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Original Article

Renal cortical transit time as a predictor for pyeloplasty in pediatric patients with unilateral hydronephrosis

ABSTRACT

Majority of patients with unilateral hydronephrosis (HN) detected on ultrasound do not require pyeloplasty. The measurement of the cortical transit time (CTT) has been demonstrated by several authors to predict the need for patients who may require pyeloplasty. The study aimed to assess if CTT would have predicted a drop in differential renal function (DRF) in patients with unilateral HN on the affected side and to assess whether CTT would differ on the first renogram between those patients who had a pyeloplasty and those who did not have a pyeloplasty. Sixty-eight patients with at least two renograms with unilateral HN with a normal contralateral kidney were observed retrospectively. The CTT was recorded for each kidney. Renograms were processed three times to measure the DRF. The mean of the three DRF measurements was used for analysis. The mean CTT of the left and right hydronephrotic kidneys was 6.0 min and 6.7 min, respectively. The relationship between CTT and DRF as well as CTT and anterior posterior diameter in the first renogram of those patients who did not have a pyeloplasty was statistically significant ($P < 0.05$). In the 20 patients who had a pyeloplasty, there was a drop of more than 10% in the DRF of three patients. No significant difference was found in CTT or DRF when comparing the group who had surgery against the group who did not have surgery. The current study was unable to demonstrate in our series of patients that CTT can predict a drop in DRF in those patients who would require pyeloplasty.

Keywords: Cortical transit time, pediatrics, pyeloplasty, renography

INTRODUCTION

The accepted methods for the calculation of the relative renal function (also known as the differential renal function [DRF]) of each kidney (expressed as a percentage of the sum of the right and left kidneys) in technetium-99m mercaptoacetyltriglycine (^{99m}Tc-MAG3) renography are the Rutland-Patlak (RP) and the integral methods. In the integral method, the DRF is calculated from the background-corrected area under the renogram curve between 1 and 2 min after injection of ^{99m}Tc-MAG3 . The RP plot is a graphical representation of the DRF, where the slope represents the relative function of each kidney and the ordinate at the origin represents the portion corrected for intravascular background activity.[1] In 2002, Josephson critically reviewed six patient series based on a diagnosis of antenatally detected hydronephrosis (HN), compliance with defined criteria and publication during the 1990s to allow for a longer follow-up and better diagnostic tools. He found that 88%–90% of patients with unilateral HN detected antenatally do not require a pyeloplasty.[2] In the same year, Ulman *et al*.[3] reported that in their study population of 104 patients with antenatally detected severe unilateral HN, 22% required surgical intervention to prevent loss of renal function. The generally accepted indications for pyeloplasty are symptomatic obstruction (recurrent flank pain), complications

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such as urinary tract infection, a decrease in DRF of more than 10% on subsequent renal scintigraphic studies, poor drainage after furosemide administration on diuretic renography, and a progressive increase in the anterior posterior diameter (APD) in subsequent ultrasound (US) studies.[4] The size of the APD on US is used to classify the severity of HN and is a useful predictor for the resolution of HN.[5] Accurate, repeated postnatal evaluation is therefore required to identify hydronephrotic kidneys that require surgical intervention. Schlotmann *et al*.,[6] Piepsz *et al*.,[7] and Harper *et al*.[8] have demonstrated that the measurement of the cortical transit time (CTT) can be used to predict the need for pyeloplasty.

The purpose of this retrospective study was to assess if the criteria used by Schlotmann *et al*.,[6] Piepsz *et al*.,[7] and Harper *et al*.[8] would have predicted a drop in DRF on the affected side. In addition, did the CTT differ on the first renogram in patients who had a pyeloplasty and those who did not undergo surgery. Schlotmann *et al*.,[6] Piepsz *et al*.,[7] and Harper *et al*.[8] used the time of arrival of activity in the subcortical structures as a measure of the CTT.

SUBJECTS AND METHODS

A database search was performed for patients who had at least two renograms between December 2000 and August 2015. The hospital folders of these patients were then reviewed to confirm the diagnosis of unilateral HN with a normal contralateral kidney. A normal contralateral kidney was defined as a kidney with an APD <10 mm and normal corticomedullary differentiation on US. One hundred and seventy-eight patients were identified and 110 excluded; 105 did not have an US report in the clinical notes and 5 had an APD of <10 mm, leaving 68 patients.

All renograms were performed using ^{99m}Tc-MAG3 (Mallinckrodt Medical), with the dose determined using the EANM dosage card.[9,10] Patients were hydrated intravenously before injection of ^{99m}Tc-MAG3 with 100–200 ml of 0.9% NaCl solution. The F +20 protocol was used as recommended in the guidelines for standard and diuretic renogram in children,[4,11] with 1.0 mg/kg furosemide being administrated up to a maximum of 20 mg.

The raw data were acquired with a Philips Axis Dual Head camera (Picker International Inc., Cleveland, Ohio, USA) with a low-energy high-resolution collimator on a 128 × 128 matrix. The duration of the renogram was 42 min: 1 s/frame for the first 2 min and 15 s/frame for 40 min. The child was then held erect or stood up for 5 min after which a static postmicturition postgravity drainage image was acquired for 5 min.

The raw data were retrieved from the electronic archive and reprocessed. The visual procedure described by Piepsz *et al*.[7] was used to determine CTT. The time of arrival of activity in the subcortical structures, calyces of the upper, and middle and lower third of each kidney and pelvis were recorded. The mean of the times activity appeared in the calyces was used as the CTT of the kidney. Each renogram was processed three times on the HERMES Gold™ software (HERMES, Stockholm, Sweden) package to measure the DRF using the RP and integral methods.[4,11] The mean of the three DRF measurements was used for analysis.

The study was approved from the Human Research Ethics Committee of the University (HREC Reference no. 839/2015).

Statistical analysis

Statistical analysis was performed using the Stata software package (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX, USA: StataCorp LP). The Shapiro–Wilk test was used to test distribution. The median, 25th and 75th centiles, and minimum and maximum were used as descriptive statistics. The Wilcoxon signed-rank test was used for paired data and the Mann–Whitney U-test to compare groups. Spearman's rank correlation test was used to assess the association between variables.

RESULTS

Patient demographics

Of the 68 patients with unilateral HN and a normal contralateral kidney, 43 were male and 25 were female. The median age at presentation for the initial renogram was 2.2 months (range, 0.2–115.3 months). Thirty-six patients had left-sided HN with a median CTT of 6 min and 32 right-sided HN with a median CTT of 6.7 min on the initial renogram. The median APDs of the left and right HN kidneys were 18.3 mm and 23 mm, respectively [Tables 1 and 2].

Comparing differential renal function and cortical transit time in the patients who did not have a pyeloplasty

Table 3 summarizes the DRF and CTT in the normal contralateral kidneys and the left and right HN kidneys of the 48 patients who did not have a pyeloplasty. There was no difference between DRF of the first and second renograms ($z = -0.858$, $P > 0.05$, $n = 47$; in the first renogram of one child, the left hydronephrotic kidney extended to the body outline, making it impossible to draw the standard regions of interest used to calculate DRF). In five patients, there was a drop of more than 10% in the DRF, but no record of the reasons for not doing a pyeloplasty. The ages of these patients ranged between 0.1 and 43.2 months, and the APDs ranged between 11.4 and 40 mm. In the first renogram, the

Table 1: Summary of data of all patients

Demographics	Total number
Sex	
Male	43
Female	25
Time between initial and second renogram (months), median	4.9
Age (months)	
Median	2.2
Range	0.24-115.3
Affected sides	
Left	36
Right	32
Ultrasound data, APD*(	
Left side	
Median	18.3
Range	10-57
Right side	
Median	23
Range	10-69.7
Cortical transit time (min)	
Left side, median (R1, R2)	6.0, 5.3
Right side, median (R1, R2)	6.7, 5.7

R1: Renogram 1, R2: Renogram 2, APD: Anterior posterior diameter on ultrasound

Table 2: Summary of data of 48 patients who did not have a pyeloplasty

Demographics	Total number
Affected sides	
Left	24
Right	24
Ultrasound data, APD (mm)	
Left side	
Median	17
Range	10-40
Right side	
Median	21.9
Range	10-69.7
Cortical transit time (min)	
Left side, median (R1, R2)	6.0, 5.0
Right side, median (R1, R2)	6.7, 5.7

R1: Renogram 1, R2: Renogram 2, APD: Anterior posterior diameter on ultrasound

longest CTT in a normal kidney was 3 min, while the shortest CTT in a hydronephrotic kidney was 3.7 min. In 32 of the 48 patients, the second renogram showed a decrease in CTT with the CTT of one hydronephrotic kidney falling into the range of the CTT of normal kidneys. The change in the CTT of the first and second renograms was significant ($z = 4.029$, $P < 0.0001$). Figure 1 illustrates the relationship between the CTT and DRF in the first renogram of the patients who did not have a pyeloplasty ($P = -0.2731$, $P < 0.05$) and Figure 2 illustrates the relationship between CTT and APD ($P = 0.2864$, $P < 0.05$).

Comparing differential renal function and cortical transit time in the patients who had a pyeloplasty

In the 20 patients who had a pyeloplasty, there was a drop of more than 10% in the DRF of three patients. No difference was seen in the DRF ($z = 0.355$, $P > 0.05$) or in the CTT ($z = 1.217$, $P > 0.05$) between the first and second renogram. CTT was shorter in the second renogram in nine of the 20 patients who had a pyeloplasty.

No significant difference was found in the CTT ($z = -0.054$, $P > 0.05$) or DRF ($z = 0.452$, $P > 0.05$) when comparing the group who had surgery against the group who did not have surgery.

Data of pyeloplasty group compared to the control group

The indication for doing or not doing a pyeloplasty was not clearly stated in the clinical notes of every patient, so undertook a supplementary analysis in those patients who had a pyeloplasty. Each of the children who had a pyeloplasty was matched with a child who did not have surgery based on age within a month and APD within two standard deviations from the median of the APD of the patients who had surgery. The control group was selected from the 48 patients who did not undergo pyeloplasty. Fifteen patients were male and five were female with a

Table 3: Cortical transit time and differential renal function in the normal contralateral kidney and left or right hydronephrotic kidneys of the patients who did not have a pyeloplasty

	Median		Interquartile range				Minimum		Maximum	
			25		75					
	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2
Normal contralateral kidney										
Left CTT (min)	2		2		2		2		3	
Right CTT (min)	2		2		2.5	2.7	2		3	
Left hydronephrotic										
CTT (min)	6	5.0	4.0	3.8	7.0	7.0	3.7	3.0	10	10
DRF (%)	49	47	42	37	53	51	28	3	63	62
Right hydronephrotic										
CTT (min)	6.7	5.7	6.0	4.5	9.5	6.7	4.0	2.0	10	8.3
DRF (%)	42	45	34	33	51	51	1	9	56	56

Please note that the DRF calculations were performed on 47 patients. R1: Renogram 1, R2: Renogram 2, DRF: Differential renal function, CTT: Cortical transit time

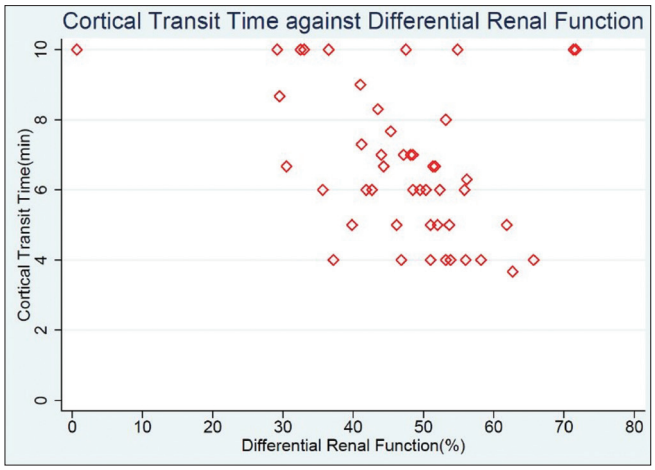

Figure 1: Scatter plot of the cortical transit time versus differential renal function in affected hydronephrotic kidneys in those patients who did not have a pyeloplasty

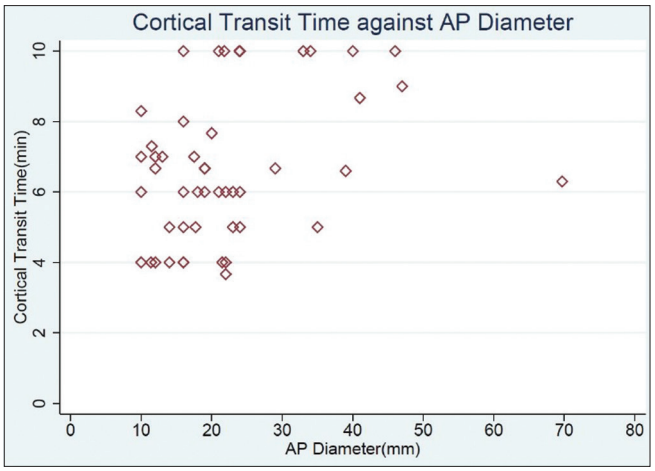

Figure 2: Scatter plot of the cortical transit time versus anterior posterior diameter in those kidneys which did not have a pyeloplasty

median age of 1.9 months (range, 0.2–86.4 months). Twelve patients had left-sided HN with a median CTT of 6.3 min and eight right-sided HN with a median CTT of 6.5 min. The median APDs of the left and right HN kidneys were 21.6 mm and 25 mm, respectively. The results of the control group are presented in Table 4.

The median interval between the initial renogram and pyeloplasty was 2.7 months (range, 0.2–72 months), and the median interval between the first and second renogram was 5.2 months (range, 0.46–22.2 months). The pyeloplasty was performed between the first and second renogram. In the control group, the median interval between the first and second renogram was 4.4 months (range 0.1–31.8 months).

Table 5 presents the CTT and DRF of the pyeloplasty group and the control group. There was no difference in CTT ($z = -0.027$, $P > 0.05$) or DRF ($z = -1.799$, $P > 0.05$) on the first renogram, but a deterioration in DRF of more than 10% was seen in three patients on their postpyeloplasty renogram. Figure 3 illustrates the relationship between the CTT ($P = 0.3418$, $P > 0.05$) and DRF ($P = 0.0950$, $P > 0.05$).

Table 4: Summary of data of 20 patients who had a pyeloplasty and the control group

	Pyeloplasty group	Control group
Sex		
Male	12	14
Female	8	6
Age (months)		
Median	1.6	2.2
Range	0.2-86.4	0.7-77.9
Affected sides		
Left	12	13
Right	8	7
Ultrasound data, APD (mm)		
All		
Median	24	21.4
Range	12-57	10-46
Right side		
Median	25	19
Range	14-50	11.5-46
Left side		
Median	21.6	24
Range	12-57	10-39
Cortical transit time		
Left side, median	5.8	6.0
Right side, median	6.5	7.3

APD: Anterior posterior diameter

DISCUSSION

Most children with an antenatal diagnosis of HN do not require surgical intervention.[2,3] Those likely to benefit from a pyeloplasty are usually symptomatic[11] or identified using an imaging modality. Currently, the most widely used practice is serial imaging with US and diuretic renography to detect the earliest signs of a progression in the HN or deterioration in the DRF.[12]

Several reports have described the use of CTT to predict deterioration in the function of the hydronephrotic kidney.[6-8,13-15] The use of this parameter stems from the postulate that in an obstructed kidney, there is an increase in the pelvic pressure which will lead to a decrease in the renal blood flow, thereby a decrease in the glomerular filtration rate (GFR).[16] This ultimately leads to activation of the renin angiotensin system with a series of events which leads to sclerosis. Sclerosis is a very late event in renal outflow obstruction. Increased intrarenal pressure from pelviureteric junction obstruction is enough to impair GFR and lead to prolongation of CTT. Therefore, the effect is decreased washout of radiotracer from the renal parenchyma on scintigraphy.[6,16]

Table 5: Quantitative data relating to the patients who had surgery against the patients who are part of the control group comparing cortical transit time and differential renal function

	Median		Interquartile range				Minimum		Maximum	
			25		75					
	R1	R2	R1	R2	R1	R2	R1	R2	R1	R2
Pyeloplasty patients										
CTT (min)	6.3	5.5	5.0	4.7	7.8	7.0	4.0	4.0	10.0	10.0
DRF (%)	46	44	41	32	50	49	18	16	56	57
Control group										
CTT (min)	6.3	4.7	5.5	3.8	7.5	6.3	4.0	3.0	10.0	8.3
DRF (%)	50	49	46	42	53	52	29	12	63	58

R1: Renogram 1, R2: Renogram 2, DRF: Differential renal function, CTT: Cortical transit time

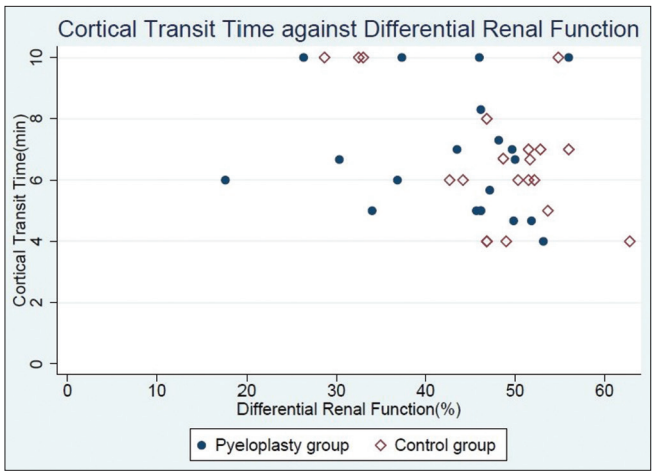

Figure 3: Scatter plot details the cortical transit time versus the differential renal function of the affected hydronephrotic kidney in the group who had a pyeloplasty against the control group

The studies performed by Schlotmann *et al*.,[6] Piepsz *et al*.,[7] and Harper *et al*.[8] all demonstrated the feasibility of using the time of arrival of activity in the subcortical structures as an index for CTT to predict the kidneys which would benefit from surgical intervention. Neither Schlotmann nor Harper reported the time of appearance of activity in the subcortical structures in normal or hydronephrotic kidneys. They only stated that the time of appearance of activity in the hydronephrotic kidneys was abnormal. The CTTs in the HN kidneys in our study were comparable to those in Piepsz *et al*.'s study (3 – 8 min).[7] In our patients, the CTT of each hydronephrotic kidney was longer than the CTT of the normal contralateral kidney on the first renogram.

In our patients, there was a significant change in CTT between the first and second renogram in those patients who did not have a pyeloplasty. Thirty-two of the 48 patients showed a drop in the CTT between the first and second renogram. This is in contrast with Harper *et al*. and Schlotmann *et al*.'s groups, where Harper *et al*.[8] only identified two patients with abnormal CTT who did not have surgery. One patient had an improvement in their CTT, and the other had a deterioration in their CTT. It is not stated whether this patient had further intervention. Schlotmann *et al*.[6] identified three of 14 patients with abnormal CTT who had no surgery of which two deteriorated and one remained stable. The change in the CTT was not reported in Piepsz *et al*.' group[7] between the first and second renogram.

There was no significant change in DRF between the first and second renogram in our patients who did not have a pyeloplasty. A drop of more than 10% in the DRF between the first and second renogram was seen in five patients, a frequency consistent with Josephson.[1] A possible reason for this may be the fact that these renograms were performed in a state of renal immaturity. With subsequent maturation of renal function, there is a higher extraction of the tracer by the kidney and this may account for the drop in DRF in those patients who did not have a pyeloplasty.[17] Even though a drop in DRF of more than 10% in subsequent studies is an acceptable criterion for a pyeloplasty, the CTT did not identify these patients who may have qualified for surgery. In the ten patients who had no surgery in Piepsz *et al*.'s group,[7] four had a deterioration in their DRF, with the remaining six patients having no deterioration in DRF.

We were also able to assess if there was a significant difference in the CTT and DRF in the group of patients who had a pyeloplasty and compare them to the patients who did not have surgery as well as a control group. This was not demonstrated in our study. Three patients were identified who had a deterioration in DRF of more than 10% on their postpyeloplasty renogram. We were unable to identify reasons for this deterioration from the clinical records. In comparison, Harper *et al*.[8] showed an improvement in CTT postpyeloplasty (however this was not quantified); Schlotmann *et al*.[6] demonstrated in 8 out of 13 an improvement in the CTT postsurgery. Piepsz *et al*.[7] demonstrated that in 10 of the 16 patients who had surgery had an improvement in the DRF. The remainder of the patients showed no significant change in DRF.

Limitations of the study

One of the limitations of this study was that it was retrospective, relying on the standard hospital record system to access data relating to the US information and notes on surgery. There were missing data in terms of the US reports and the indications for the pyeloplasty and reasons for not doing a pyeloplasty were not clearly recorded in some of the notes.

CONCLUSION

The current study was unable to demonstrate in our series of patients that CTT can predict a drop in the DRF, thereby identifying those patients who would require pyeloplasty. As stated previously, this may be owing to our study being retrospective and our reliance on the clinical notes for the US data and surgical notes.

In future, a prospective study evaluating the relationship between CTT and a drop in the DRF should be undertaken in this unit.

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Conflicts of interest

There are no conflicts of interest.

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