

*Original Article*

## **Assessment of radioisotopic micturating cystography for the diagnosis of vesicoureteric reflux in renal transplant recipients with acute pyelonephritis**

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### **Abstract**

**Background.** The gold standard for documenting vesicoureteric reflux is direct (retrograde) micturating cystography (MC). In children, radioisotopic MC has been advocated for increased sensitivity and lesser radiation exposure. In renal transplant recipients, where reflux can induce acute pyelonephritis, this technique has not been evaluated. The aim of this study was to assess the radioisotopic technique in these patients.

**Methods.** Seventeen renal transplant recipients had developed acute pyelonephritis following the surgical grafting procedure. They were investigated using both MC techniques. Radioisotopic MC was performed using <sup>99m</sup>Tc-pertechnetate.

**Results.** Reflux was documented in nine patients by radioisotopic MC but in only seven with the conventional technique. All negative patients remained symptom free after the pyelonephritis was cured and it was assumed that they had no reflux. Consequently, using the radioisotopic MC as gold standard, the conventional X-ray technique had a sensitivity of 78% and a specificity of 100%.

**Conclusions.** Direct radioisotopic MC allowing continuous cystogram recording is more accurate than conventional X-ray MC for the diagnosis of vesicoureteric reflux in transplanted patients with acute pyelonephritis.

**Key words:** renal transplantation; vesicoureteric reflux; cystography; radioisotopic cystography; pyelonephritis

### **Introduction**

Although technically a straightforward procedure, the vesicoureteral anastomosis is the greatest potential cause of complication of the transplant operation [1–3]. Urological complications occur in about 5–15% of renal allografts during the perioperative period [4]. Urinary infection associated with pyelonephritis may result from an anatomical dysfunction such as ureteric stenosis or vesicoureteric reflux [5–7] and indicates the need for prompt urological investigation [5–7].

Vesicoureteric reflux can be detected by direct and indirect techniques [8]. Indirect micturating cystography (MC) is obtained at the end of intravenous urography or radioisotopic renal scintigraphy. Instead of emptying the bladder, the patient is encouraged to drink fluids until the bladder is full, and then micturates while pictures are taken sequentially. The limitation of these indirect techniques is their inability to detect lesser degrees of reflux reliably.

Direct MC remains the 'gold standard' for the diagnosis of vesicoureteric reflux. This investigation is usually necessary to establish the diagnosis and to provide the anatomical information necessary for the management of the renal transplant recipient. One of the drawbacks of the technique is the requirement for retrograde catheterization of the bladder, which increases the risk of infection, and in addition carries a relatively high radiation dose. Micturating cystography is performed using intravesical administration of a radiolabelled compound and has been successfully used in children. This technique delivers a much lower radiation dose [9–12] and can be made more quantitative by using continuous imaging with the gamma camera. Direct radioisotopic MC has not previously been evaluated in adult renal transplant recipients with acute pyelonephritis occurring outside of the perioperative period.

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## Subjects and methods

### Patients

We reviewed the charts of the last 230 patients who received a renal cadaveric transplant in our institution. Twenty-one patients developed pyelonephritis 2 months or longer after the procedure and 17 were included in the study, because they were investigated by both X-ray and radioisotopic MC. Five were male and 12 female. Infection was diagnosed at  $21.3 \pm 19.0$  months (2–70) post-transplantation.

Prior to grafting, all had careful urological investigations, which included cystoscopy. None of the patients was anephric: the ureterovesical anastomosis was made according to the extravesical technique of Lich-Gregoir [13]. The ureter of the transplant was anastomosed to the bladder through a new vesical hiatus with a submucosal tunnel designed to prevent ureter angulation.

### Direct radioisotopic micturating cystography

The procedure derived from the standard MC technique, was performed after a flash dose of cefotaxime had been administered intravenously 1 h prior to the test. A catheter was carefully inserted into the bladder. The patient was kept supine under a gamma camera (Gammatome 2, Sopha Medical, France) equipped with a parallel colimator positioned over the lower part of the abdomen. A dose of 17–20 MBq of  $^{99m}\text{Tc}$ -pertechnetate diluted in normal saline was administered into the bladder through the catheter. It was estimated that a total of 25 mrad was given to the bladder, 1 mrad to the ovaries or 0.5 mrad to the testis during the test, which lasted less than 30 min. The bladder was inflated with normal saline at 37°C, at a rate of 50 ml/min. The infusion was stopped when the patient complained of fullness. At completion, a mean volume of 610 ml of saline had been administered. Then a clamp was put on the catheter for a few minutes before voiding. The gamma camera recording gave one image per 15 s for 30 min. Image analysis was made using a computerized program which improved image contrast and generated a time-activity curve on the ureteral, renal or vesical region of interest. Reflux was passive (low-pressure reflux) or active (high-pressure reflux) according to its occurrence during bladder filling or voiding respectively. It was reported according to the international grading system [14].

In all instances the urinary infection was successfully treated prior to cystography. When indicated, the results were used to guide reconstructive surgery or endoscopic submucosal Teflon injection (results not included in the study).

### Analysis of data

Based on the diagnosis of vesicoureteric reflux both MC techniques were compared. Classical formulae [15] were used to calculate specificity, sensitivity, and positive and negative predictive values as follows.

$$\text{Sensitivity (\%)} = \frac{\text{true positive results}}{\text{total patients with disease}} \times 100$$

$$\text{Specificity (\%)} = \frac{\text{true negative results}}{\text{total patients without disease}} \times 100$$

$$\begin{aligned} \text{Positive predictive value (\%)} \\ &= \frac{\text{true positive results}}{\text{true positive} + \text{false positive results}} \times 100 \end{aligned}$$

$$\begin{aligned} \text{Negative predictive value (\%)} \\ &= \frac{\text{true negative results}}{\text{true negative} + \text{false negative results}} \times 100 \end{aligned}$$

## Results

Both MC techniques were well tolerated. The day after every investigation, urine sterility was documented.

Figure 1 shows a representative case of a patient with vesicoureteric reflux of the transplanted kidney demonstrated by the direct micturating cystogram using  $^{99m}\text{Tc}$  pertechnetate. The activity-time curve shows intermittent peaks, which correspond to reflux into the graft during bladder filling and emptying.

The diagnosis of vesicoureteric reflux was established in seven patients by the standard X-ray MC technique and in nine patients by the radioisotopic MC technique. In eight patients the procedure was negative with both techniques. The reflux was documented in the transplanted kidney in eight patients and in a remaining kidney in one. Massive intrarenal reflux was observed in only one patient (grade IV), and was mild to moderate in the others (grades I–III).

The radioisotopic technique was more accurate than the X-ray one, since two cases were not detected by the latter. All negative cases remained symptom-free after the cure of pyelonephritis. Consequently we assumed that they had no reflux. Considering the radioisotopic MC technique as the gold standard, the conventional X-ray MC technique has a sensitivity of 78% and specificity of 100%. Its positive predictive value is 100% and its negative predictive value 80%.

## Discussion

In this series of acute pyelonephritis of late onset after renal transplantation, the search for vesicoureteric reflux was made with direct X-ray and radioisotopic MC. The conventional technique was less accurate than the radioisotopic technique, since only 78% of affected patients were found positive. The two patients in whom vesicoureteric reflux was not proven by the conventional MC technique had a low-grade reflux. This suggests that the single X-ray picture taken during voiding did not catch the reflux at the moment of its occurrence.

Radioisotopic MC using fast kinetic imaging (one image every 15 s) and derived activity-time curves is particularly well designed for the diagnosis of transient vesicoureteric reflux. In addition the technique allows the distinction between passive reflux occurring during bladder filling and active reflux observed during voiding. This distinction, the clinical significance of which may be questioned in the absence of intravesical pres-

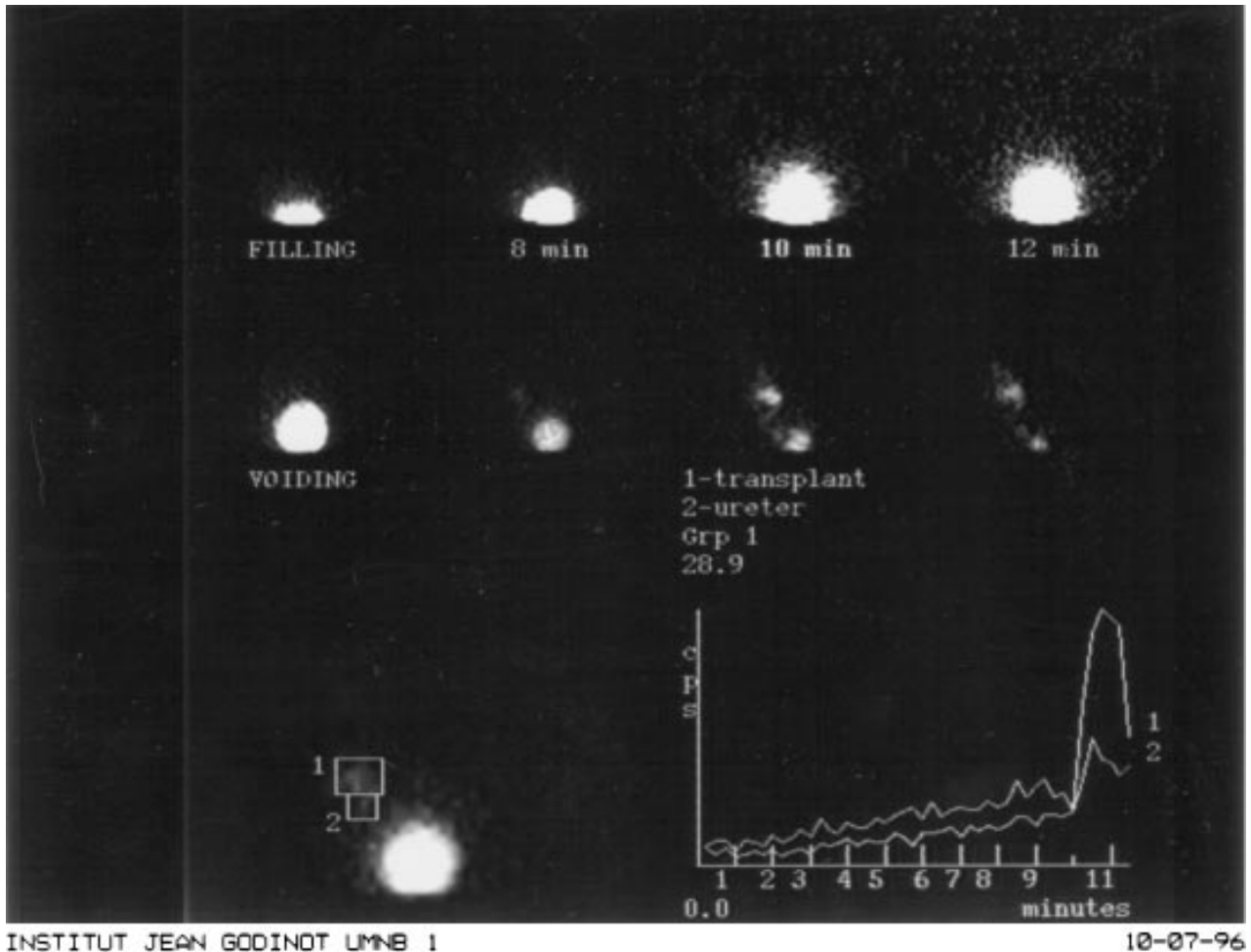


Fig. 1. Radioisotopic micturating cystography (patient no. 3). Dynamic imaging showing active vesicoureteral reflux during voiding. Activity-time curves are derived from area of interest (1, renal transplant; 2, ureter).

sure recording, is still possible with the conventional MC technique but requires more pictures and increases the radiation exposure, thereby counterbalancing the advantages of digital luminescence radiography [15], which is universally recommended.

Radiation exposure was not calculated in the present study but reference studies have been published elsewhere [9–12] particularly in children. These have documented that radioisotopic MC delivers less than 30 mrad to the bladder and 4–5 mrad to the testis, whereas conventional MC (without the digital luminescence technique) delivered 30–100 times more radiation to the bladder and gonads. Avoiding radiation exposure, new developments in Doppler ultrasonography have made possible the detection of vesicoureteric reflux in children [16]. The preliminary results, which appear highly operator-dependent, have to be evaluated in adults.

The radioisotopic MC technique documented vesicoureteric reflux in 53% of transplant recipients with acute pyelonephritis outside of the perioperative period. Such a high prevalence of reflux raises questions about the Lich-Gregoir technique of ureterovesical

anastomosis, which has been considered the most efficient [17]. It suggests the possibility of retractile sclerotic changes occurring at the level of the anastomosis, which could be induced by ischaemia and/or incipient chronic rejection. Spontaneous resolution of low-grade reflux is possible [18] but has not been documented in the setting of transplantation.

In conclusion, radioisotopic MC in renal transplant recipients with late pyelonephritis is more reliable than conventional MC to document vesicoureteral reflux. This advantage is associated with fast and continuous kinetic recording of urine radioactivity. The technique does not avoid the risk of infection since it requires bladder catheterization, but it requires less radiation exposure to the pelvis and particularly to the gonads.

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