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Percent of tracer clearance at 40 min in MAG3 renal scans is more sensitive than $T_{1/2}$ for symptomatic UPJ obstruction

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Abstract

Objective—To increase the diagnostic sensitivity of standard MAG3 diuretic renal scans for ureteropelvic junction obstruction (UPJO) by exploring the utility of an alternative measurement $P_{40,}$ the percentage of maximal tracer counts present at 40 minutes.

Methods—Patients with strong clinical and anatomic evidence for UPJO may have a normal $T_{1/2}$, making definitive diagnosis difficult. We reviewed the charts of 142 consecutive patients who underwent successful laparoscopic or robotic-assisted laparoscopic pyeloplasty for UPJO between 2005 and 2015. Both pre- and post-operative renal scan images were available for 37 symptomatic patients with primary unilateral UPJO and two kidneys. We defined P_{40} as the percentage of maximal tracer counts present at 40 minutes. We identified the upper limit of normal (97.5th percentile, +2SD) for P_{40} using the pre-operative renal scans from the unaffected kidney. We compared the sensitivity of P_{40} to $T_{1/2}$ to identify symptomatic UPJO.

Results—In our cohort, 51% of symptomatic patients (n=19) had a normal $T_{1/2}$ (Median 8.9 min; IQR: 7.5 min) and 49% (n=18) had an abnormal $T_{1/2}$ (Median: 40 min; IQR: 0 min). No patients had an abnormal P_{40} on their unaffected kidney. All patients with an abnormal $T_{1/2}$ also had an abnormal P_{40}. P_{40} increased the sensitivity of the renal scan from 49% (n=18/37) to 73% (n=27/37) when compared to $T_{1/2}$. The majority of patients (95%) demonstrated an improvement in P40 after pyeloplasty.

Conclusion—P_{40} markedly increases the sensitivity of a renal scan for diagnosing symptomatic UPJO and may be another valuable marker in addition to $T_{1/2}$ to document functional improvement in drainage after pyeloplasty.

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Keywords

UPJ obstruction; renal scans; pyeloplasty; radiology; renogram; pyeloplasty

Introduction

The diagnosis of clinically significant ureteropelvic junction obstruction (UPJO) requires a comprehensive work-up including a history, physical examination, functional imaging and an endoscopic evaluation.[1] Diuretic renography can provide functional evidence to help identify patients who may benefit from surgical intervention and is a mainstay of the preoperative work-up. The traditional interpretation of renal scans depends on the calculation of the time to 50% tracer clearance after diuretic administration ($T_{1/2}$).[2]

The optimal approach for both the interpretation of excretory renogram curves (i.e. visual analysis versus a quantitative index) and the timing of diuretic administration with various protocols (F-15, F0, F+20) remains controversial. The Consensus Committee of the Society of Radionuclides in Nephrourology recommends the F+20 protocol that prescribes furosemide injection at 20 minutes following tracer administration.[3] A $T_{1/2}$ of > 20 min is strongly suggestive of obstruction. Improvement in $T_{1/2}$ to ≤ 20 min following pyeloplasty is deemed evidence for resolution of obstruction.[2] However, a significant number of patients present preoperatively with compelling clinical symptoms and anatomic evidence of UPJO but equivocal $T_{1/2}$ (>10 but <20min) and many continue to show a delayed $T_{1/2}$ despite complete resolution of symptoms postoperatively.[4]

The use of $T_{1/2}$ to assess obstruction has significant limitations, as this value captures only a small subset of the information stored in a renal scan drainage curve. In many cases, the $T_{1/2}$ conflicts with a patient's clinical status and can confuse diagnosis and counseling. A substantial number of patients who have compelling clinical histories of flank pain and anatomic imaging consistent with UPJO have “non-obstructed” renal scans by $T_{1/2}$.[4] How to use this information in both the pre and postoperative settings remains controversial.

The morphology of 99mTc-MAG3 diuretic renogram drainage curves can vary between patients. We hypothesized that $T_{1/2}$ may not be adequately conveying the information needed to assess obstruction in some cases, and we hypothesized that a measurement that does not depend on the maximal tracer being present at furosemide administration (e.g. large collecting systems continue to fill after furosemide) would identify additional patients with clinically relevant UPJO. We defined a new measurement which is the percent of maximal tracer that is still present at 40 minutes (P_{40}). P_{40} can be easily abstracted from a standard MAG3 renogram (Figure 1).

Materials and Methods

Data collection and database use were approved by our institutional review board and compliant with the terms of the Health Insurance Portability and Accountability Act (HIPAA) with waiver of requirement for informed consent. We retrospectively reviewed records of 146 consecutive adult patients undergoing laparoscopic or robotic-assisted dismembered pyeloplasty for UPJO between 2005 and 2015 by one of two surgeons (REL and WAM).

Inclusion criteria were adult patients who had undergone successful pyeloplasty with two native kidneys and symptoms of unilateral obstruction who had undergone both pre-operative and post-operative 99mTc-MAG3 diuretic renography. Exclusion criteria included: (1) vesicoureteral reflux, (2) chronic kidney disease as defined by glomerular filtration rate (GFR) < 60 mL/min/1.73m^2, (3) ectopic pelvic kidneys and (4) prior renal transplantation. Patients with secondary UPJO following previous endopyelotomy were not excluded from the analysis. In all cases, a standard 99mTc-MAG3 diuretic renal scan protocol was performed with recording for at least 40 minutes and IV furosemide (40 mg) was injected at the 20-minute time point in the majority of patients (78%, n=29). Patient demographics are listed in Table 1.

We identified two groups of patients who had undergone successful pyeloplasty for symptomatic UPJO and were followed with renal scans. Success in this setting was defined as (a) complete resolution of UPJO symptoms and (b) stable differential renal function on follow up renal scan. By comparing patients with preoperative $T_{1/2} \leq 20$ min and > 20 min both before and after surgery, we sought to determine if P_{40} could identify more patients with clinically relevant UPJO than $T_{1/2}$. We defined P_{40} as the percent of maximal tracer that is still present at 40 minutes (Figure 1).

We utilized the renogram data from the pre-operative contralateral unaffected kidney to determine an upper limit of normal for the P_{40} value (97.5th percentile, +2SD). We validated the reproducibility of this value by comparing the pre-surgical P_{40} values in the unaffected kidneys to the post-surgical P_{40} values in the unaffected kidneys. We compared the sensitivity of P_{40} to identify symptomatic UPJO to $T_{1/2}$. We also investigated which patients had normalization of their abnormal P_{40} value after surgery. Statistical analysis utilizing paired t-test was performed with R version 3.2.3. P-values of <0.05 were considered statistically significant.

Results

Thirty-seven patients met inclusion criteria and were included for analysis (Table 1). 19 patients (51%) presented with a normal $T_{1/2}$ (Median 8.9 min; IQR: 7.5 min) and 18 (49%) with an abnormal $T_{1/2}$ (Median: 40 min; IQR: 0 min). Using data from the unaffected kidney, we determined that the upper-limit of normal (97.5th percentile) for P_{40} in our population was 0.244 (24.4%). We validated this range using values from the unaffected kidney on the post-operative renal scan and found that no unaffected kidneys had an abnormal P_{40} (Figure 2). Pre-operatively, 73% (n=27) of patients had an abnormal P_{40}, whereas only 49% (n=18) had abnormal $T_{1/2}$. All patients with an abnormal $T_{1/2}$ also had an abnormal P_{40} (Figure 3).

In the diagnostically challenging subset of patients with symptomatic UPJO and a normal $T_{1/2}$, P_{40} identified an additional 47% (n=9) of patients as abnormal, increasing the sensitivity of the renal scan from 49% to 73% (Figure 3; p = 0.032). All patients with an abnormal preoperative $T_{1/2}$ showed an improvement in P_{40} after pyeloplasty (Median: 0.842 vs. 0.336, p<0.01). 84% (n=16) of patients with a normal preoperative $T_{1/2}$ had a significantly lower P_{40} post-pyeloplasty (Median: 0.206 vs. 0.136, p<0.01) (Figure 2). Normalization of P_{40} occurred in 15 patients (56%) with a pre-operatively abnormal P_{40} value. Patients with a normal $T_{1/2}$ and an abnormal P40 had a normalization rate of 78% (n=7/9; Figure 3). 12 (32%) patients had <40% differential renal function (DRF) in their affected kidney.

Comment

Here we demonstrate that P_{40} is a simple measurement requiring no additional testing that can substantially improve the sensitivity of a diuretic renogram to detect clinically significant renal obstruction even in the setting of a normal $T_{1/2}$. The reduction in P_{40} following pyeloplasty with resolution of symptoms supports this measurement as an indicator of flow.

A renal scan is an important test to support surgical intervention in a suspected case of UPJO. While there are specific recommendations on how a renogram should be performed in suspected UPJO, we encountered significant institution-to-institution variation in practice.[3, 5] Variation was frequently due to nonstandard performance of the test or inaccurate interpretation. Even when the renal scan is performed correctly, it may not indicate obstruction despite the presence of clinical symptoms and hydronephrosis on imaging. An equivocal renal scan in a patient with symptoms of UPJO presents the clinician with a dilemma regarding definitive management. There is conflicting data on patients with an equivocal renal scan.[6] A recent study from Fontenot et al. reported less symptom relief in patients with a normal preoperative $T_{1/2}$ but symptom relief was not recorded in a standardized manner. A second study from Ozayer et al. reported mutual symptom relief in patients after pyeloplasty regardless of any evidence of obstruction on the preoperative renal scan.[7] In our cohort, a relatively high number of patients had a normal T1/2 that ultimately underwent pyeloplasty and achieved symptomatic relief. We confirmed the presence of UPJO with retrograde ureterograms for patients who had a compelling history for UPJO with a normal $T_{1/2}$ hprior to pyeloplasty. In our own clinical practice, we consider relief of symptoms the single most important data point. While subjective improvement is difficult to capture numerically the patient's satisfaction will guide further management. Postoperative renal scans should also be utilized to document stable kidney function over time.

The F+20 diuretic protocol is the accepted initial technique of choice to differentiate between a non-obstructive dilatation and clinically relevant obstruction. The estimated reporting of ‘equivocal results’ in most series is 15%.[7-9] In our series, 52% had equivocal $T_{1/2}$ which may be attributed to testing at various independent radiological centers outside of our tertiary referral institution. We found a wide range of nonstandard protocols being used at these centers to perform MAG3 renal scans and great divergence in the interpretation of results on radiographic reports. For patients with an equivocal renal scan, the recourse may be to repeat the study with a standard diuretic protocol or to perform a Whitaker antegrade pressure flow study which requires more invasive intervention and is not readily available in all clinical settings.

Alternative renal scan measurements have been described such as the renal tissue tracer transit time (TTT) or the “single (or differential) kidney function <40%” in identifying kidneys that require surgical repair.[10, 11] The TTT is conceptually somewhat similar to P_{40} and illustrates the tracer transit from parenchyma to the collecting system. TTT monitors kidneys with a large collecting system that show a delayed drainage pattern but no obstruction. Nevertheless it has the disadvantage of relying on a visual assessment of the actual scan images and appears to be less reproducible than the calculated tracer clearance and less objective than the quantifiable P_{40} clearance parameter. Our series did not identify differential renal function (DRF) to be indicative of outcome. While DRF did differ between the affected and control kidneys pre-operatively, it did not improve significantly following surgery. This pattern was consistent throughout both groups and may be related to irreversible kidney damage from long term UPJO.

P_{40} is a novel variable that can be easily extracted from the diuretic curve and is defined as the percent uptake of tracer at 40 minutes compared to maximum tracer uptake. On assessment of the renogram curves, there are several characteristics of P_{40} that lend credibility to its potential utility. The longer time interval provides a more accurate measurement of slower filling and draining collecting systems. By measuring tracer counts at 40 minutes, large collecting systems are given time to clear the tracer in the absence of an obstructive component. Furthermore, taking the value at maximum tracer uptake instead of tracer at time of furosemide exclusively covers the entire excretion phase, which is crucial for drainage assessment. To start at the time of furosemide injection may include the tail end of tracer uptake or miss the initial part of the excretion phase on the descending curve, which may not incorporate the true excretory urodynamics of the upper tracts.

The strength of P_{40} is that it identified all patients who would have been diagnosed with a significant obstruction by $T_{1/2}$, and captures additional patients that $T_{1/2}$ missed. Furthermore, the majority of patients with a normal $T_{1/2}$ but an abnormal P_{40} had complete normalization of their P_{40} value after surgery, which strongly supports the capability of P_{40} to identify clinically relevant obstruction. Future prospective studies will be required to validate P_{40} for the diagnosis of UPJO and to determine if P_{40} should supplant $T_{1/2}$ as the diagnostic measurement of choice or if it should be used as an adjunct in those patients with symptoms of UPJO and an equivocal $T_{1/2}$.

There are several key strengths and weaknesses of our study that merit discussion. One of the strengths was our ability to make comparisons between pre and postoperative P_{40} and $T_{1/2}$ values, and to compare these changes to an internal control, the unaffected contralateral kidney. In most published studies, the preoperative scans were used solely for deduction and analysis of diagnosis without taking into consideration postoperative outcomes. This is important as there are cases of persistently prolonged $T_{1/2}$ on post-operative renal scans that could represent a ‘reservoir effect’ with increase pelvis capacity as compared to a true secondary UPJO. P_{40} may potentially address this. In this study, all included patients were determined to have clinically significant UPJO that resolved after surgery. The number of patients studied was limited by the availability of both pre and postsurgical renograms of suitable quality and standard protocol in the majority of patients screened. Our practice is a tertiary referral center for many secondary UPJO cases. Because of this, most preoperative imaging studies were done at outside institutions which often did not adhere to the standard renal scan protocol. Lastly, this study is retrospective in nature and as a result our findings will need to be validated in a prospective cohort.

Conclusions

P_{40} markedly increases the sensitivity of a renal scan for the diagnosis of a clinically significant UPJO and may be particularly useful in diagnosing the patient with symptoms of UPJO despite an equivocal $T_{1/2}$.

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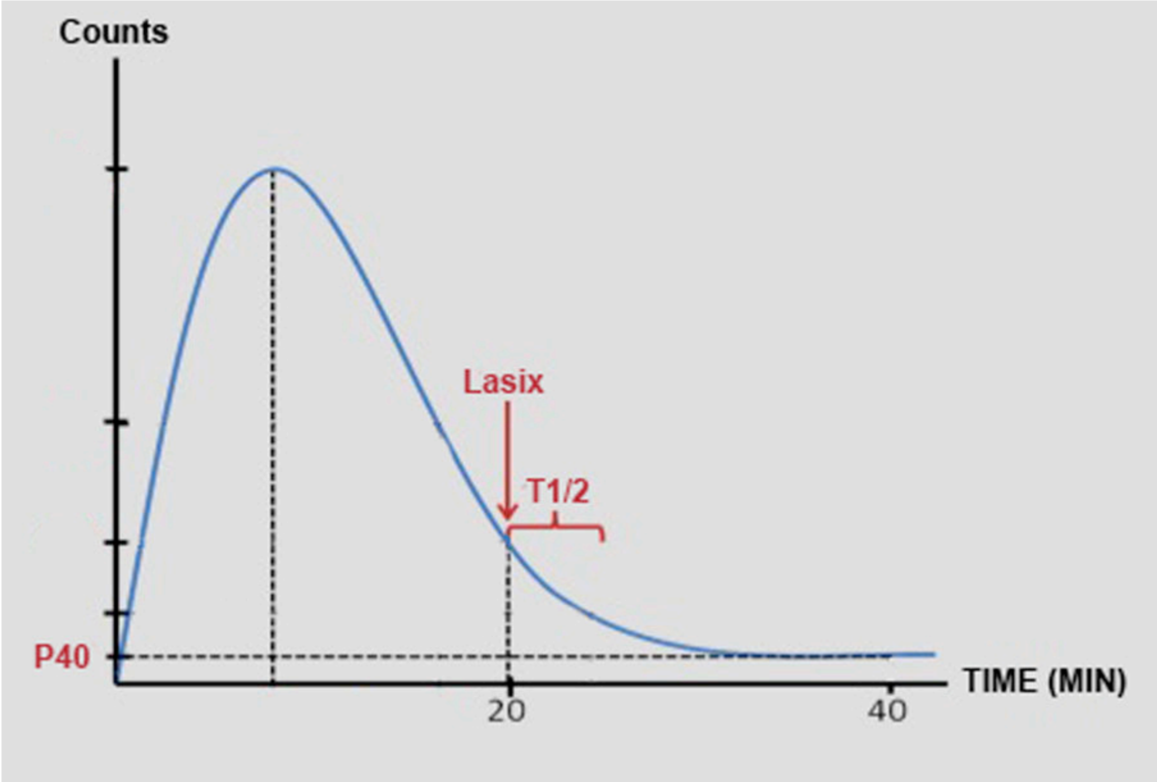

Figure 1.
Representative renogram curve demonstrating the $T_{1/2}$ and P_{40} value measurements.

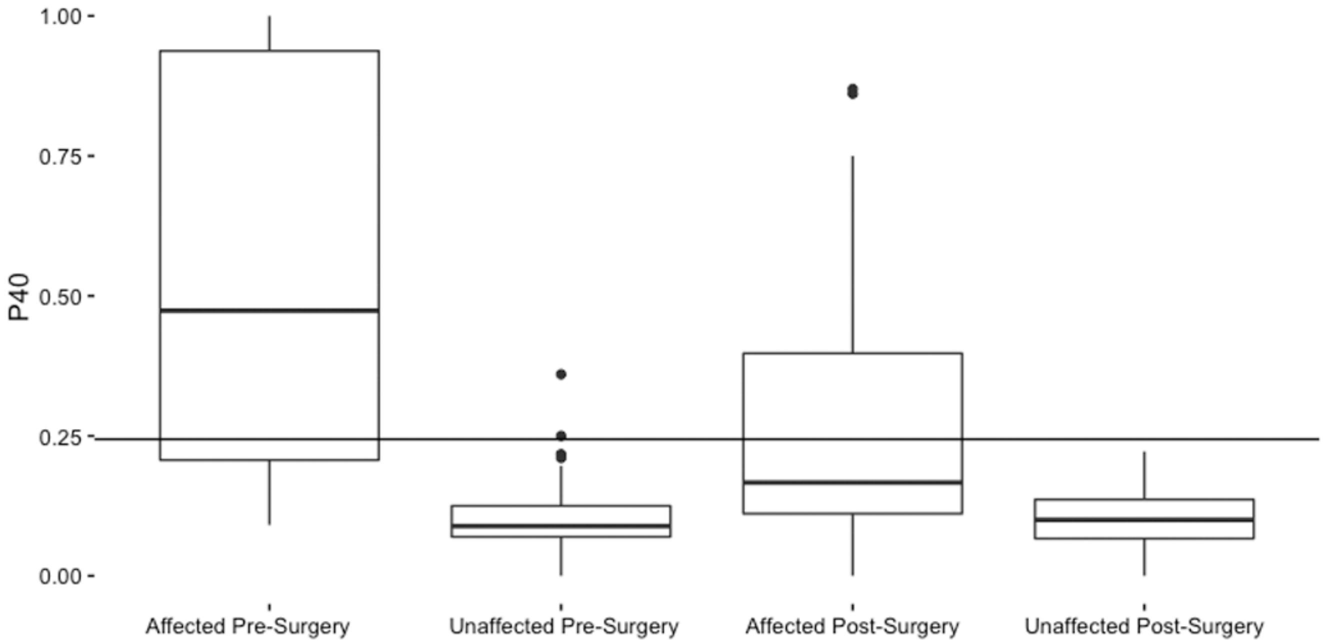

Figure 2.

Pre- and post-surgical P_{40} values in the affected and unaffected kidneys. The horizontal line represents the upper limit of normal for P_{40} (97^{th} percentile).

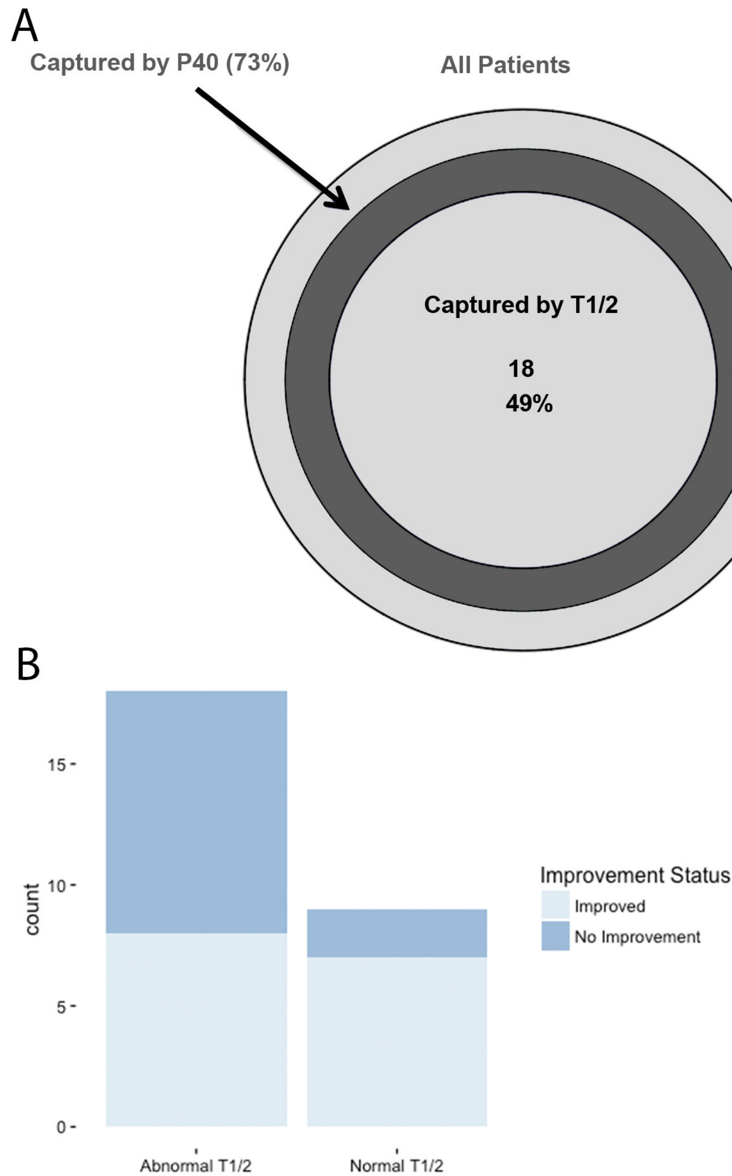

Figure 3.

(A) Euler diagram representing the patients that were identified as abnormal by $T_{1/2}$ (innermost circle), patients that were abnormal by P_{40} (second circle, encompassing all abnormal $T_{1/2}$ patients). The outer circle represents all patients included in the study, including those with normal P_{40} and $T_{1/2}$ despite having clinically relevant UPJO. (B) The number of patients who had normalization of their P_{40} after surgery with a pre-operatively abnormal P_{40} and either a normal or abnormal $T_{1/2}$.

Table 1

Subject demographics

	N = 37
Age (y)	42 ± 16
Gender	12M/25F
Abnormal $T_{1/2}$	18/37 (48.6%)
Abnormal P_{40}	27/37 (73.0%)
Differential Renal Function <40%	12/37 (32.4%)