

# Renal cortical transit time in the evaluation of prenatally detected presumed pelvi ureteric junction like obstruction: A systematic review

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## ABSTRACT

**Introduction:** Differentiating nonobstructive from obstructive dilatation of the kidney is a clinical dilemma in prenatally detected hydronephrosis. Many radionuclide renogram parameters have been used to differentiate obstructed from non-obstructed units, including cortical transit time (CTT). We evaluate the role of CTT in identifying obstruction through a systematic review.

**Methods:** A literature search of the MEDLINE, MEDLINE In-Process, and MEDLINE Epub Ahead of Print, EMBASE, Google scholar, Pub Med, and Cochrane Library was done using key words – radionuclide renogram, CTT, parenchymal transit time, cortical transit, renography to identify articles on the subject. The identified articles were assessed for appropriateness and reviewed.

**Results:** The initial search yielded a total of 1583 articles, after adding the articles from references and applying the inclusion and exclusion criteria a total of 28 articles were selected. CTT showed good inter observer agreement in identifying obstruction. The use of CTT as a single parameter for determining the need for surgery and to identify those kidneys which will have functional improvement after surgery has been evaluated and has been found to be useful. CTT is best used in conjunction with ultrasonography to make clinical decisions.

**Conclusion:** The commonly used visual method of estimating the CTT, is a promising parameter for the evaluation of prenatally detected pelviureteric junction obstruction. Further well-designed multicenter prospective studies are needed to establish it as the most specific parameter to differentiate obstructive from nonobstructive dilatation of the pelvicalyceal system.

## INTRODUCTION

With the widespread use of ultrasonography in the prenatal period, antenatal hydronephrosis is seen in nearly 1%–5% of all pregnancies.<sup>[1,2]</sup> Categorization of these patients into mild, moderate, and severe hydronephrosis has been proposed either by measuring the anteroposterior diameter or by using the Society of Fetal Urology grading system.<sup>[3]</sup>

Postnatally, the babies are born with a presumptive diagnosis of hydronephrosis. A correct diagnosis

and deciding the need for surgical intervention is often the greatest worry for the parents.<sup>[4]</sup> The clinician faces the dilemma of differentiating a nonobstructive from an obstructive dilatation of the pelvicalyceal system.<sup>[5]</sup> A majority of such prenatally detected hydronephrosis are transient and subside over a period of time, but those which persist need close observation and regular follow-up or definitive management in future.<sup>[6-9]</sup>

There is Level I evidence that infants with prenatally detected hydronephrosis should be evaluated by ultrasonography not

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earlier than 48–72 h after birth and preferably 5–7 days after birth.<sup>[10]</sup> If hydronephrosis persists, then further evaluation is mandatory either by ultrasonography or by radionuclide studies at 4–12 weeks, depending on the degree of hydronephrosis.<sup>[2]</sup>

Ultrasonography gives good anatomical delineation of the dilated pelvicalyceal system, but functional evaluation and the need to determine the nature of the hydronephrosis is best done by a Tc99 Mercapto Acetyl Triglycine (MAG 3) or Ethylene dicysteine (EC) diuretic renogram. With these two tests, it is possible to determine whether the hydronephrosis is obstructive or nonobstructive in nature.<sup>[11]</sup> This differentiation is important because an untreated, obstructed kidney may sustain an irrevocable loss of function.

A dilated system will necessarily have a slow rate of clearance of radiotracer despite the lack of functional obstruction as the system has to fill before the drainage is appreciable. Therefore, dilatation in a growing kidney, on ultrasonography, is not a very reliable indicator of the presence of obstruction.<sup>[12]</sup> Conventionally, the T1/2 values or the presence of an obstructive curve on a renogram or a differential function <40% have been taken as indicative of obstruction.<sup>[13]</sup> However, many studies have questioned the usefulness of these criteria. This has led to the search for more reliable parameters to differentiate an obstructed from a non-obstructed system.<sup>[5,14-17]</sup>

One such parameter has been the cortical transit time (CTT) estimated on the renogram.<sup>[5]</sup> It is defined as the time taken by the tracer to pass from the cortex to the pelvicalyceal system.<sup>[17]</sup> This article aims to review the usefulness of CTT to differentiate obstructive from nonobstructive dilatations of the pelvicalyceal system with special emphasis on presumed pelvic-ureteric junction obstruction (PPUJO) in prenatally detected hydronephrosis.

The objectives of the review were (1) to evaluate the usefulness of CTT to differentiate obstructive from nonobstructive dilatation of the pelvicalyceal system, especially in PPUJO, (2) to describe the pathophysiology in the use of CTT as a parameter to diagnose obstruction, (3) to evaluate the accuracy of visual estimation of CTT, and (4) to compare the usefulness of CTT with other parameters.

## METHODS

### Search strategy and study selection

This systematic review was done as per the preferred reporting items for systematic reviews and meta-analysis guidelines.<sup>[18]</sup> A comprehensive search was made from the MEDLINE, MEDLINE In-Process, MEDLINE Epub Ahead of Print, EMBASE, Google scholar, PubMed, and Cochrane Library was done using keywords – radionuclide renogram, CTT, parenchymal transit time, cortical transit, renography.

All articles with these keywords were selected and further articles from references were also included. The full text of all the articles were studied and analyzed to identify any further studies for inclusion. The study period was from the inception of the databases to March 2020.

### Inclusion criteria

All English language articles describing CTT, and its application to diagnose obstruction, and its comparison with Whitaker test and diuretic renogram were included in this review.

### Exclusion criteria

Technical studies which have emphasized on the physics of measuring the CTT on a gamma camera were excluded from the study. Figure 1 gives the details of the selection of the articles.

### Data extraction and analysis

The selected articles were studied and evaluated under the various categories, as described in Table 1. In the end, the authors have given their own perspective on the role of CTT in future independently and in conjunction with the other parameters of ultrasonography and diuretic renogram.

## RESULTS

A total of 28 articles were included. Two articles by Britton *et al.*<sup>[19]</sup> and by Schlotmann *et al.*<sup>[20]</sup> gave an insight into the pathophysiology of CTT. Initially, the terminology used was parenchymal transit time or tissue transit time, but later, these were replaced by CTT which is now the accepted nomenclature.<sup>[21]</sup> Although a number of articles have described the methods used to calculate CTT,<sup>[22]</sup> the International Scientific Committee of Radionuclides in Nephrourology consensus on renal transit time has been used as the reference standard.<sup>[23]</sup> The visual method of CTT calculation was followed by most researchers who tried to co-relate CTT with clinical parameters for diagnosing an obstructed system.<sup>[24,25]</sup> Santos *et al.*<sup>[26]</sup> and Cichocki *et al.*<sup>[27]</sup> have looked into inter-observer agreement of measurement of CTT using the visual images and the deconvolution analysis method, respectively. Studies by Schlotmann *et al.*<sup>[28]</sup> Song *et al.*<sup>[29]</sup> and Jain *et al.*<sup>[30]</sup> have also looked at this aspect. Five studies have specifically dealt

**Table 1: Various aspects of cortical transit time studied in this review**

Pathophysiology of delayed CTT as a parameter for obstruction
Methods describing the measurement of CTT
Inter-observer agreement on measurement of CTT
Usefulness of CTT to differentiate obstructed from a non-obstructed but dilated system
Comparison of CTT with Whitaker test
Comparison of CTT with parameters on diuretic renogram
Limitations in using CTT as a parameter of obstruction

CTT=Cortical transit time

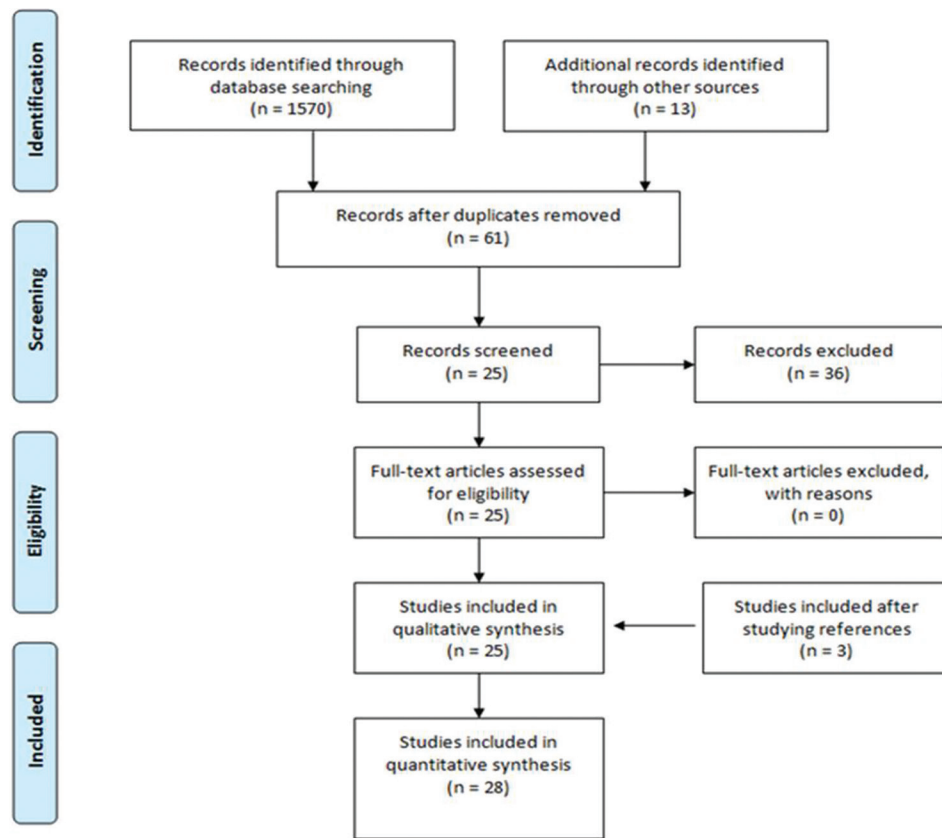


Figure 1: Preferred reporting items for systematic reviews and meta-analysis Flow Diagram

with the clinical outcome of using CTT as a parameter to decide the need for surgery.<sup>[28,31-34]</sup> Five studies have looked at the predictive value of CTT to identify renal units which would benefit from surgery.<sup>[18,24,28,29,34]</sup> Two studies have compared the CTT with the Whitaker test.<sup>[18,35]</sup> Studies by Britton *et al.*,<sup>[36]</sup> were the initial studies which compared the CTT with parameters on diuretic renography. Verboven *et al.*<sup>[37]</sup> and Lupton *et al.*<sup>[38]</sup> also made similar comparisons. No study has emphasized any drawback of using CTT as a parameter in the management of patients with prenatally detected hydronephrosis.

## DISCUSSION

Initially, the terminology used to describe CTT was Parenchymal Transit Time or Tissue Transit Time. It was first described in 1977, but it was after the study by Schlotmann *et al.* in 2008<sup>[20]</sup> that the interest in CTT rekindled.

### Pathophysiology of delayed cortical transit time in an obstructed system

Whitfield and Britton *et al.* proposed a distinction between obstructive uropathy, which occurs when there is an obstruction to flow of urine from the pelvis and obstructive nephropathy-where the obstruction of the outflow tract has an effect on the function of the nephron.<sup>[39]</sup> They mentioned that the outflow of urine may be impeded in a system, but the uptake

function would not be impaired initially. Thus, the glomerular filtration would continue, but due to outflow resistance, the pressure in the tubules would increase. This would lead to increased absorption of salt and water in the tubules, and the solutes would have a slower transit through the nephron. This results in a delayed transit time on renography.<sup>[19,36,39]</sup>

Schlotmann *et al.* in 2008<sup>[20]</sup> stated that obstruction leads to a reduction in filtration fraction, which in turn activates the renin-angiotensin system. This concept was also described by Bajpai *et al.* using captopril renography.<sup>[40,41]</sup> Schlotmann proposed that the reduction in filtration fraction leads to delayed transit of the tracer across the tubules, and the activation of renin-angiotensin system causes morphological reorganization with eventual sclerosis mediated by transforming growth factor  $\beta$ .<sup>[20]</sup>

### Measurement of cortical transit time

There have been two approaches described to measure CTT. One method uses a gamma camera, and the other is a visual method. By using the gamma camera, deconvolution analysis or factor analysis are the techniques used to determine the parenchymal transit time.<sup>[22,23]</sup> A detailed discussion is not within the scope of this review.

The other method uses the interpretation of the images or curves visually. The Belgian group, led by Prof. Piepsz, has

been a strong advocate of measuring the CTT by assessment of visual images.<sup>[24,25]</sup> Most of the clinical studies assessing the usefulness of CTT have also used this method.

### **Interpreting a cortical transit time by the assessment of visual images**

Initially described by Kuyvenhoven *et al.* in 2004,<sup>[24]</sup> the maximum activity appears in the kidney in normal subjects between 2 and 3 min. By 3–4 min, the radioisotope tracer appears in the pelvicalyceal system. The arrival of the tracer in the pelvicalyceal system has been quantified and was described as the corticopelvic transfer index by Makoba *et al.*<sup>[42]</sup>

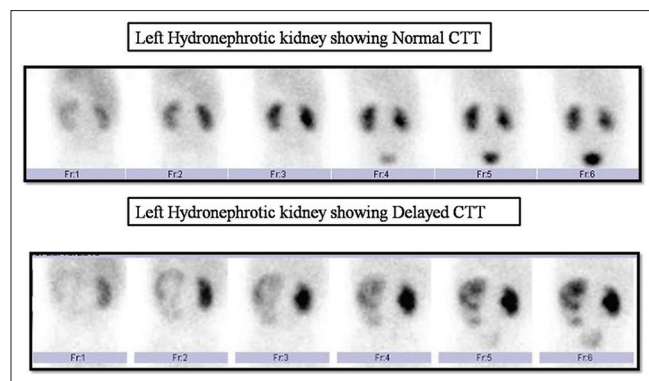
Schlotmann in 2009 described the criteria they used for visual estimation of CTT.<sup>[28]</sup> Subsequently, all the studies with the exception of the study by Song *et al.*<sup>[29]</sup> have used the description of visual estimation of CTT, as described by Piepsz *et al.* in 2011. They state that when 1-min sum images are evaluated, the cortical transit is considered impaired when no or almost no activity appears in the subcortical structures, i.e., in the calyces and medulla for at least 3 min and only a semilunar cortical rim is seen.<sup>[25]</sup> Figure 2.

### **What is normal cortical transit time?**

Earlier studies by Whitfield *et al.* and Britton *et al.*<sup>[19,35,39]</sup> measured CTT using deconvolution analysis and found it to be around 3 min. However, the study by Schlotmann *et al.*<sup>[28]</sup> mentioned 2–6/10 min as the delayed CTT. Song *et al.* also have used these time frames.<sup>[29]</sup> Recent studies have followed the 3 min cutoff to differentiate the normal from the delayed CTT.<sup>[30–34]</sup> Table 2 gives the normal CTT as reported by the various studies.

### **Inter-observer agreement on the measurement of cortical transit time**

This aspect is important when visual images are used to measure CTT. Out of the nine clinical studies that have used visual images to measure CTT, five have mentioned the use of inter/intraobserver agreement in their studies. Only one study, i.e., by Santos *et al.* in 2017<sup>[25]</sup> specifically looked



**Figure 2:** Renogram Images showing Normal cortical transit time <3 minutes and Delayed cortical transit time of >3 min

only at the inter-observer agreement. In this study two groups of four nuclear medicine consultants in one group and two nuclear medicine residents in the other group were compared. All the consultants had an agreement in 61 out of the 69 cases studied (88.4%) and agreement of at least three out of the four was reached in 98.6% (68 out of the 69 cases). The residents agreed on 48 out of the 69 cases (69.6%). Further analysis of the study showed perfect agreement between the final year resident and consultant and fair agreement with the 1<sup>st</sup>-year resident. This clearly indicates the value of experience in these cases. Song *et al.* also found a very good ICC of 0.843 when two urologists have assessed the images.<sup>[29]</sup> In the study by Jain *et al.*<sup>[30]</sup> the CTT was calculated by the visual method by two different observers, blinded to each other's observations. The average of their findings was taken. The Cohen's kappa statistic value for the interobserver variation in interpretation of CTT in the preoperative and the postoperative scan was 0.61 and 0.62. This indicated substantial strength of agreement. Table 3 has the details of the various studies on this aspect of CTT.

### **Usefulness of cortical transit time to differentiate obstructed from a nonobstructed but dilated system**

Parameters of radionuclide renograms, for example, the T<sub>1/2</sub> and drainage curves are considered as “gold” standards to make the diagnosis of obstruction in dilated systems. However, both the degree of hydronephrosis and the renogram parameters are affected by a host of factors like the state of hydration and fullness of the bladder.<sup>[4]</sup> The reservoir effect of a dilated and compliant renal pelvis resulting in slow drainage is one of the strongest arguments for not relying on T<sub>1/2</sub> values and drainage curves.<sup>[15]</sup> While drainage curves and T<sub>1/2</sub> values are reliable to rule out obstruction, they remain unsatisfactory to diagnose obstruction.<sup>[15,44]</sup>

Dilatation is easy to understand and decipher from investigations evaluating the anatomy of the pelvicalyceal system—ultrasonography, computerized tomography, or by magnetic resonance imaging. Unfortunately, obstruction is less well defined. Koff defined it as “any restriction to urinary flow which, if left untreated, would cause damage to the kidney.”<sup>[45]</sup> Unfortunately, this can only be ascertained retrospectively during follow-up when a decrease in function would conclusively prove the diagnosis of obstruction. Asymptomatic patients may be lost for follow-up or may present late when surgical intervention may not be completely able to recover the loss of function.<sup>[8,12]</sup>

For CTT to be used as a parameter to differentiate an obstructed from a non-obstructed system – a delayed CTT should identify kidneys at risk of deterioration if surgery is postponed and a normal CTT should imply that these kidneys are not a risk of deterioration of function. In addition can a delayed CTT identify renal units whose function will improve after surgery?

**Table 2: Normal values of cortical transit time in various studies along with the radioisotope used and the methods used in estimation**

References	Normal CTT (s)	Method	Radioisotope
Whitfield <i>et al.</i> 1977 <sup>[35]</sup>	230	Deconvolution analysis	DTPA
Whitfield <i>et al.</i> 1978 <sup>[39]</sup>	144-230	Deconvolution analysis	DTPA
Britton <i>et al.</i> 1979 <sup>[19]</sup>	156	Deconvolution analysis	DTPA
Britton <i>et al.</i> 1987 <sup>[36]</sup>	180	Deconvolution analysis	DTPA
Verboven <i>et al.</i> 1988 <sup>[37]</sup>	120-300	Deconvolution analysis	DTPA
Kuyvenhoven <i>et al.</i> 2004 <sup>[24]</sup>	120-240	Visual images	DTPA
Schlotmann <i>et al.</i> 2008 <sup>[20]</sup>	120-360-480	Visual images	MAG 3
Durand <i>et al.</i> 2008 <sup>[23]</sup>	120-180	Deconvolution analysis	DTPA/MAG 3
Schlotmann <i>et al.</i> 2009 <sup>[28]</sup>	120-360-480	Visual images	MAG 3
Piepsz <i>et al.</i> 2011 <sup>[25]</sup>	Upto 180 s	Visual images	MAG3
Harper <i>et al.</i> 2013 <sup>[31]</sup>	Upto 180 s	Visual images	MAG3
Duong <i>et al.</i> 2013 <sup>[34]</sup>	Upto 180 s	Visual images	MAG3
Duong <i>et al.</i> 2014 <sup>[43]</sup>	Upto 180 s	Visual images	MAG3
Song <i>et al.</i> 2017 <sup>[29]</sup>	120-600 s	Visual images	MAG 3
Lee <i>et al.</i> 2017 <sup>[32]</sup>	Upto 180 s	Visual images	MAG3
Sharma and Sharma 2017 <sup>[33]</sup>	Upto 180 s	Visual images	EC-Ethylene dicysteine
Jain <i>et al.</i> 2020 <sup>[30]</sup>	Upto 180 s	Visual images	MAG3

CTT=Cortical transit time

**Table 3: Studies which looked at the inter and intra observer agreement of cortical transit time**

References	Isotope used	Renograms studied	Interobserver agreement/disagreement	Intraobserver agreement/disagreement
Schlotmann <i>et al.</i> 2009 <sup>[28]</sup>	MAG3	169	142/27	Not studied
Piepsz <i>et al.</i> 2011 <sup>[25]</sup>	MAG3	26	26/0	Not studied
Harper <i>et al.</i> 2013 <sup>[31]</sup>	MAG3	37	Not studied	37/37
Santos <i>et al.</i> 2017 <sup>[26]</sup>	MAG3	69	61/8	Not Studied
Song <i>et al.</i> 2017 <sup>[29]</sup>	MAG3	126	ICC-0.843	Not Studied
Jain <i>et al.</i> 2020 <sup>[30]</sup>	MAG3	31	Cohen; s Kappa value 0.61	Not studied

CTT=Cortical transit time, ICC=Intra class correlation coefficient

**Can delayed cortical transit time identify those kidneys which are at risk of deterioration if surgery is delayed?**

Table 4 compares the data from the studies utilizing CTT to evaluate deterioration in differential renal function (DRF) in patients with delayed CTT on the initial renogram. The striking feature is the small number of patients, in all these studies, which fulfill the criteria to answer the question. Except for the study by Sharma and Sharma,<sup>[33]</sup> all others are retrospective studies. Furthermore, except the study by Piepsz *et al.*<sup>[25]</sup> and Sharma and Sharma<sup>[33]</sup> who have used only the deterioration in DRF as the primary parameter as an indicator for surgery, others have also used increasing hydronephrosis, abnormal drainage curves as the indications for pyeloplasty.

Out of the 22 patients in the article by Harper *et al.*<sup>[31]</sup> 20 underwent surgery and of the two patients with delayed CTT who did not undergo surgery, one showed improvement in CTT during follow-up and the other had a stable function during follow-up. The length of follow-up has not been specified in this article. This suggests that there could be factors other than impedance to the urine flow from the renal pelvis, which can affect the CTT. It has been the personal experience of the authors that pyelonephritis can affect the CTT and which can improve after the treatment of infection. In the study by Lee *et al.*,<sup>[32]</sup> four patients with

**Table 4: Deferment of surgery in patients with delayed cortical transit time and the patients with deterioration of renal function during follow up**

References	Number of patients showing delayed CTT	Deterioration of function
Schlotmann <i>et al.</i> 2009 <sup>[28]</sup>	3	2
Piepsz <i>et al.</i> 2011 <sup>[25]</sup>	4	4
Harper <i>et al.</i> 2013 <sup>[31]</sup>	2	0
Lee <i>et al.</i> 2017 <sup>[32]</sup>	4	0
Sharma and Sharma 2017 <sup>[33]</sup>	11	11

CTT=Cortical transit time

delayed CTT did not undergo surgery. They all had an anteroposterior diameter of renal pelvis <20 mm, and the mean age at the time of last follow-up was 18.9 months. The period of follow up is important as usually the follow-up in such patients is till the age of 6 years.<sup>[2]</sup>

Whether delayed CTT can identify the kidneys which are at risk of deterioration due to delay in surgery can be answered by a well-designed multicenter prospective study of asymptomatic prenatally detected Presumed Pelvi Ureteric Junction like Obstruction (PPUJO). The initial renogram has to be done at 4-6 weeks and subsequent follow up can be done by ultrasonography; with the need for a follow-up renogram if there are signs of increasing hydronephrosis. Sharma and Sharma have proposed an

algorithm of using ultrasonography and CTT for the evaluation and management of patients with prenatally detected PPUJO.<sup>[33]</sup>

### **Can a normal cortical transit time assure the clinician that these kidneys are not at risk of deterioration of function?**

Irrespective of the T ½ values and drainage curves, if the CTT is normal, then ideally, these kidneys should not deteriorate during follow-up. Evidence [Table 5] suggests that a normal CTT is like having a good drainage pattern on a diuretic renogram, which rules out obstruction. Only a single patient in the study by Lee *et al.*<sup>[32]</sup> had surgery, but the authors did not mention whether it was solely due to deterioration in function. Furthermore, the methodology of following up these patients have not been clearly defined or specified in any of the studies. Duong *et al.* have mentioned that CTT alone cannot be taken as parameter and it should be used in conjunction with structural parameters, as seen on ultrasonography.<sup>[43]</sup> This has also been emphasized by Sharma and Sharma<sup>[33]</sup> who classified the kidneys into obstructed, non obstructed, and equivocal categories and suggested close follow-up with ultrasonography in patients having CTT >3 min and pyeloplasty if hydronephrosis increased during follow-up.

### **Can a delayed cortical transit time identify kidneys which will show improvement in function after surgery**

Many studies suggest that function does not always improve after pyeloplasty.<sup>[46-48]</sup> Delayed CTT has been found to be an important parameter, which suggests that the function could improve after surgery. Britton *et al.* were the first in 1979<sup>[19]</sup> to suggest that delayed CTT can help in classifying kidneys with unilateral hydronephrosis into those in whom surgery will improve the function and in those it will not. Similar results were noted by other investigators. Song *et al.*, in their study, evaluated the value of delayed CTT as a predictor of function improvement after pyeloplasty. They concluded that substantial renal improvement is seen in patients with delayed CTT and decreased DRF.<sup>[29]</sup> Jain *et al.* did not notice any improvement in function in most of their patients whose preoperative DRF was <40%. Undetected and irreversible damage due to delayed diagnosis was thought to be the reason for the same. They concluded that in poorly functioning kidneys, delayed CTT does not predict improvement postoperatively.<sup>[30]</sup> However, the majority of these patients had very poor DRF [Table 6].

**Table 5: Studies which looked at renal function when patients with normal cortical transit time were under follow up**

References	Patients with normal CTT	Patients showing deterioration of function during follow up
Schlotmann <i>et al.</i> 2009 <sup>[28]</sup>	85	3
Piepsz <i>et al.</i> 2011 <sup>[25]</sup>	3	0
Harper <i>et al.</i> 2013 <sup>[31]</sup>	11	0
Lee <i>et al.</i> 2017 <sup>[32]</sup>	17	1
Sharma and Sharma 2017 <sup>[33]</sup>	25	0

CTT=Cortical transit time

### **Comparison of Whitaker test with cortical transit time**

Whitaker test has long been considered the gold standard to diagnose obstruction in a dilated system,<sup>[49,50]</sup> Whitfield in 1977 and Britton *et al.* in 1979 compared the pressure values with the CTT (called Parenchymal transit time in those days) with what we know as the Whitaker test today. This was described as pressure-flow study or urodynamics of the renal pelvis.<sup>[19,35]</sup>

Whitefield found that out of the 12 cases diagnosed to have obstruction, 7 also showed obstruction on pressure-flow study, while 3 had equivocal and 1 had nonobstructive pattern.<sup>[35]</sup> Britton *et al.* found that there was perfect correlation between the CTT and pressure flow study of the renal pelvis in the 9 cases diagnosed as having obstruction and 4 having been diagnosed as non obstructive on pressure studies<sup>[18]</sup>. The drawback of both the studies was that they defined obstruction as pressure rise >15 cm of H<sub>2</sub>O as compared to 22 cm of H<sub>2</sub>O as mentioned by Whitaker test and there was no clear mention of indeterminate values on the pressure-flow study. Recently, Jain *et al.* did not do pressure-flow studies but measured the renal pelvic pressure intraoperatively and found it to be high in all the patients. However, they did not find any correlation between it and the CTT.<sup>[30]</sup>

### **Comparison of diuretic renography with cortical transit time**

Since the description of a furosemide induced diuretic renogram by O' reilly *et al.*,<sup>[51,52]</sup> the T ½ values and the drainage curves have been widely followed as parameters to define obstruction. There is now increasing evidence that because of the reservoir effect of the dilated renal pelvis and the variable protocols followed for diuretic renograms, these parameters can no longer be accepted as the gold standard.<sup>[14]</sup> While CTT has been evaluated as an alternative since 1977, only four studies have compared these parameters.

Britton *et al.* in 1987 were the first to compare Furosemide induced diuretic renogram with CTT. They found a good correlation between the two (<90%) and stated the combination of both these parameters would give an accurate assessment of outflow obstruction.<sup>[36]</sup>

However, in 1988, Verboven *et al.* did not find any correlation between CTT and response to furosemide.<sup>[37]</sup> Schlotmann *et al.* in 2009 found that of the 115 paired studies, 14 had a delayed CTT (described as Tissue Transit Time) and all these also had an obstructed response to furosemide. Out of the 85 kidneys with Normal CTT, 15 had an obstructive, 36 had an equivocal and 34 had a normal response to furosemide.<sup>[28]</sup> They, however, had a CTT in a range of 2-6-8 min which again, thus cannot be compared with many present studies which follow the now more widely accepted 3 min cut off.

**Table 6: Studies which looked at improvement of function after surgery and its relation to the preoperative cortical transit time**

Reference	Number of patients showing delayed CTT	Number of patients showing improvement after surgery	Number of patients undergoing surgery with normal CTT	Number of patients with normal CTT showing improvement in function postsurgery
Britton <i>et al.</i> 1979 <sup>[19]</sup>	14	11	4	0
Schlotmann <i>et al.</i> 2009 <sup>[28]</sup>	13	8	15	0
Piepsz <i>et al.</i> 2011 <sup>[25]</sup>	15	10	3	1
Duong 2013 <sup>[33]</sup>	6	5	11	2
Song <i>et al.</i> 2017 <sup>[29]</sup>	37	17	89	12

CTT=Cortical transit time

### What does the future hold?

Evidence shows that there is good interobserver agreement on estimating the CTT, but the importance of experience cannot be overlooked.<sup>[26]</sup> A question which should be solved by a multidisciplinary consensus is regarding the cutoff value of CTT. Although majority of the recent studies have used 3 min as the cutoff, this value has come from research by a single center and it needs to be confirmed by a multicenter study involving urologists and nuclear medicine experts. The question remains, whether 3 min be accepted as the cutoff with anything above it as delayed CTT or there should values which should be considered as indeterminate.

Most of the recent studies have used MAG3 as the radioisotope with the exception of Sharma and Sharma<sup>[33]</sup> who have used EC. Are the results comparable? Studies seem to suggest that the two isotopes are comparable.<sup>[53-55]</sup> However, again this needs confirmation from other centers utilizing EC for the estimation of CTT.

Another area of interest for investigators should be to look at the variation in CTT values in the renogram done at 1 month with those done later, i.e., at 3 months when the kidneys have matured and have better-excreting ability.

Although rationally CTT looks a very promising parameter and Piepsz *et al.*<sup>[25]</sup> have suggested that it may be the only parameter which could predict the need for surgery and functional improvement after surgery; a study from the same institute suggested that it cannot be the sole parameter and increasing hydronephrosis with thinning of the parenchyma cannot be overlooked.<sup>[43]</sup> A well-designed multicenter prospective trial can solve this dilemma. In a diuretic renogram a normal T<sub>1/2</sub> and a normal drainage curves exclude obstruction; similarly, a normal CTT excludes significant obstruction and combining ultrasonography with CTT to evaluate and manage these patients may be superior to CTT alone.<sup>[33,43]</sup>

There are parameters which evaluate the emptying, i.e., the excretory ability of the pelvis (e.g., – T<sub>1/2</sub> values) and there are parameters which look at the excretory ability of the parenchyma, perhaps combining the variables may be the method of choice. What the future studies could answer is how the data from both i.e., pelvic emptying and

concentrating and excretory ability of the parenchyma can be utilized to solve the dilemma to differentiate a dilated and obstructed system from a dilated but non obstructed system.

### CONCLUSION

Any new parameter has to stand the test of time against the established indices to prove its efficacy and superiority. As a predictive marker, CTT appears to be very promising and possibly better than the currently used T<sub>1/2</sub> and the renogram curve. With an increasing understanding of the pathophysiology of renal outflow obstruction and the pharmacokinetics of the present generation radionuclide tracers, CTT can answer important questions which are of clinical importance while dealing with a prenatally detected PPUJO.

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