Diuretic Renography with the Addition of Quantitative Gravity-Assisted Drainage in Infants and Children

David C. Wong, Monica A. Rossleigh, and Robert H. Farnsworth

Department of Nuclear Medicine, The Prince of Wales and Sydney Children's Hospitals, Sydney, Australia

The aim of this study was to evaluate the use of quantitative gravity-assisted drainage (GAD) using >50% residual activity as an indicator to confirm obstruction in diuretic renography in the investigation of hydronephrosis and hydroureteronephrosis in infants and children. This was evaluated in 2 groups: furosemide clearance half-time ($t_{1/2}$) > 20 min (obstructed range) and $t_{1/2}$ = 10–20 min (indeterminate range). **Methods:** Two hundred children (155 boys, 45 girls; age range, 2 d to 16 y; median age, 26 wk) were studied over a 2-y period. One hundred thirty-five F+20 (diuretic given 20 min after radiopharmaceutical) and 65 F+0 (simultaneous administration of diuretic and radiopharmaceutical) studies were performed with intravenous administration of ^{99m}Tc-mercaptoacetyltriglycine (MAG3) and furosemide. At the end of the 20-min diuretic phase, a 5-min post-GAD image was obtained, and the percentage of residual activity was calculated by comparison with the last 5 min of the diuretic phase. All patients were monitored for 6–12 mo, and the final diagnoses were based on either surgical findings or conservative management with follow-up sonography or ^{99m}Tc-MAG3 studies. Results of the diuretic renography using quantitative GAD were then compared with the final diagnoses. **Results:** A renal unit was defined as a kidney and its ureter. In the 200 patients studied, 256 hydronephrotic renal units were analyzed: 10 units showed no function, 1 unit showed poor function, 131 units had $t_{1/2}$ < 10 min, 62 units had $t_{1/2}$ > 20 min, and 52 units had $t_{1/2}$ = 10–20 min. Of the 131 renal units with $t_{1/2}$ < 10 min, there was only 1 case of obstruction. Using GAD > 50% residual activity for the diagnosis of obstruction in 62 renal units with $t_{1/2}$ > 20 min, the sensitivity was 88.4%, the specificity was 73.7%, and the accuracy was 83.9%. Similarly, using GAD > 50% residual activity for the diagnosis of obstruction in 52 units with $t_{1/2}$ = 10–20 min, the sensitivity was 100%, the specificity was 79.5%, and the accuracy was 82.7%. **Conclusion:** The quantitation of GAD > 50% residual activity in diuretic renography can help to differentiate between obstruction and nonobstruction in renal units with $t_{1/2}$ > 20 min and $t_{1/2}$ = 10–20 min. The quantitation of GAD when $t_{1/2}$ < 10 min is not useful because obstruction has already been excluded.

Key Words: diuretic renography; pediatrics; hydronephrosis

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For correspondence or reprints contact: Monica A. Rossleigh, MD, Department of Nuclear Medicine, The Prince of Wales Hospital, High St., Randwick, New South Wales 2031, Australia.

There has been a marked increase in the early detection of hydronephrosis (distention of the pelvicaliceal system) and hydroureteronephrosis (distention of the pelvicaliceal system and ureter) in infants with the widespread use of antenatal sonography. This has resulted in the investigation of many infants with diuretic renography (*1,2*). Obstruction in the urinary tract can be located anywhere from the renal pelvis to the urethra, with the most common site being at the ureteropelvic junction (UPJ). Obstruction can also occur more distally at the ureterovesical junction (UVJ) (*3,4*). The purpose of diuretic renography is to differentiate a true obstruction from a dilated nonobstructed system (stasis) by imaging after the intravenous administration of furosemide (*3,5*). Diuretic renography in the investigation of hydronephrosis has been shown to be reliable in the investigation of UPJ and UVJ obstruction (*6,7*). The furosemide clearance half-time ($t_{1/2}$) in diuretic renography has been used to define whether obstruction is present. A $t_{1/2}$ < 10 min usually means the absence of obstruction, whereas a $t_{1/2}$ > 20 min usually identifies obstruction. A $t_{1/2}$ = 10–20 min is an equivocal result (*3,5,8*). The need for an additional view after gravity-assisted drainage (GAD) using visual assessment to determine whether there is further drainage, particularly after pyeloplasty, has been emphasized (*9*). In this study we evaluated the use of quantitative GAD using >50% residual activity as an indicator to confirm obstruction in diuretic renography in 2 groups: $t_{1/2}$ > 20 min (obstructed range) and $t_{1/2}$ = 10–20 min (indeterminate range). Comparisons were also made with GAD > 60% and GAD > 40% residual activities to confirm renal obstruction.

MATERIALS AND METHODS

Two hundred children (155 boys, 45 girls; age range, 2 d to 16 y; median age, 26 wk) with a diagnosis of hydronephrosis or hydroureteronephrosis based on sonographic examinations were enrolled in this study over a 2-y period. The serum creatinine levels ranged from 0.02 to 0.17 mmol/L, with a mean of 0.04 mmol/L (normal ≤ 0.05 mmol/L). Sixteen patients had creatinine levels > 0.05 mmol/L. A renal unit was defined as a kidney and its ureter. In the 200 patients studied, there were 256 dilated renal units, of which 219 were hydronephrotic and 37 were hydroureteronephrotic. Fifty-one postsurgical patients had 49 renal units with

previous pyeloplasties and 9 renal units with postreduction ureteroplasties and reimplantations; 2 patients had previous renal transplants. Five patients also had solitary kidneys. Patients with duplex kidneys were not included in this study because of difficulties in drawing the regions of interest around the upper and lower pole moieties. Patients with neuromuscular disorders, such as prune-belly syndrome and neurogenic bladder, were also not included.

All patients had prior evaluation for vesicoureteric reflux with micturating cystourethrograms. A urinary catheter was inserted before beginning the study only if the patient was suspected of having UVJ obstruction or grade II or higher vesicoureteric reflux on micturating cystourethrograms. Antibiotic coverage (amoxicillin or gentamycin) was provided if catheterization was required because of the known risk of introducing infection.

One hundred thirty-five F+20 (diuretic given 20 min after the radiopharmaceutical) and 65 F+0 (diuretic given simultaneously with the radiopharmaceutical) studies were performed. The F+0 diuretic renography study was recently validated (*10*). All children who had difficulty with venous access or with remaining still for the standard F+20 study were enrolled in the F+0 study. Children were hydrated orally before beginning the study. Babies were usually breast-fed and older children were given 400–600 mL of water to drink, depending on age. Children requiring sedation received replacement intravenous fluids for hydration.

A weight-adjusted dose of ^{99m}Tc-mercaptoacetyltriglycine (MAG3) (using Gilday's graph (*11*)) (maximum dose, 200 MBq; minimum dose, 20 MBq) and 1 mg/kg furosemide (maximum dose, 40 mg) were given. All studies were performed on either a model 400 AC or a model 300 γ camera attached to a Starcam computer (General Electric Medical Systems, Milwaukee, WI). Initial dynamic images were acquired at 40 1-s frames followed by 62 20-s frames. These images formed the diuretic phase of the F+0 study. For the F+20 study, after administration of furosemide at 20 min, further acquisition of 120 10-s frames was obtained. At the end of the diuretic phase, babies and sedated children were held upright for about 5 min to achieve GAD; this was followed by acquisition of a 5-min static image. If the post-GAD image showed poor drainage in the presence of a full bladder, a further image was obtained after voiding; this image with an empty bladder was then used for the GAD quantitation. Patients who were able to get up and void were requested to do so, and static images were then obtained after voiding.

Differential renal function was calculated using the total counts of the renogram curve for each kidney minus background during the interval between 1.5 and 2.5 min after injection of the radiopharmaceutical. The renogram included the entire kidney and the renal pelvis. The $t_{1/2}$ values were generated from the exponential fit of the maximal slope of the washout component of the renogram curves between 2 points, starting at the peak of the renogram curve. The percentage of residual radioactivity was calculated by comparison of the counts in the post-GAD 5-min image with the counts in the last 5 min of the diuretic phase.

For the purpose of this study, the following criteria were used to confirm renal obstruction. Significant UPJ or UVJ obstruction was diagnosed if $t_{1/2} > 20$ min and GAD > 50% residual activity. Significant UPJ or UVJ obstruction was also diagnosed if $t_{1/2}$ = 10–20 min and GAD > 50% residual activity. A significantly obstructed renal unit was also diagnosed if poor or no function in the presence of hydronephrosis or hydroureteronephrosis was evident on sonographic examination. No significant renal obstruction (referred to as nonobstructed) was diagnosed if $t_{1/2} < 10$ min or if $t_{1/2} \geq 10$ min and GAD < 50% residual activity.

All patients were monitored for 6–12 mo, and the results of the diuretic renography based on the above criteria were compared with the final diagnoses. All patients had 3-mo to 1-y clinical follow-up with sonographic examinations performed at 3- to 6-mo intervals depending on the clinical assessment. Repeated diuretic renography was performed if increasing dilatation was found on the sonographic study. The final diagnoses were based on either surgical findings of obstruction or conservative management with repeated sonography and ^{99m}Tc-MAG3 examinations indicating nonobstruction. The decision to have surgical intervention or conservative management was determined by the pediatric urologist, who considered the results of the diuretic renography, including the relative function of the kidney, the child's clinical findings, and serial sonographic examination appearances, before making the management decision.

RESULTS

Of the 256 hydronephrotic renal units analyzed, 10 units had no function, 1 unit (16%) had poor function, 131 units had $t_{1/2} < 10$ min, 62 units had $t_{1/2} > 20$ min, and 52 units had $t_{1/2}$ = 10–20 min. Analysis of GAD was not possible and also was not required in the 11 renal units that showed no or poor function in the diuretic renography studies. Nephrectomies were performed in the 10 renal units with no function, with histologic examination showing hydronephrotic dysplastic kidneys associated with tight UPJ obstruction in 5 units; xanthogranulomatous pyelonephritis associated with staghorn calculus, abscesses, and UPJ obstruction in 1 unit; and hypoplastic renal dysplasia in 4 units. A pyeloplasty was performed in the 1 renal unit with poor function because there was a tight UPJ obstruction.

Figure 1 shows graphs of $t_{1/2}$ versus GAD residual activity for the 245 functioning hydronephrotic renal units. The GAD residual activity for the renal units with $t_{1/2} < 10$ min ranged from 5% to 112% with a wide scatter of values (Fig. 1A). The reason for this scatter is that further drainage may or may not be evident in nonobstructed kidneys because significant clearance occurs in response to the diuretic. Only 1 (0.76%) case of obstruction was evident in the 131 hydronephrotic renal units with $t_{1/2} < 10$ min. This was in a patient with left hydronephrosis on sonographic examination and, on the diuretic renogram, $t_{1/2}$ = 9.4 min with a post-GAD of 29% residual activity. The patient was asymptomatic at the time of the diuretic renography and experienced no flank pain with administration of furosemide but continued to complain of intermittent left loin pain; surgery revealed anomalous lower renal pole vessels, causing intermittent ureteric obstruction. This patient has been free of pain since the operation.

Sixty-two hydronephrotic renal units had $t_{1/2} > 20$ min. Using GAD > 50% residual activity as an indicator for obstruction, there were 38 true-positive studies, 5 false-positive studies, 14 true-negative studies, and 5 false-negative studies. The 5 false-positive studies were classified as 3 UPJ obstructions and 2 UVJ obstructions, and the 5

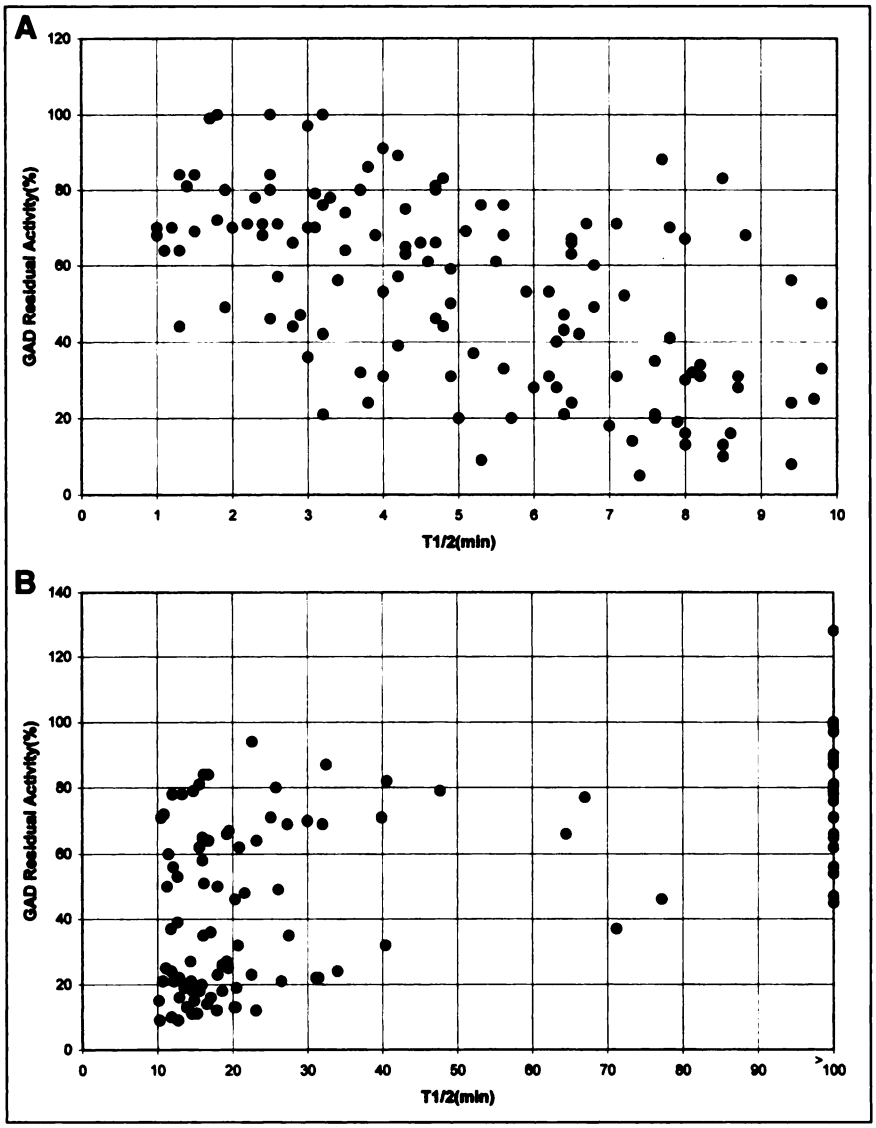

FIGURE 1. (A) Range of GAD residual activities for studies with $t_{1/2}$ < 10 min. (B) Range of GAD residual activities for studies with $t_{1/2}$ = 10–20 min and $t_{1/2}$ > 20 min.

false-negative studies were all associated with UPJ obstruction. Of the 3 false-positive studies for UPJ obstruction, 2 were F+0 studies and 1 was an F+20 study. Of the 2 false-positive studies for UVJ obstruction, 1 was an F+0 study and 1 was an F+20 study. Of the 5 false-negative studies, 1 was an F+0 study and 4 were F+20 studies. The sensitivity was 88.4%, specificity was 73.7%, and accuracy was 83.9%. Figure 2 shows a patient with left hydronephrosis on sonography, and the diuretic renogram shows $t_{1/2}$ = 67.8 min for the left kidney with a GAD residual activity of 74%, thus indicating obstruction; UPJ obstruction was confirmed at surgery. Figure 3 shows a patient with bilateral hydronephrosis on sonography, and the diuretic study shows a $t_{1/2}$ of infinity for both kidneys with a GAD residual activity of 128% for the left kidney and 47% for the right kidney. The left kidney underwent surgery, and pyeloplasty was performed for a tight UPJ obstruction. The right kidney was treated conservatively and was found to be nonobstructed on follow-up.

Similarly, for the 52 hydronephrotic units with $t_{1/2}$ = 10–20 min, using GAD >50% residual activity for obstruction, there were 8 true-positive studies, 9 false-positive studies, 35 true-negative studies, and no false-negative study. The 9 false-positive studies were classified as 5 UPJ and 4 UVJ obstructions. Of the 5 false-positive studies for UPJ obstruction, 2 were F+0 studies and 3 were F+20 studies. Of the 4 false-positive studies for UVJ obstruction, 1 was an F+0 study and 3 were F+20 studies. The sensitivity was 100%, specificity was 79.5%, and accuracy was 82.7%. Figure 4 shows the results in a patient with previous bilateral pyeloplasties in which the $t_{1/2}$ for the left kidney was 20.2 min and the $t_{1/2}$ for the right kidney was 11.9 min, with GAD residual activities of 13% and 10%, respectively, thus demonstrating no significant obstruction in either kidney after surgery.

The above data were also analyzed using GAD > 60% and > 40% residual activities as indicators to confirm renal obstruction. Table 1 shows the comparison of using GAD > 50%, GAD > 60%, and GAD > 40% residual activities in renal units with $t_{1/2}$ > 20 min. The accuracy is highest using

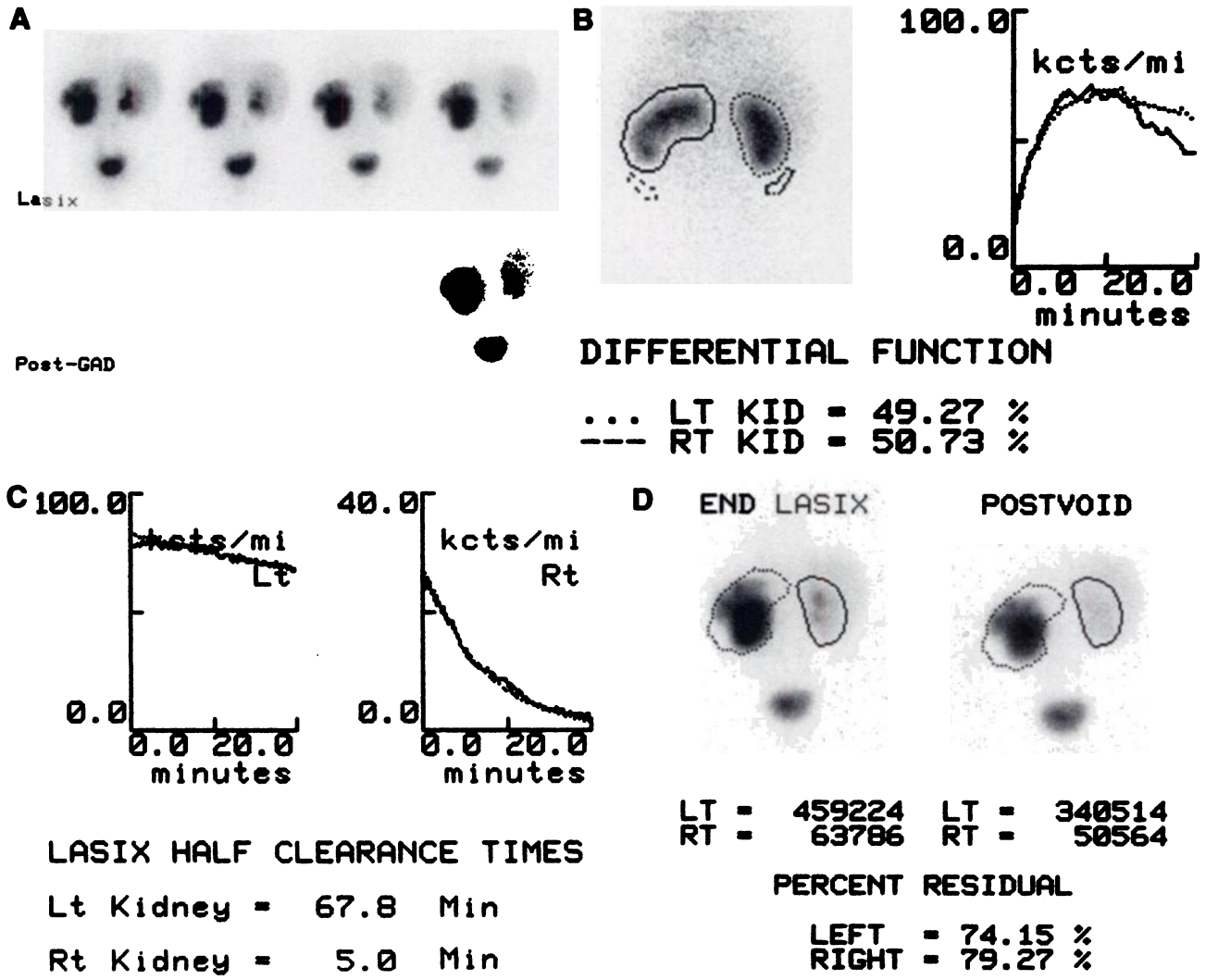

FIGURE 2. A 10-mo-old boy who presented with urinary tract infection. (A) F+20 diuretic renogram to evaluate left hydronephrosis. Furosemide (Lasix; Hoechst Marion Roussel Australia Pty. Ltd., Lane Cove, New South Wales, Australia) was given 20 min after radiopharmaceutical. (B) Differential renal function calculation confirms good relative function in obstructed left kidney. (C) $t_{1/2}$ for left kidney is prolonged at 67.8 min, supporting diagnosis of obstruction. (D) GAD residual activity for left kidney is high (74%), further supporting diagnosis of obstruction. Left UPJ obstruction was confirmed surgically.

50%. Applying the Student *t* test with 3 degrees of freedom, the difference is significant when compared with 60% ($P = 0.001$) and 40% ($P = 0.09$). Using 40% as the cutoff results in a marked reduction of the specificity to 47%.

Table 2 shows the comparison of using GAD > 50%, GAD > 60%, and GAD > 40% residual activities in renal units with $t_{1/2}$ = 10–20 min. The accuracy is highest using 50% as the cutoff. Applying the Student *t* test with 3 degrees of freedom, the difference is significant when compared with 60% ($P = 0.001$) and 40% ($P = 0.02$). The sensitivity drops when 60% is used as the cutoff and the specificity drops when 40% is used.

DISCUSSION

Assessment of diuretic renography in infants and children is problematic. No gold standard is applicable when diuretic renography is evaluated in the diagnosis of functionally significant obstruction. In this study, follow-up data of up to 12 mo were used to ascertain whether the patients required surgery for obstruction, with the subsequent operative findings or required conservative management with clinical assessment, serial sonographic examinations, and follow-up diuretic renography to confirm nonobstruction as a means of validating the usefulness of this technique. The pediatric urologist takes into account not only the findings on diuretic renography, including the relative function of the kidney, but also the child's clinical presentation and sonographic examination findings before embarking on surgical intervention.

The operative findings may vary in the neonatal group. Some children may have classic fibromuscular hyperplasia at the UPJ, whereas others may have proximal ureters with a corkscrew appearance that may result in obstruction at the UPJ associated with kinking of the ureter at the site of tortuosity (*10*). Obstruction may resolve spontaneously or

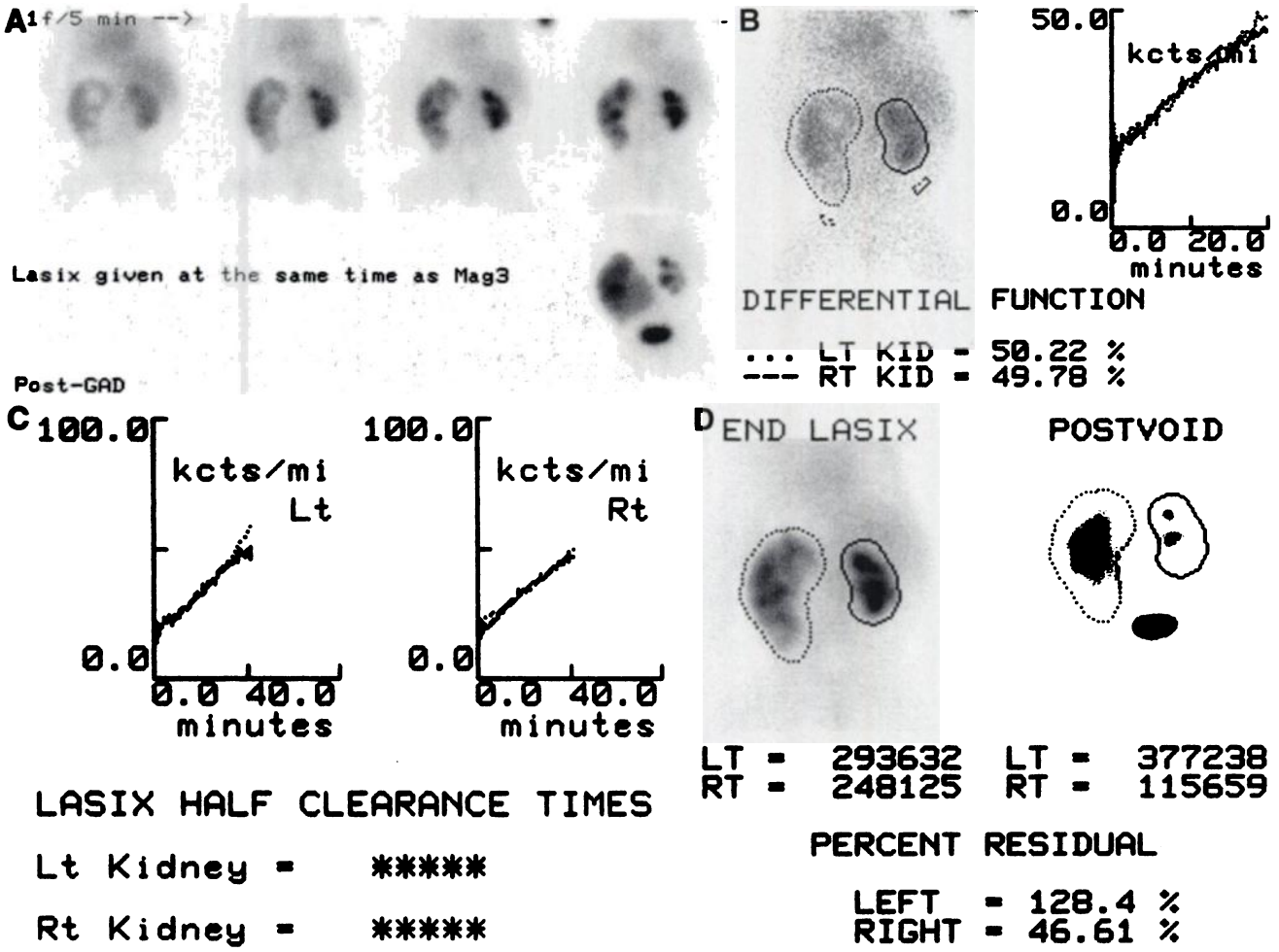

FIGURE 3. An 8-d-old boy with bilateral hydronephrosis, more marked on left, detected antenatally on routine sonographic examination. (A) F+0 diuretic renogram to evaluate bilateral hydronephrosis. Furosemide (Lasix; Hoechst Marion Roussel Australia Pty. Ltd., Lane Cove, New South Wales, Australia) was given at same time as radiopharmaceutical. (B) Differential renal function calculation reveals symmetric function. (C) $t_{1/2}$ for each kidney is infinity because no response to diuretic was evident. (D) GAD residual activity for left kidney is 128% and for right kidney is 47%. UPJ obstruction was confirmed surgically in left kidney; nonobstruction was confirmed in right kidney on follow-up sonography and follow-up diuretic renography.

develop with time, particularly in infants and children. The postulated reason for this is the phenomenon of transitional hydronephrosis (*12–15*). Diuretic renography is used to help classify which children need to proceed to surgery for relief of obstruction.

The "well-tempered" diuretic renogram was advocated as the standard method to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis (*16*). This was published in 1992 and, to our knowledge, since that time no studies have confirmed the necessity of using this methodology. We disagree with several aspects of the well-tempered diuretic renogram. These children do not have bladder outlet obstruction and will void spontaneously, particularly as a diuretic has been administered. Therefore, we believe that the routine use of a bladder catheter is not indicated. This is an invasive procedure that should be performed only when necessary, as outlined earlier. Furthermore, nuclear medicine techniques reflect physiology. We believe that the children should be in a normally hydrated state and not be fluid overloaded with intravenous volume expansion, as required by the well-tempered renogram. The success of our technique in infants and children has been reported (*7,10*). Criticism of the requirements of the well-tempered renogram has also been made by others (*17*). Comments regarding the procedure guideline for diuretic renography in children have been encouraged (*3,18*).

Armstrong and Oates (*19*) reported that using quantitation of additional clearance <50% after GAD during diuretic renography can confirm an obstructed system or reclassify an equivocal response as obstructed or nonobstructed in a study involving 77 hydronephrotic renal units in 41 patients. Our findings support their data. Other data supporting this technique were provided by Piepsz et al. (*17*), who described a study involving 93 hydronephrotic kidneys in 84 patients in which renal drainage was assessed using residual renal activity after micturition, expressed in percentage of activity at the moment of injection of furosemide. Responses were

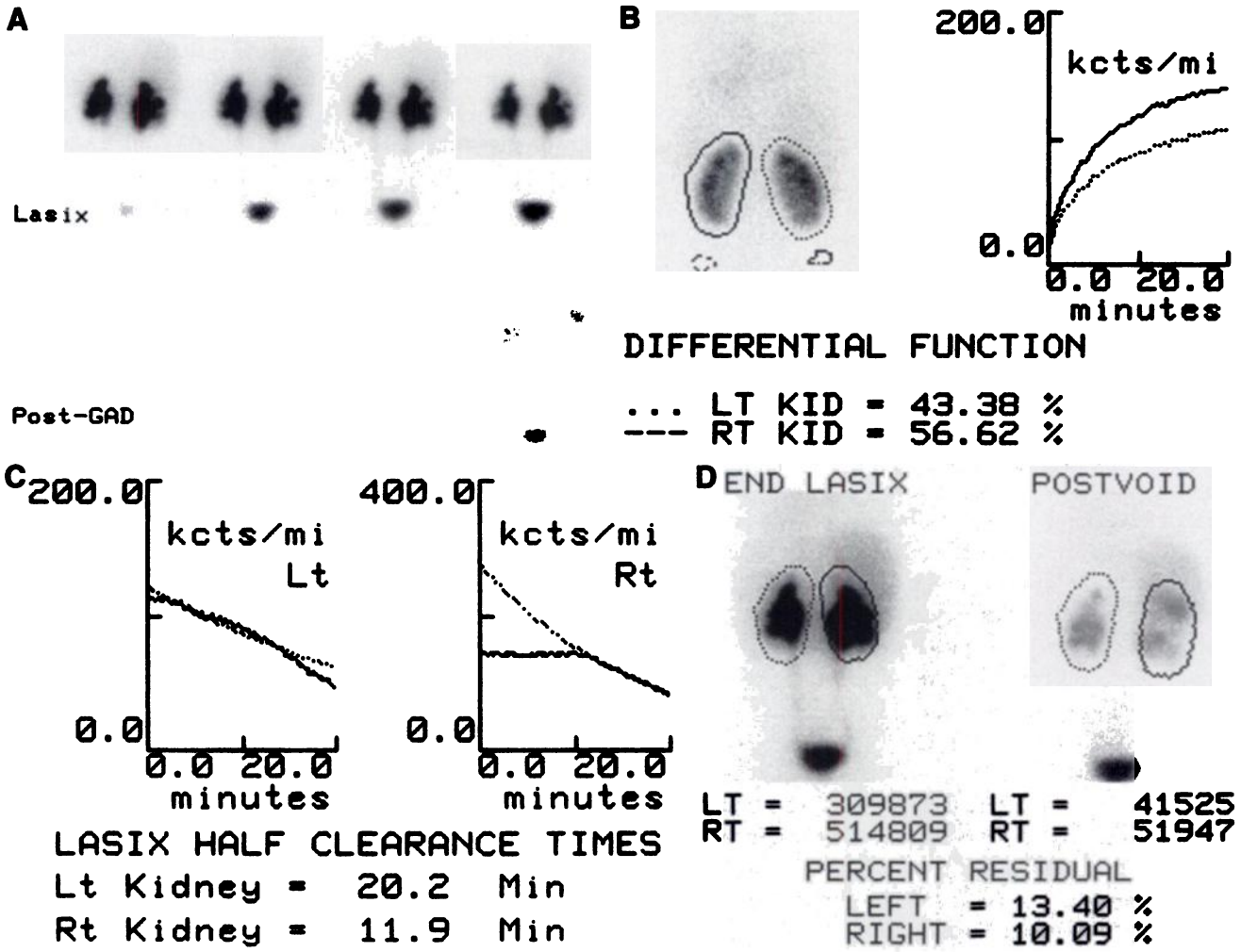

FIGURE 4. A 4-y-old boy who had undergone bilateral pyeloplasties at 6 wk of age. (A) F+20 diuretic renogram. Patient was well clinically, and study was requested for routine follow-up. Furosemide (Lasix; Hoechst Marion Roussel Australia Pty. Ltd., Lane Cove, New South Wales, Australia) was given 20 min after radiopharmaceutical. (B) Differential renal function calculation confirms that left kidney contributes less to total renal function than does right kidney. (C) $t_{1/2}$ for each kidney is in abnormal range, suggesting that ongoing obstruction cannot be excluded. (D) GAD residual activity for each kidney is well below 50%, confirming nonobstruction. Reliance on GAD is commonly found in postpyeloplasty patients.

divided into 3 groups: type 1, >60% residual activity, which corresponded visually to poor or no emptying of the kidney; type 2, <30% residual activity, in which good kidney emptying was obtained; and type 3, 30%–60% residual activity, which was considered to be an equivocal response. Their analyzed data showed a type 2 response in 83 hydronephrotic kidneys (74 patients). Type 1 response was observed in 9 kidneys (9 patients), and each of these patients

TABLE 1
Comparison of GAD Residual Activity in 62 Hydronephrotic Units with $t_{1/2}$ > 20 Minutes

GAD residual activity (%)	TP (n)	FP (n)	TN (n)	FN (n)	Sensitivity (%)	Specificity (%)	Accuracy (%)
>50	38	5	14	5	88.4	73.7	83.9
>60	36	4	15	7	83.7	78.9	82.3
>40	38	10	9	5	88.9	47.4	75.8

TP = true-positive; FP = false-positive; TN = true-negative; FN = false-negative.

TABLE 2
Comparison of GAD Residual Activity in 52 Hydronephrotic Units with $t_{1/2}$ = 10–20 Minutes

GAD residual activity (%)	TP (n)	FP (n)	TN (n)	FN (n)	Sensitivity (%)	Specificity (%)	Accuracy (%)
>50	8	9	35	0	100.0	79.5	82.7
>60	6	8	36	2	75.0	81.1	80.8
>40	8	10	34	0	100.0	77.3	80.8

TP = true-positive; FP = false-positive; TN = true-negative; FN = false-negative.

underwent a pyeloplasty. In 1 kidney (1 patient), a type 3 response was observed, and the patient also had surgery.

Our study confirms that those hydronephrotic renal units with $t_{1/2} < 10$ min usually mean the absence of obstruction, with only 1 renal unit in 131 renal units with $t_{1/2} < 10$ min requiring pyeloplasty for intermittent UPJ obstruction. In addition, quantitation of GAD residual activity is not useful in renal units with $t_{1/2} < 10$ min. A wide range of values occurred between 5% and 112%; these values have no real meaning because drainage has already occurred in response to the diuretic.

Although $t_{1/2} > 20$ min usually means obstruction, renal units without obstruction still occur in this group, especially in patients with impaired renal function or postpyeloplasty (*9*). In postpyeloplasty patients, despite the surgical relief of the obstruction, the renal pelvis often remains dilated and hypotonic, making response to the diuretic stimulus difficult because of the reservoir effect of a large dilated system. Furthermore, the operation requires incision of the muscle intrinsic to the pelviureteric system and results in the loss of normal pelviureteric dynamics for at least 1 y. Therefore, for approximately 3 y postoperatively, the normal mechanics for urinary drainage have been altered, and these patients rely on gravity assistance (*9,19*). On the basis of our data and those of Armstrong and Oates (*19*), the use of GAD > 50% residual activity to differentiate between renal obstruction and nonobstruction appears feasible. Our data indicate that the accuracy is highest using a 50% cutoff, compared with the 40% and 60% levels, and this finding is supported statistically by applying the Student *t* test.

A $t_{1/2} = 10$–20 min is an equivocal result. Similar to the findings of Armstrong and Oates (*19*), the use of GAD > 50% residual activity in this study has allowed reclassification of an equivocal result as obstructed or nonobstructed. In this group, the accuracy is highest using 50% as the cutoff.

The specificity of diuretic renography for GAD > 50% residual activity to confirm obstruction in the groups with $t_{1/2} > 20$ min and $t_{1/2} > 10$–20 min may seem lower than acceptable, being 73.7% and 79.5%, respectively, for each group. An explanation for this is that obstruction was defined as being present if the clinicians thought the obstruction was sufficiently severe enough to require surgical repair. It is recognized that, particularly in infants and children, obstruction may resolve spontaneously (*12–15*).

We have applied GAD > 50% residual activity to both conventional diuretic renography (i.e., F+20 method) and the recently validated modified diuretic renography using the F+0 technique (*10*). GAD > 50% residual activity appears to be applicable to both methods. The addition of quantitative GAD > 50% residual activity is further assessment that can be applied to diuretic renography to aid in the determination of whether functionally significant renal obstruction is present.

CONCLUSION

The quantitation of GAD > 50% residual activity as an indicator to confirm obstruction in diuretic renography can help to differentiate between obstruction and nonobstruction in hydronephrotic renal units with $t_{1/2} > 20$ min (obstructed range) and $t_{1/2} = 10$–20 min (indeterminate range). There is no requirement for quantitation of GAD when $t_{1/2} < 10$ min because these kidneys are almost always not obstructed.

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