of the ureter and its mucosa. The various forms of ureteritis – mostly observed in chronic urinary tract infections – diverticulitis, intrinsic and extrinsic stenosing processes, traumatic injuries and neoplasms can all be accurately detected by IVU, better than with any other method. Computed tomography, on the other hand, should be considered complementary because it documents wall thickness, if increased, and the urinary tract in the non-functioning kidney and after kidney transplantation [60].

In summary, the indications left for IVU are very few because most of the conditions which affect the urinary system can be accurately diagnosed using cross-sectional imaging techniques.

Briefly, it is stated that IVU is still the examination of choice where there is a need to visualize the entire urinary system and to evaluate the state of the papillae and calyces, especially as regards tuberculosis. Documenting papillary necrosis of other origin does not seem to affect therapy.

Recent studies have advocated the use of CT urography and MR urography.

The use of CT urography still causes concern [61, 62]: opacification of the calyces is not optimal given its scarce spatial resolution; visualization of the entire urinary system, in particular the urinary tract, requires a greater radiation dose compared with IVU; and the processing time is still long. This technique, however, has the advantage of allowing accurate evaluation of the whole renal parenchyma. Computed tomography urography should, therefore, be further investigated particularly in light of the new multi-slice CT technology.

Magnetic resonance urography seems more interesting especially in view of the satisfactory results obtained in determining degree, level and cause of obstructive uropathies. In other cases the technique is still under validation, although the use of new sequences and the administration of diuretics and gadolinium seem to be promising also in the non-dilated urinary tract [63, 64]. The technique has the advantage of sparing the patient exposure to ionizing radiation while allowing visualization of the urinary system on the various spatial planes. The preliminary results justify, for the time being, its use in pregnancy, in children and in patients who are hypersensitive to contrast media.

In conclusion, although not actually dead, IVU can be said to have started to agonise but, to paraphrase the writer Mark Twain, the news of its demise are somewhat premature.

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