How Should We Measure the Anteroposterior Diameter (APD) of the Renal Pelvis in Congenital Hydronephrosis?

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III. Abstract

Introduction

The anteroposterior diameter (APD) of the renal pelvis is a commonly used ultrasound parameter in the evaluation and management of hydronephrosis. It has been established that an APD value associated with pyeloplasty is around 25 mm. Some believe the APD should be measured at the innermost part of the renal pelvis while others suggest that it should be done at the renal contour. However, there is no consensus on the optimal APD measurement technique including whether it should be measured supine or prone. This study compared six different techniques of APD measurements, in both supine and prone positions, and further evaluated their association with pyeloplasty.

Methods

Data was obtained by retrospectively reviewing patients' charts that had initial high-grade hydronephrosis (HGH) from 2008 to 2014. We recorded the patients' demographics, ultrasound data and management choice. In the mid-renal transverse plane, the APD was measured by 2 blinded investigators, at the intra-renal, renal contour and extra-renal regions of the renal pelvis in supine and prone positions. We compared the six APD measurements based on the outcome of management (pyeloplasty vs. conservative management). The ROC curve obtained was then used to assess the ability of various APD measurements in predicting surgical intervention. The cutoff value chosen that predicts pyeloplasty was the lowest diameter with 100% specificity.

Results

We included 129 patients (134 renal units). Forty-four renal units (42 patients) underwent pyeloplasty whereas 90 renal units (87 patients) were managed conservatively. Patients' demographics were grouped by both SFU grade and clinical outcome. Regardless of grade, the

APD measurements were different in all 6 techniques. All APD measurement techniques showed good inter-rater reliability. Based on the ROC curve, all APD measurements were associated with pyeloplasty with an AUC from 0.89 to 0.91. The supine extra-renal APD measurement of 24mm was the most sensitive cutoff value. The cutoff values ranged from 18 to 27mm when including patients from all grades of hydronephrosis. The median APD measurements were significantly less for SFU grade 3 than grade 4 hydronephrosis in all positions ($P<0.001$ for all measurements), yet the predictive cutoff value of 24mm for the supine extra-renal was similar for both grades.

Conclusion:

APD measurements differ based on the technique, but they are all equally associated with the clinical outcome of pyeloplasty. The inter-rater reliability of all techniques were excellent. Though the median APD measurements are smaller in SFU grade 3, it appears that the cutoff for a predictive renal pelvic APD does not differ between SFU grades 3 and 4 for the supine extra-renal technique. We conclude that the technique for measuring the APD needs to be specified in studies of hydronephrosis and in any grading systems.

IV. RÉSUMÉ

Introduction

Le diamètre antéropostérieur (DAP) du bassinet rénal est un paramètre échographique couramment utilisé dans l'évaluation et la gestion de l'hydronéphrose. Il a été établi qu'une valeur DAP pour prédire une pyéloplastie est d'environ 25 mm. Certains croient que le DAP devrait être mesuré à la partie la plus interne du bassin rénal tandis que d'autres suggèrent qu'elle devrait être faite au niveau du contour rénal. Cependant, il n'y a pas de consensus sur la technique de mesure optimale de DAP, y compris si elle doit être mesurée en décubitus ventral ou dorsal. Cette étude a évalué six techniques différentes de mesure du DAP, en position couchée et couchée, afin de trouver la méthode optimale pour prédire une pyéloplastie.

Méthodes

Les données ont été obtenues en examinant rétrospectivement les dossiers des patients présentant avec une hydronéphrose de haut grade (HGH) initiale de 2008 à 2014. Nous avons enregistré les données démographiques des patients, les données échographiques et le choix de prise en charge. Dans le plan transversal mi-rénal, le DAP a été mesuré par 2 investigateur aveugle, au niveau intrarénal, du contour rénal et des régions extrarénales du bassinet rénal en décubitus ventral et dorsal. Nous avons comparé les six mesures APD sur la base des résultats de la gestion (pyéloplastie vs gestion conservatrice). La courbe ROC obtenue a ensuite été utilisée pour évaluer la capacité de diverses mesures APD à prédire une intervention chirurgicale. La valeur limite choisie pour prédire la pyéloplastie était le diamètre le plus bas avec une spécificité de 100 %.

Résultats

Nous avons inclus 129 patients (134 unités rénales). Quarante-quatre unités rénales (42 patients) ont subi une pyéloplastie alors que 90 unités rénales (87 patients) ont été gérées de façon conservatrice. Les données démographiques des patients ont été regroupées par grade SFU et résultat clinique. Indépendamment du grade, les mesures APD étaient différentes dans les 6 techniques. Toutes les techniques de mesure de l'APD ont montré une bonne fiabilité inter-juges. Sur la base de la courbe ROC, toutes les mesures d'APD étaient associées à une pyéloplastie avec une ASC de 0,89 à 0,91. La mesure d'APD extra-rénale en décubitus dorsal de 24 mm était la valeur seuil la plus sensible. Les valeurs seuils variaient de 18 à 27 mm en incluant des patients de tous les grades d'hydronéphrose. Les mesures médianes de l'APD étaient significativement inférieures pour l'hydronéphrose de grade 3 SFU par rapport au grade 4 dans toutes les positions (P <0,001 pour toutes les mesures), mais la valeur seuil prédictive de 24 mm pour l'extra-rénal en décubitus dorsal était similaire pour les deux grades.

Conclusion

Les mesures d'APD diffèrent selon la technique, mais elles sont toutes également associées au résultat clinique de la pyéloplastie. La fiabilité inter-évaluateurs de toutes les techniques était excellente. Bien que les mesures médianes d'APD soient plus petites dans le grade 3 de la SFU, il semble que le seuil pour une APD pelvienne prédictive ne diffère pas entre les grades 3 et 4 de la SFU pour la technique extra-rénale en décubitus dorsal. Nous concluons que la technique de mesure de l'APD doit être précisée dans les études sur l'hydronéphrose et dans tout système de classement.

IV. Acknowledgement

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V. Contribution of Authors

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VI. Review of Literature

i. Prevalence of ureteropelvic junction anomalies:

Congenital hydronephrosis is detected prenatally in 1-2 % of total pregnancies during routine prenatal sonography [1,2]. The incidence of ureteropelvic junction (UPJ) anomalies, known also as isolated hydronephrosis, comes second to transient hydronephrosis (10-30%)[3].

ii. Nature and Pathogenesis of Isolated hydronephrosis:

Isolated hydronephrosis (IH) is defined by an exclusive dilatation of the pelvicalyceal system without ureteral dilatation. It can be caused by UPJ stenosis or obstruction (**Figure 1**). In the majority of cases, IH is caused by atretic UPJ but few cases can present later in childhood due to a crossing vessel that externally compresses the UPJ (**Figure 2**) [4]. Other causes of UPJO include valvular mucosal folds, persistent fetal ureteral convolutions, and ureteral polyps [5,6].

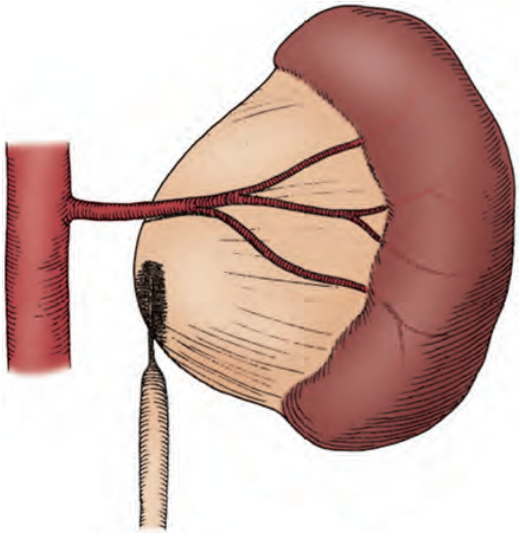

Figure 1 Atretic segment causes ureteropelvic junction obstruction.

From: L. Henning Olsen,and Yazan F. H. Rawashdeh. Surgery of the Ureter in Children. Campbell Walsh Urology. Eleventh ed. Philadelphia,: Elsevier,inc; 2016: 3057-74

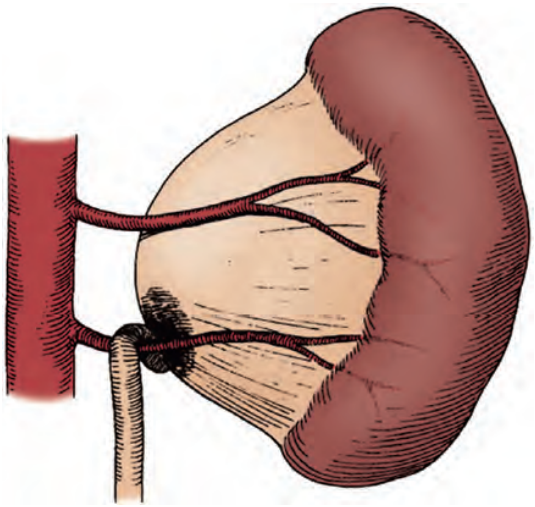

Figure 2 A crossing vessel contributes to a significant kinking of ureteropelvic junction

From: L. Henning Olsen,and Yazan F. H. Rawashdeh. Surgery of the Ureter in Children. Campbell Walsh Urology. Eleventh ed. Philadelphia,: Elsevier,inc; 2016: 3057-74

iii. **Presentation of isolated hydronephrosis**. (**Prenatal vs postnatal)**

Isolated hydronephrosis can be presented either prenatally or postnatally.

A) <u>Prenatal presentation:</u>

The majority of cases are detected during routine prenatal ultrasound follow up of pregnancy. Fetal ultrasonography is typically performed in the mid-second trimester. has significantly changed the presentation, evaluation, and management of prenatal hydronephrosis. Prenatally, isolated hydronephrosis is by far the most common entity detected. APD is the most commonly used grading system in the prenatal assessment of hydronephrosis[7]. Although APD cannot specifically help identify pathology, the ultrasonographic finding of unilateral renal pelvic dilation without ureteral dilatation is usually suggestive for isolated hydronephrosis [8].

In 1991, Corteville et al descried the standard for renal pelvic dilation. In their study, an APD greater than 4 mm at 33 weeks of gestational age or greater than 7 mm at 40 weeks had a sensitivity of 100% in predicting patients with abnormal renal function or those who required surgical intervention postnatally[9]. In their metanalysis, Zhang et al. found that a cutoff fetal APD with 25 mm had sensitivity and specificity of 0.81 (95% CI 0.60 to 0.92) and 0.78 (95% CI 0.68 to 0.86), respectively, for predicting pyeloplasty [10].

B) <u>Postnatal presentation:</u>

Most children present during their first year of life due to prenatally detected hydronephrosis. The minority of cases could present with febrile UTI or later in life with renal colic [4]. The postnatal assessment of prenatal hydronephrosis includes a

postnatal ultrasound during the first 1-2 months after delivery. Only patients with bilateral severe prenatal hydronephrosis should be evaluated immediately after delivery to avoid compromised renal function. If the pelvic dilatation disappears after delivery, it is considered transient hydronephrosis and the patient should be discharged [11]. Patients with febrile UTI present in **most cases** with high fever (>39 °C) and the diagnosis is confirmed by the presence of pyuria and at least 50 000 CFUs per mL of a single organism in an appropriately collected specimen of urine [12]. Renal colic in older children is likely caused by the presence of a crossing renal vessel and mostly associated with nausea and vomiting [13].

IH or UPJ obstruction may be associated with other genitourinary anomalies, for instance, a horseshoe kidney [14]. Moreover, it could be a component of a syndrome such as CHARGE syndrome (coloboma, heart anomaly, choanal atresia, retardation, genital and ear anomalies) [15].

iv. Ultrasound role in the detection of UPJO (Prenatal and postnatal)

Ultrasound plays a crucial role in the evaluation and following up of children diagnosed with congenital hydronephrosis. The majority of congenital anomalies of the kidney and urinary tract associated with fetal hydronephrosis can be detected by ultrasonography without the risk of radiation exposure [16]. This can be evident when we realize that before the extensive use of prenatal screening ultrasound, hydronephrosis was merely diagnosed with loin pain or Febrile UTI, and these patients were typically managed surgically after the diagnosis of the underlying pathology. These days, with the high probability of prenatal diagnosis, the majority of cases are asymptomatic [17].

The routine prenatal assessment of the fetal kidneys begins in the mid-second trimester, between 18 and 22 weeks of gestation [18]. Prenatally, hydronephrosis can be detected as pelvic dilatation which is often called “pyelectasis”. Even though pyelectasis can reflect obstructive uropathy, it is can reflect a normal physiological process. So, the need for objectively define significant pelvic dilation has been raised to avoid following up non-significant pyelectasis [19].

Isolated hydronephrosis is originally suspected if significant renal pelvic dilatation is observed without hydroureter; however, hydroureter is difficult to be assessed in utero unless hugely dilated [20]. The most famous grading system that objectively classifies hydronephrosis in utero is APD grading system which measures the maximal intrarenal pelvis dilatation [9]. Despite the fact that APD is the most important tool that predicts the postnatal outcome, other parameters can be assessed by ultrasound and significantly impact the outcome of congenital hydronephrosis. These parameters include oligohydramnios, parenchymal thinning and echogenicity [20].

Postnatally, ultrasound should be avoided in the first 48-72 hours after birth, because hydronephrosis may be underestimated due to extracellular fluid shifts. Nevertheless, infants with bilateral hydronephrosis and those with hydronephrosis of a solitary kidney likely require urgent evaluation within the first two days of life because of the high possibility of significant renal function deterioration and may need early intervention[3]. Despite the presence of many grading systems that evaluate postnatal hydronephrosis, APD is considered the most important objective tool for assessment [21-23]. Due to its importance in predicting the outcome of hydronephrosis, APD is

included within the six parameters in the newly developed Urinary Tract Dilation Classification System that was introduced the Society for Fetal Urology in 2014 [20].

Isolated hydronephrosis or UPJ obstruction is highly suspected when the pelvicalyceal system is severely dilated without distal ureteral dilatation. This is because the probability of the diagnosis of vesicoureteral reflux is very low[24]. Interestingly, the role of ultrasound is not limited to the initial evaluation of hydronephrosis but also it is considered a crucial tool for hydronephrosis follow-up [25]. The need for other investigations in patients with improving isolated hydronephrosis is very low and not recommended [26].

v. APD role in the management of IH

- *Advantages and disadvantages of APD*

Corteville et al evaluated possible renal pelvis diameters including length of the renal pelvis, transverse renal pelvic diameter and renal pelvic length in addition to renal parenchymal thickness and renal length. The transverse diameter of the renal pelvis, which resembles the APD, was measured in the axial plane through the fetal abdomen. They found that is the most accurate predictor for the diagnosis of postnatal hydronephrosis[9]. Over many decades, the APD measurement showed to have many advantages in the prediction of pyeloplasty. One of these advantages is being easy to be measured. Moreover, it can perfectly predict the need for surgical intervention as well as the postoperative outcome [27,28]. One more merit is that is can be used prenatally and postnatally[9,10]. Lastly, it is an objective predictor which may have superior results in comparison with subjective grading systems[10].

Despite its usefulness in the assessment and follow up of hydronephrosis, APD has some limitations. Firstly, APD only measures the collecting system dilatation and may not accurately reflect the hydronephrosis grade. Secondly, the inter- and intra-observer reproducibility of APD measurement are not well determined. Moreover, calyceal dilation or parenchymal status (as echogenicity or thinning) are no considered in the APD grading [3].

– ***Methods of APD measurement:***

Although APD is measured in the transverse renal plan, there is no wide agreement about the ideal way to measure it. APD could be measured at the renal contour or the widest diameter of the intrarenal pelvis. In their multidisciplinary consensus, Nguyen et al. recommended measuring APD at the maximal diameter of the intrarenal pelvis (Figure 3) [20]. Other studies measured APD at the renal contour in the mid-renal transverse view [27,29,30]. APD measurement of the extrarenal pelvis was never reported in the literature. Nevertheless, there is no direct comparison of different measurement locations especially the intrarenal and extrarenal locations.

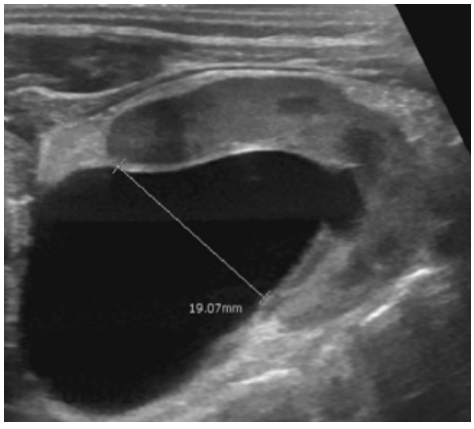

Figure 3 APD was measured at the maximal intrarenal pelvis diameter

From Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). J Pediatr Urol. 2014;10(6):982-998. doi:10.1016/j.jpurol.2014.10.002

Regarding the patient position, APD can be measured in both supine and prone positions. Despite being less popular than the supine position, the prone position has a better interobserver agreement and more frequently visualize calyceal dilatation. It is also observed that APD in the prone position is greater than that in the supine position for the same renal unit [31]. **Despite the fact that APD has been implicated in the evaluation of isolated hydronephrosis, the measurement agreement (interrater reliability) is not well evaluated in most studies. This is considered a pitfall in the literature especially if we depend on APD as an important tool in evaluating every single patient with hydronephrosis. The need for a study to evaluate the interrater reliability of all possible APD measurements methods is intensely needed.**

- ***Interpretation of APD***

In utero, AHN is classified into 3 categories according to APD measurement in the 2nd and 3rd trimester (**Table1**).

Degree of ANH	Second trimester	Third trimester
Mild	4 to <7 mm	7 to <9 mm
Moderate	7 to ≤10 mm	9 to ≤15 mm
Severe	>10 mm	>15 mm

Table 1Degree of AHN according to APD

From *Nguyen HT, Herndon CD, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. J Pediatr Urol. 2010;6(3):212-231. doi:10.1016/j.jpurol.2010.02.205*

Until the moment, there is no wide agreement on the best APD value that determines the need for postnatal follow up. Coplen et al. used the maximum APD measurement for analysing the outcome of prenatal hydronephrosis. They recommended a 15 mm

cut-off value for determining obstructive pathology (sensitivity 73% and specificity 82%)[32]. In another study by Ismaili et al., they observed that a cut-off of 10mm, measured in the axial plane, in late gestational age could detect 23% of cases, while a cut-off of 7 mm defined 68% of cases [33]. However, during the relatively short follow up period (24 months), they did not limit their study to isolated hydronephrosis and included many types of hydronephrosis which can compromise their results. Lee et al. found in their metanalysis that only 11.9% of total cases presented with a 3rd-trimester

Time of detection of ANH	Severity of ANH	APD (mm)	Recommendations
2nd Trimester	Mild	<7	Consider 3rd Trimester US
	Moderate	7–10	3rd Trimester US
	Severe	>10	Repeat US in 3–4 weeks
3rd Trimester	Mild	<9	Postnatal evaluation
	Moderate	9–15	Postnatal evaluation
	Severe	>15	Repeat US in 2–3 weeks

Table 2 SPU recommendation for prenatally detected hydronephrosis

From *Nguyen HT, Herndon CD, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. J Pediatr Urol. 2010;6(3):212-231. doi:10.1016/j.jpurol.2010.02.205*

33.9) in moderate AHN and 54.3% (21.7- 83.6) for severe AHN [34]. Depending on the prenatal APD, the SPU suggested some recommendations regarding hydronephrosis follow up either prenatally or postnatally (**Table 2**) [3].

The Canadian Urological Association recommends performing renal ultrasound within the first 2 weeks of life if APD >15 mm in the 3rd trimester. Moreover, when APD ranges from 7 to 10 mm in the 3rd trimester, postnatal US can be performed in 1-3 months after birth. APD between 10 and 15 mm could be managed according to the SFU grade [11].

Despite the fact that APD showed to be associated with surgical intervention, the cutoff value of APD varied from one study to another. In a prospective multivariate analysis, Arora and colleagues evaluated the maximal APD of the renal pelvis as a predictor of pyeloplasty. APD was measured one week after birth on a transverse renal image. They found that initial postnatal APD and pre-operative differential renal function were the only independent predictors for pyeloplasty. Furthermore, they found that APD > 24 mm has a 73.1% sensitivity and 88% specificity[28]. Another study conducted by Dhillon, measured APD in the transverse renal plane one week after birth, recommended pyeloplasty in children who have APD more than 20 mm [35]. Dias and colleagues conducted a multivariate analysis to assess the accuracy of immediate postnatal maximal APD measurement in the prediction of pyeloplasty. They found that APD >16 mm (sensitivity of 99.8%, specificity of 89.5%, and OR 106) has been correlated with pyeloplasty[16]. Longpre et al. retrospectively evaluated possible predictors for hydronephrosis resolution. In addition to APD, they also evaluated parenchymal thinning and the SFU grade of hydronephrosis. They defined APD as the distance between the two parenchymal lips at the renal hilum in the mid-section transverse view. They found that APD and SFU grade of hydronephrosis were

independent predictors for resolution [36]. These studies lack standardized indications of pyeloplasty. Moreover, some did not clearly describe how APD was measured.

Sharma and colleagues evaluated the APD in the supine and prone positions to determine if the measurement difference between both positions predicted the outcome of hydronephrosis. APD was measured at the level of renal hilum initially in the transverse plane with the infant in supine position then in prone position. They observed that the APD was smaller in the prone position than in the supine position in patients with improved hydronephrosis, whereas those with no APD change in both positions had worsening of hydronephrosis and required subsequent surgical intervention [30]. In addition to the small number of included patients, the indications of pyeloplasty in this study were limited to the renogram findings which can be affected by the prematurity of the newborn kidneys.

- APD as a part of other hydronephrosis scoring systems

- Urinary Tract Dilation (UTD) classification system:In 2014, the Society for Pediatric Urology introduced a new system to replace the SFU grading system. The new system consists of two components (prenatal and postnatal) (**Figure 4**). Both components include APD as a primary parameter. APD in the UTD system

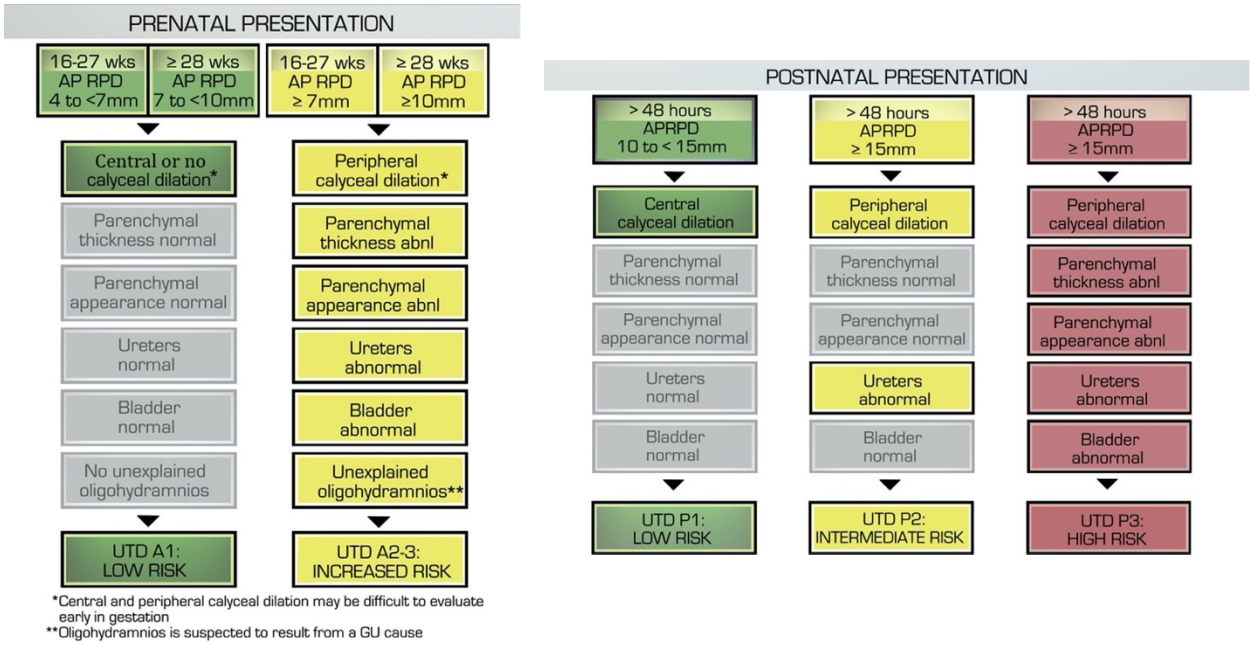

Figure 4 Prenatal and postnatal component of the UTD classification system

From Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). J Pediatr Urol. 2014;10(6):982-998. doi:10.1016/j.jpurol.2014.10.002

is defined as the maximal diameter of the renal pelvis in transverse renal scan**.** Normal dilatation is considered if APD <4 mm at <28 weeks gestation, <7 mm at 28 weeks, and <10 mm postnatally. Postnatal APD >15 mm is the lowest APD threshold for both moderate risk and high-risk UTD groups.

- Combined grading system:

A group from the sick kids' hospital in Toronto has proposed a new grading system of combined measures of the APD of the renal pelvis and calyceal dilatation. They compared the ability of the new grading system to better predict surgical intervention beyond standard assessments of the APD or SFU grading system. In their study, APD was defined as the greatest diameter of the renal pelvis acquired in a transverse plane on ultrasound images. APD was divided into 4 groups (APD,6 mm, APD>6–9 mm, APD>9–15 mm, and APD >15 mm). The combined grading system consists of one of the four APD groups in addition to the presence or absence of diffuse calyceal dilatation of all minor and major calyces. This system helped predict surgery fourteen folds higher for APD >9–15 mm with diffuse caliectasis than APD>9–15 mm alone [37]. As stated in most studies that evaluated pyeloplasty predictors, surgery is undertaken at the clinical discretion of the treating surgeon. Moreover, this study suffered from selection bias 12% of patients were excluded due to unavailable ultrasound studies. Even more, the definition of diffuse caliectasis is greatly subjective.

- APD ratios and percentages

- APD to parenchymal thickness (APD/PT)

APD/PT was introduced by Mudrik-Zohar et al as the best in-utero ultrasonographic predictor of postnatal surgical outcome. It showed better sensitivity than APD and PT separately. They found that the mean APD/PT ratio was 5.4 ± 4.5 for patients underwent pyeloplasty and 2.1 ± 1.4 for those conservatively managed. Moreover, they observed that an APD/PT ratio of >2.1 had a sensitivity of 87% and specificity of 65%

for predicting surgical intervention [38]. The authors did not clearly define the indications for pyeloplasty in their retrospective analysis. Despite the promising results of in-utero APD/PT ratio, there is a paucity of publications that evaluate the postnatal APD/PT ratio.

- Percentage worsening of APD (PW-APD)

PW-APD aims to quantify worsening hydronephrosis using serial APD measurements before pyeloplasty in patients with failed initial conservative management. The percentage worsening of the APD (PW-APD) was calculated by comparing APD at two time points; the First-Last US and the Previous-Last US. The PW-APD was significantly different between the Pyeloplasty and the Control group. It was noted that 100% worsening of the APD in the First-Last US and 59% APD worsening in the Previous-Last US was observed in renal units that had surgeries for worsening hydronephrosis [39]. These results are limited to a small group of pyeloplasties which were indicated due to worsening hydronephrosis. The definition of hydronephrosis is still subjective despite being reviewed by a single investigator.

- Role of APD in the postoperative assessment of IH

It was agreed that diuretic renogram is required after pyeloplasty to evaluate the persistence of obstruction. In 1996, Amling and colleagues evaluated the usefulness of ultrasound in the assessment of hydronephrosis post-pyeloplasty. They found that less than 91% of patients had improvement after pyeloplasty while pelvicalyceal dilatation completely resolved in only 19% of cases. However, they used the SFU grading system in their cohort which is interpreted subjectively [40]. Similar findings were

observed by Almodhen et al. who found that 90% of patients had improved hydronephrosis within the first 3 months after pyeloplasty [41]. The major limitation of these studies is that they used the SFU system to judge improvement which is highly subjective.

Being an objective tool that can predict pyeloplasty, APD was also studied to evaluate improvement of hydronephrosis after pyeloplasty. In a prospective study of 52 patients who underwent pyeloplasty, the preoperative APD and APD/PT ratio showed to be associated with the improvement of renal function. APD and APD/PT ratio were less than 50 mm and 15, respectively, in all patients with improved kidney function[41]. In another prospective study, APD was an independent predictor of improvement of hydronephrosis after pyeloplasty. Another study observed that a postoperative APD less than 11.5 mm or less was associated with success (100% sensitivity and 55% specificity) [29].

Rickard et al. evaluated the percentage improvement of APD (PI-APD) as a predictor of pyeloplasty success. In their study, pyeloplasty success was defined as resolved hydronephrosis (SFU ≤2 or APD ≤15 mm), symptoms free and/or drainage time on renal scan <20 min. PI-APD was calculated using the preoperative and 8-12 weeks APD postoperatively. In their study, 95% of patients who had post-pyeloplasty hydronephrosis improvement/resolution had PI-APD >40%. Therefore, they recommend to just follow such patients with APD >40% using ultrasound only and reserve postoperative renogram to patients with lower PI-APD if needed. Moreover, they noted that all recurrent UPJO patients had PI-APD of less than 20% and 5 out of

6 patients had 0% PI-APD [27]. Despite the fact that drainage times on renogram is better than ultrasound in evaluation of success of pyeloplasty in the first few months postoperatively, only 39% of patients had renograms to confirm resolved obstruction. However, this could be explained by that most urologists order renograms when hydronephrosis is worsening or not improved after pyeloplasty.

The value of postoperative APD/PT ratio was evaluated prospectively. Babu and Sai found that both APD and PT alone did not improve significantly at 3-months postoperatively. Interestingly, the APD/PT ratio showed great improvement post-pyeloplasty from 13.48 preoperatively to 5.73 at 3-month follow up [42]. Although this study was prospective, it included a small number of patients (24 patients). Hence, larger studies are mandatory to establish the usefulness of the APD/PT ratio.

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Study	Population	Study Design	Method of measurement	Outcome	Limitations
Preoperative Assessment					
Coplen et al [32]	257 patients	Retrospective	The maximum APD on a transverse plane	15 mm prenatal APD can be used as a threshold to detect obstruction.	- Retrospective. - Included pyeloplasties due to renal colic.
Ismaili et al [33]	5643 patients	Prospective	Measured in axial plane	APD≥7 mm was the best ultrasound criterion to predict postnatal uropathies	- No clear description of APD measurement. - Short follow up period. - Not confined to specific hydronephrosis pathology.
Arora et al [28]	84 patients	Prospective	The maximum APD on a transverse renal image.	APD >24 mm could predict the need for surgery.	- Multiple radiologists were involved. - Pyeloplasty indications were affected by financial and familial factors
Dhillon et al [35]	39 patients	Prospective	In the transverse renal plane.	Pyeloplasty is recommended when APD > 20 mm.	- Small group of patients. - Method of APD measurement is not clearly described.
Dias et al [16]	312 patients	Prospective	Maximal APD in the transverse plane	Postnatal APD > 16mm is predictive for pyeloplasty.	- Method of measurement is not clear. - Pyeloplasty indications were dependant on renogram findings.
Longpre et al [36]	100 patients	Retrospective	At the renal contour in the transverse plane.	The mean initial APD in resolved cases was 9.4 mm as opposed to 29.0 mm in cases requiring surgery	- Retrospective. - Two investigators measured APD.
Sharma et al [30]	38 patients	Prospective	At the renal contour in the transverse plane in supine and prone positions	No positional change in APD is associated with surgical intervention.	- Small number of population. - Indications of pyeloplasty is limited to renogram findings.

Dos Santos et al [37]	348 patients	Retrospective	Greatest diameter of the renal pelvis in a transverse plane	- The LR+ for surgery for diffuse caliectasis and APD>6–9 mm was higher than for APD>6–9 mm alone	- Retrospective. - Selection bias.
Mudrik-Zohar et al [38]	39 patients	Retrospective	At the transverse section of the fetal abdomen, in a sagittal cross section.	- APD14 mm was the best single predictor of the need for surgery. - A ratio of >2.1 of APD/PT suggests UPJO.	- Retrospective. - Small number of patients. - Indications of pyeloplasty are not clearly stated.
Hodhod et al [39]	37 patients	Retrospective	At the renal contour in a supine transverse plane	100% percent worsening of the APD in the First-Last US and 59% APD worsening in the Previous-Last US was observed in pyeloplasty	- Retrospective. - Small population. - Limited to pyeloplasties indicated due to worsening HN
Postoperative Assessment					
Romao et al [29]	192 patients	Retrospective	At the renal contour at the mid-renal transverse plane	A PI-APD of 38% or greater or postoperative anteroposterior diameter of 11.5 mm or less was associated with pyeloplasty success	- Retrospective. - Pyeloplasty is influenced by subjective judgment of the surgeon
Richard et al [27]	138 patients	Retrospective	At the renal contour at the mid-renal transverse plane.	<20% PI-APD permitted identification of all r recurrent UPJO cases	- Retrospective. - Poor definition of successful pyeloplasty.
Babu and Sai[42]	24 patients	Prospective	Maximum APD in coronal section	- APD reduction was not significant after 3 months. - The reduction in APT/PT ratio was significant at 3 months	Small population

Appendix 1: A summary table compares all prior studies that looked at measures of APD

Aim of thesis

1) To evaluate the interrater reliability and internal consistency of different techniques of APD measurements (inner, contour and extrarenal), in both supine and prone positions for patient presented in the first year of life with antenatal hydronephrosis due to isolated hydronephrosis.
2) To find if there are differences among these techniques according to the severity of hydronephrosis (SFU grade 3 and 4) and in the prediction of surgical intervention for antenatally detected isolated hydronephrosis.
3) To define the best cutoff value of each method in terms of incidence of pyeloplasty and renogram $T_{1/2}$ values ($T_{1/2}$ >20 minutes and >75 minutes).

VII. Manuscript:

How Can We Measure the Renal Pelvic Anteroposterior Diameter in Postnatal Isolated Hydronephrosis?

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Abstract:

Introduction

The anteroposterior diameter (APD) of the renal pelvis is a commonly used ultrasound parameter in the evaluation and management of hydronephrosis. It has been established that an APD value associated with pyeloplasty is around 25 mm. Some believe the APD should be measured at the innermost part of the renal pelvis while others suggest that it should be done at the renal contour. However, there is no consensus on the optimal APD measurement technique including whether it should be measured supine or prone. This study compared six different techniques of APD measurements, in both supine and prone positions, and further evaluated their association with pyeloplasty.

Methods

Data was obtained by retrospectively reviewing patients' charts that had initial high-grade hydronephrosis (HGH) from 2008 to 2014. We recorded the patients' demographics, ultrasound data and management choice. In the mid-renal transverse plane, the APD was measured by 2 blinded investigators, at the intra-renal, renal contour and extra-renal regions of the renal pelvis in supine and prone positions. We compared the six APD measurements based on the outcome of management (pyeloplasty vs. conservative management). The ROC curve obtained was then used to assess the ability of various APD measurements in predicting surgical intervention. The cutoff value chosen that predicts pyeloplasty was the lowest diameter with 100% specificity.

Results

We included 129 patients (134 renal units). Forty-four renal units (42 patients) underwent pyeloplasty whereas 90 renal units (87 patients) were managed conservatively. Patients' demographics were grouped by both SFU grade and clinical outcome. Regardless of grade, the

APD measurements were different in all 6 techniques. All APD measurement techniques showed good inter-rater reliability. Based on the ROC curve, all APD measurements were associated with pyeloplasty with an AUC from 0.89 to 0.91. The supine extra-renal APD measurement of 24mm was the most sensitive cutoff value. The cutoff values ranged from 18 to 27mm when including patients from all grades of hydronephrosis. The median APD measurements were significantly less for SFU grade 3 than grade 4 hydronephrosis in all positions ($P<0.001$ for all measurements), yet the predictive cutoff value of 24mm for the supine extra-renal was similar for both grades.

Conclusion: APD measurements differ based on the technique, but they are all equally associated with the clinical outcome of pyeloplasty. The inter-rater reliability of all techniques were excellent. Though the median APD measurements are smaller in SFU grade 3, it appears that the cutoff for a predictive renal pelvic APD does not differ between SFU grades 3 and 4 for the supine extra-renal technique. We conclude that the technique for measuring the APD needs to be specified in studies of hydronephrosis and in any grading systems.

Introduction:

Prenatal hydronephrosis is diagnosed in 1-5% of all pregnancies [1-4]. These cases are evaluated with an early postnatal ultrasound that is categorized into low and high-grade hydronephrosis [5,6]. Roughly 30% of all high grade isolated hydronephrosis will result in surgical intervention with the pyeloplasty technique [7,8]. In the absence of a gold standard definition of obstruction, the decision for pyeloplasty relies on evaluation of multiple parameters, including the antero-posterior diameter of the renal pelvis (APD). APD is an objective ultrasound parameter that has been suggested as an independent predictor of pyeloplasty [9,10] . Moreover, it has been used extensively in the prenatal assessment of hydronephrosis and as a part of the UTD grading system [11]. However, there is no consensus about the best way to measure APD. Some prefer to measure it at the maximum dilated part of the transverse plane of the intra-renal pelvis whereas others recommend taking the measurement at the renal contour [12-18]. In this study, we evaluate six different techniques of APD measurements, including 3 in supine and 3 in prone positions and evaluate the inter-rater reliability of each technique as the primary objective. In addition, as a secondary objective, we compare the associated measurements with the clinical outcome of pyeloplasty. We hypothesized that the measurements would differ amongst techniques and that each technique would have a different cutoff **associated** with pyeloplasty.

Patients and methods

After obtaining the approval of the ethics committee at our institution, we conducted a retrospective review of patients' charts who presented with AHN from 2008 to 2014. Only patients with high-grade isolated hydronephrosis (HGH) presenting in the first year of life were included, defined as SFU grade 3 and 4. We excluded patients who presented with febrile UTI. Moreover, patients with vesico ureteric reflux, duplex system, posterior urethral valve, megaureter, ureterocele and neurogenic bladder were also excluded.

We collected patients' demographics, side of hydronephrosis, laterality and the SFU grade of hydronephrosis of the initial ultrasound at presentation. The diuretic drainage half-time of the last mercaptoacetyltriglycine (MAG3) nuclear renogram performed closest to surgery was also recorded. All ultrasound images were reviewed by one pediatric urologist and one pediatric radiologist, blinded to the outcome. Any measurement with a difference greater than 2 mm was adjudicated by a second pediatric urologist. Ultrasound images were retrieved from the Picture Archiving and Communications System (PACS) at Montreal children hospital. Firstly, we reviewed the grade of hydronephrosis and only patients with HGH were elected for APD measurements. APD measurements were obtained in the supine and prone positions at the mid renal transverse plane which is defined as a mid-renal horizontal plane of the kidney where the renal pelvis can be identified within the renal hilum. APD was measured at the inner pelvis, renal contour and maximal extra-renal pelvic dilatation (Figure 1). Measurement of the inner pelvis was obtained at the widest diameter of the inner part of renal pelvis proximal to the renal contour. The contour measurements were defined as the anteroposterior diameter of the renal pelvis at the renal hilum. The extra-renal APD was measured at the widest part of the renal

pelvis distal to the renal hilum. A patient was excluded if we were not able to obtain any of these six measurements or if the patient age was less than 3 days of age.

We categorized the outcome of hydronephrosis in terms of surgical management (pyeloplasty) and conservative management (control group). Pyeloplasty was indicated, one of three pediatric urologists, in cases of worsening hydronephrosis, loss of split function of greater than 10%, or delayed drainage with split function < 40%. Worsening hydronephrosis is defined as upgrading of hydronephrosis using the SFU grading system or increased APD during follow up. Despite the retrospective nature of the study, all urologists participated in this study follow the same indications of pyeloplasty. The indication of pyeloplasty was retrieved from patient's charts. APD was not used as a parameter to determine worsening of hydronephrosis. A secondary analysis of the pyeloplasty group utilized a diuretic renogram half-time greater than 20 minutes or greater than 75 minutes as objective markers of clinical severity [19,20]. Conservative management entailed follow up with ultrasound every 2-3 months until improvement of hydronephrosis. Improved hydronephrosis was followed at greater intervals between ultrasounds. The Statistical Package for the Social Sciences (SPSS) V20 was used for statistical analysis. Categorical data were presented in numbers and percentages and compared using the Chi square test. Medians and ranges were used to present continuous data which were evaluated using non-parametric tests. To assess the reliability and consistency of APD measurements, we evaluated the inter-rater reliability using the intraclass correlation coefficient (ICC). In addition, Cronbach's alpha was used to test the internal consistency. The receiver operating characteristic (ROC) curve was used to evaluate the cutoff values of different methods of APD measurements. The cutoff value chosen that predicts pyeloplasty was the lowest diameter with 100% specificity. A p value less than or equal 0.05 was considered statistically significant.

Results

Of 626 patients who presented with AHN, we reviewed the charts of 261 patients who had HGH. We excluded patients with vesicoureteric reflux (28 cases), non-obstructing megaureter (30 patients), posterior urethral valve (3 patients), neurogenic bladder (6 patients), vesicoureteral junction obstruction (7 patients), and missed follow up (20 patients). A further 37 patients whose ultrasound images were of suboptimal quality were excluded, as well as one case age less than 3 days, leaving 129 patients (134 units) with isolated hydronephrosis for inclusion. A screening VCUG was performed in 92% (119 of 129) patients.

Of total eligible units, 44 renal units (42 patients) underwent pyeloplasty whereas 90 renal units (87 patients) were assigned to conservative management (control group). Indications for surgery included worsening hydronephrosis and diuretic drainage time in 16 (38%), initial split function less than 40% with prolonged diuretic drainage time in 15 (36%), a drop in split function to less than 40% in 6 (14%) and 7 (17%) with prolonged diuretic drainage time in the setting of functionally solitary kidney in 2 , bilateral high grade HN in 1, renal colic in 1, renal stone in 1, palpable mass in 1 and parental concern with observation in 1. The median age at surgery was 4.6 months (range 1-35).

Patients' demographics are presented in **Table 1**. For all included patients, the median age at presentation was 0.47 months (range 0.3-11.7) and the median duration of follow up was 38.4 months (range 8.9 -107.8). Notably, 75% of the pyeloplasty group had SFU grade 4 compared to 10% of the observation (control) group.

The median APD measurements obtained by the 6 different techniques are listed in **(Table 2**). The different APD measurements in SFU grade 4 were almost double those of the SFU grade 3 group. Regardless of grade, the intra-renal measurements were significantly smaller than the

APD measurements by other methods ($p < 0.001$ for both). The contour and extra-renal pelvis measurements differed in grade 4 but not in grade 3 hydronephrosis. with the extra-renal values being the largest. When comparing prone versus supine measurements, we found that there were no significant differences.

Using the ROC curve, all APD measurements were similarly associated with pyeloplasty with AUCs ranging from 0.89 to 0.91 (**Figure 2**). The cutoff values ranged from 18mm for the prone-inner technique to 27 mm for the supine-contour and prone extra-renal techniques, with the majority clustering at 24mm. The supine extra-renal cutoff of 24 mm was identical for both grades 3 and 4 hydronephrosis (ROC curve not shown).

All APD measurements showed good inter-rater reliability and acceptable internal consistency (**Table 3**). The adjudication of APD measurements with differences >2 mm is presented in **Table 4.** After adjudication, these measurements were still reliable and consistent without redundancy.

The use of diuretic half-times as an endpoint confirmed that all six techniques of APD measurement were equally associated with the elevated half-time, with AUCs ranging from 0.8 to 0.84, slightly lower than that seen with pyeloplasty **(Figure 3)**. The same trend was observed with smaller APDs for the inner measures and larger APDs found with the extra-renal measurements. Overall, the APD cutoffs associated with elevated half-times were higher than those seen with surgery. The cutoffs with the greatest sensitivity in this study were seen with the grade 4 surgical cases (ROC curve not shown). The positive and negative predictive values of possible cut-off values of all measurements in relation to surgical intervention, $T_{1/2}$ >20 minutes and $T_{1/2}$ >75 minutes are presented in appedix1.

Discussion

Risk assessment in the conservative management of high grade hydronephrosis has been extensively investigated for decades using various ultrasound and nuclear renogram parameters. The fetal renal pelvic APD is the most extensively studied predictor of postnatal obstructive pathology. Though fewer studies of postnatal APD exist, they appear to confirm its predictive capacity [9,10,21,22]. However, no clear consensus exists on the location of measurement of the APD within the mid renal transverse plane. Nguyen et al., state that the appropriate location for ADP measurement is at the maximal diameter of the intrarenal pelvis [23]. This multidisciplinary consensus has been used by most centers since 2014 yet no studies have directly compared various measurement locations. Other studies measured APD at the renal contour in the mid-renal transverse plane [24-26]. To our knowledge, no studies evaluated the APD measurement at the extrarenal pelvis.

Another debate exists in the comparison of supine to prone measurements of the APD, with most studies evaluating a limited number of renal units. Calle-Toro et al., demonstrated that the APD was higher in the prone position when compared to supine and higher for the left kidney compared to the right [27]. However, other studies have contradictory data regarding the optimal patient position when measuring APD or renal length [12-18]We found that the median APD measurements were similar in both supine and prone positions with just minor differences. This can simplify abdominal ultrasounds as keeping the child supine for renal assessment reduces the number of positions required for the exam. In both patient positions, the median intra-renal measurement was significantly smaller than the median APD measurements in other methods. Our data shows that despite the fact that APD was smaller at the intrarenal pelvis in comparison to the other 2 measurements, it was still capable of associating with the clinical outcome of

pyeloplasty. Our goal when analyzing our data with ROC curves was to find the cutoff value with the highest specificity whereas a minority of other reports have used the APD cutoff with highest sensitivity. The subject of which statistical method to use to best define an optimal cutoff is beyond the scope of this study.When comparing the six APD measurements according to the SFU grading, the APD measurements were significantly less for those with SFU grade 3 than who had SFU grade 4. A surprising finding within our secondary analysis was that despite the significant difference in APD measurement between SFU grades, the predictive cutoff values were similar at 24 mm. This strengthens the position that APD is associated with pyeloplasty. Our results confirm that all APD measurements are equally associated with pyeloplasty regardless of location within the mid renal transverse plane. The supine extra-renal technique appeared to have the highest combination of sensitivity and specificity, which was corroborated by the diuretic drainage time analysis.

Cutoff values predicting the risk of pyeloplasty can therefore be useful for clinical decision-making based on the technique used for APD. We suggest that similar to the 15mm cutoff in the UTD grading system, that 25mm could be utilized as another marker of severity within grading systems. It has been shown that the inter-rater reliability of SFU grade 3 in particular is poor [28]. Our finding that the inter-rater reliability of APD measurements was excellent is corroborated by Vemulakonda et al who further reported that it was superior to that of the SFU grading system[29]. The combination of APD measurements within a modified SFU grading system deserves greater study as a simple and potentially more reliable tool for risk assessment in the management of congenital hydronephrosis.

It is important to note that we are not suggesting that APD alone can be used to indicate the need for surgery. Rather, it can contribute to the risk assessment for The strengths of our study

compared to others which have evaluated postnatal APD include the robust sample size, the review of images by multiple clinicians and the detailed description of the operative indications. The limitations of our study include the retrospective design. **The decision making of pyeloplasty could be subjective**. In addition, the interpretation of our results and in fact all studies on the subject are limited by the indications used to determine the need for pyeloplasty, as no gold standard exists. Nevertheless, our surgical cohort is described in greater detail than most publications and was managed with an intention to observe the majority of high-grade cases, as opposed to many others who indicate surgery merely on the basis of elevated diuretic drainage times. The median age at surgery was 4.6 months, similar to that in the landmark series of conservative management by Koff et al in whom 40% also underwent surgery for worsening hydronephrosis[30]. We have previously reported that worsening congenital hydronephrosis leading to pyeloplasty was characterized by a 40% increase in APD or 57 % upgrading[31]. In contrast to some authors, we excluded UTI as an indication for surgery since confounding variables such as foreskin status could bias the results. There is possibly a bias in the inclusion/exclusion criteria due to the poor inter-rater reliability of the SFU grading system**.** Finally, our results represent a young age group; hence, other studies are warranted to evaluate different methods of APD measurements that can predict pyeloplasty across all age groups.

Conclusion

Anteroposterior diameter measurements differ based on the technique but not patient position, and they are all capable of assessing the risk pyeloplasty. The inter-rater reliability of all techniques was excellent. The technique of APD measurement should be specified in publications on the subject, as well as in grading systems and should be consistent when comparing different ultrasound results over time for a patient. Measurements could be taken in the supine position only, thus simplifying the ultrasound examination of the child. APD measurements associated with pyeloplasty could be used to further define the SFU grades or UTD classification but will require additional studies for confirmation.

Parameter		Pyeloplasty Group	Control Group	P value	SFU3	SFU4	P value
Gender	**Male** *n (%)*	30 (71.4)	74 (86.2)	0.07	78 (87.6)	26 (65)	0.003
	Female *n (%)*	12 (28.6)	13 (13.8)		11 (12.4)	14 (35)	
Laterality	**Unilateral** *n (%)*	40 (95.2)	84 (96.5)	0.7	86 (96.6)	38 (95)	0.66
	Bilateral *n (%)*	2 (4.8)	3 (3.5)		3 (3.4)	2 (5)	
Side	**Right** *n (%)*	15 (34.1)	14 (15.6)	0.014	14 (15.2)	15 (35.7)	0.01
	Left *n (%)*	29 (65.9)	76 (84.4)		78 (84.8)	27 (64.3)	
SFU	**SFU grade 3** *n (%)*	11 (25)	81 (90)	<0.001	--	--	--
	SFU grade 4 *n (%)*	33 (75)	9 (10)		--	--	
T1/2 *median (range)*		35 min (6-172)	4 min (1-35)	<0.001	4 min (1-146)	19 min (3.3-172)	<0.001
Age at presentation *median (range)*		0.3 mon (0.1-11.7)	0.73 mon (0.13-6.3)	<0.001	0.6 (0.1-6.3)	0.35 (0.1-11.7)	0.007
Follow up *median (range)*		43 mon (10.9-95.2)	37.8 mon (8.9-107.8)	0.77	37.8 mon (8.9-107.8)	43.4 (10.9-95.2)	0.77

Table 1 Patients' demographics and diuretic drainage half-times grouped by SFU grade and clinical outcome.

Parameter		SFU 3	SFU 4	P value	All Units
APD measurements (in mm)					
Supine	**Inner** median (range)	8 (3.5-20.1)	16 (6-47)	<0.001	10 (3.5-47)
	Contour median (range)	10 (4-24.5)	21.5 (11.5-48)	<0.001	13 (4-48)
	Extra-renal median (range)	10.3 (4-25.3)	24.5 (9.5-56.5)	<0.001	12.2 (4-56.5)
Prone	**Inner** median (range)	8.3 (3.9-21.5)	17 (8-46)	<0.001	9.8 (3.9-46)
	Contour median (range)	10.5 (3.9-26)	21.6 (10-46)	<0.001	13 (3.9-46)
	Extra-renal median (range)	11 (4.75-25)	23.5 (7.5-57.5)	<0.001	12 (4.75-57.5)

Table 2 APD measurements for all units and according to the **SFU grading system**.

	Supine Inner	Supine Contour	Supine Extra renal	Prone Inner	Prone Contour	Prone Extra renal
			Intraclass correlation coefficient			
All Units	0.968	0.973	0.967	0.955	0.977	0.964
SFU 3	0.948	0.965	0.928	0.901	0.965	0.909
SFU 4	0.968	0.971	0.965	0.987	0.985	0.970
			Cronbach's alpha			
All Units	0.974	0.976	0.973	0.967	0.973	0.972
SFU 3	0.964	0.972	0.953	0.948	0.962	0.943
SFU 4	0.974	0.975	0.973	0.974	0.973	0.975

Table 3 The reliability of different APD measurements (measurements taken by two investigators A.H and H.E).

	Supine Inner	Supine Contour	Supine Extra renal	Prone Inner	Prone Contour	Prone Extra renal
n of units needed adjudication	4	4	9	4	7	5
			Intraclass correlation coefficient			
All Units	0.88	0.897	0.957	0.803	0.953	0.806
			Cronbach's alpha			
All Units	0.957	0.963	0.98.5	0.89	0.984	0.882

Table 4 The reliability of different APD measurements if the difference between the first two investigators > 2 mm (measurements taken by three investigators A.H, H.E and J.C).

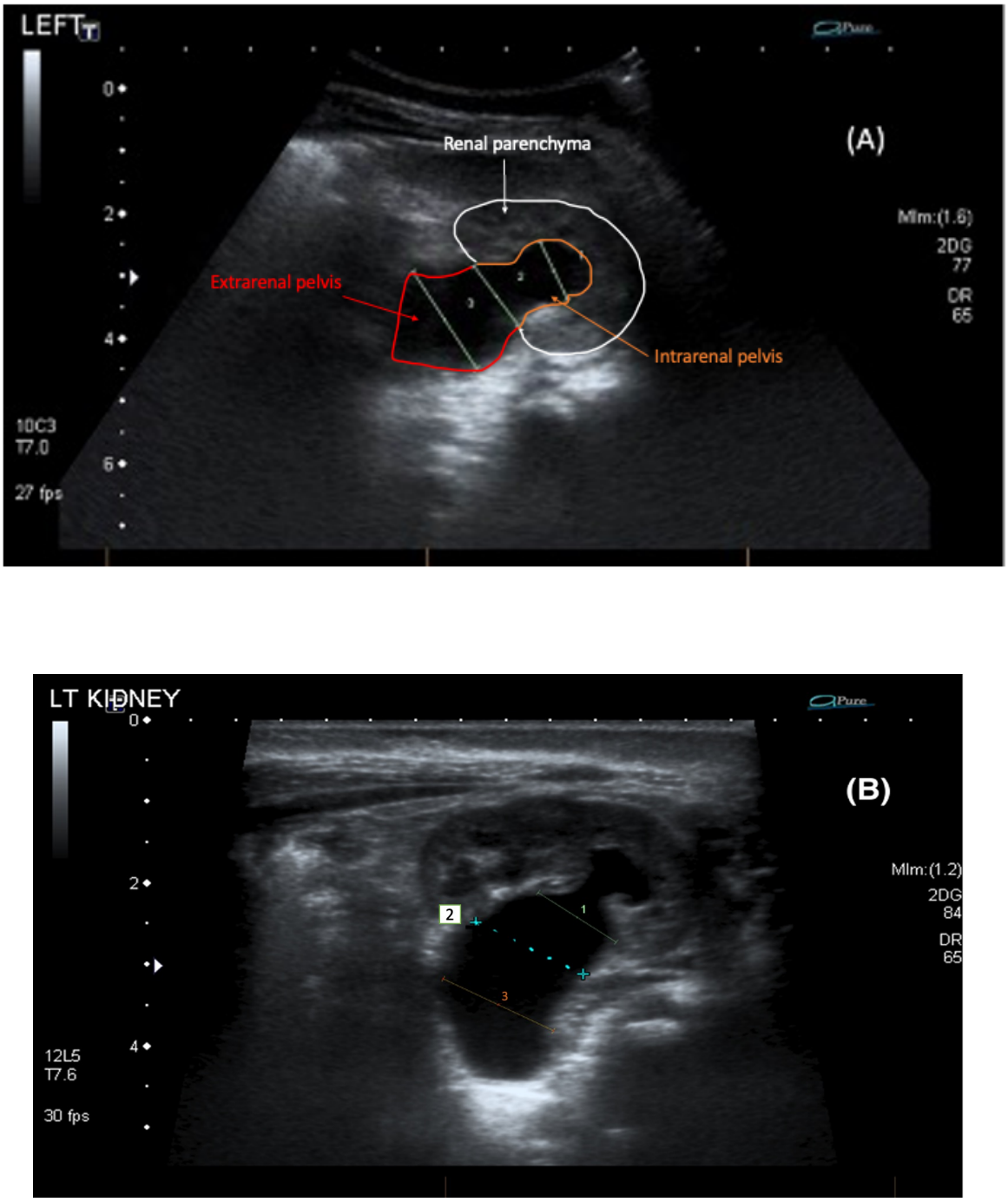
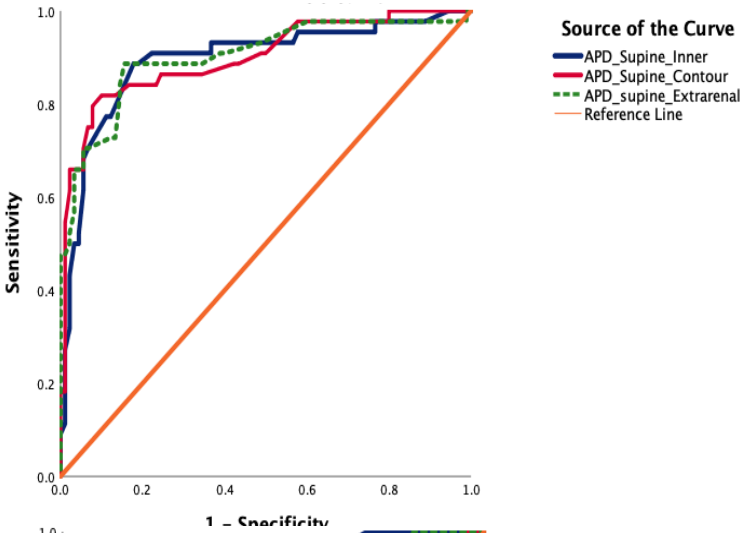
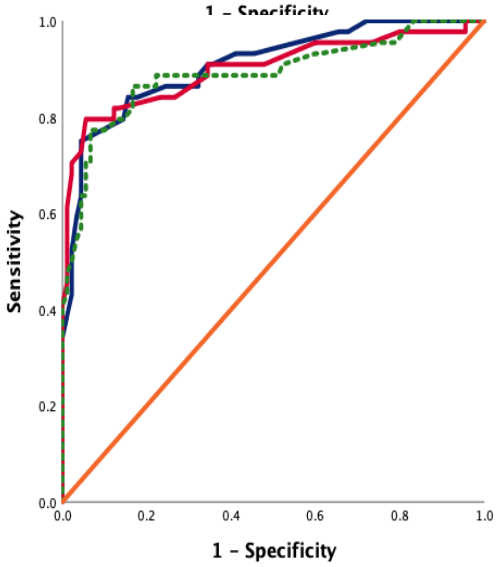


Figure 1 Illustrates how APD was measured in supine (a) and prone (b) transverse mid-renal views at the intrarenal pelvis, renal contour and extrarenal pelvis locations.

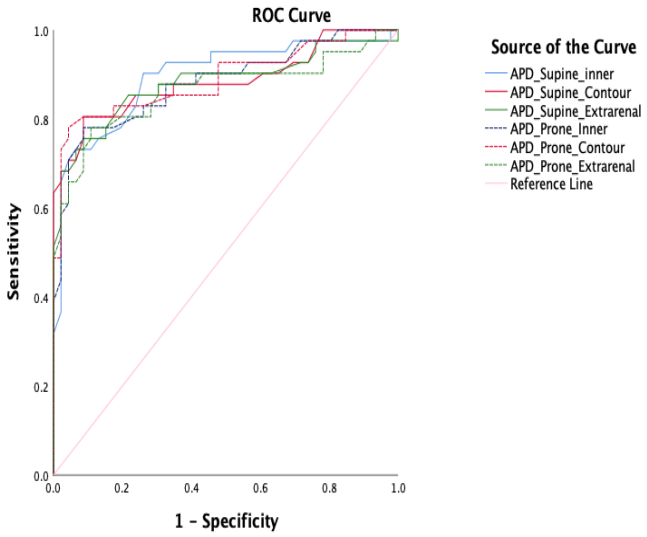


Measurement	Cutoff Point (in mm)	Sensitivity	Specificity
APD Supine Inner AUC =0.895, 95%CI= 0.83-0.96, p<0.001	>20	27.3%	98.9%
	>24	**9.1%**	**100%**
	>30	4.5%	100%
APD Supine Contour AUC =0.9, 95%CI= 0.84-0.96, p<0.001	>20	61.4%	97.8%
	>27	**18.2%**	**100%**
	>30	9.1%	100%
APD Supine Extra renal AUC =0.9, 95%CI= 0.84-0.96, p<0.001	>20	68.2%	94.4%
	>24	**47.7%**	**100%**
	>30	25%	100%

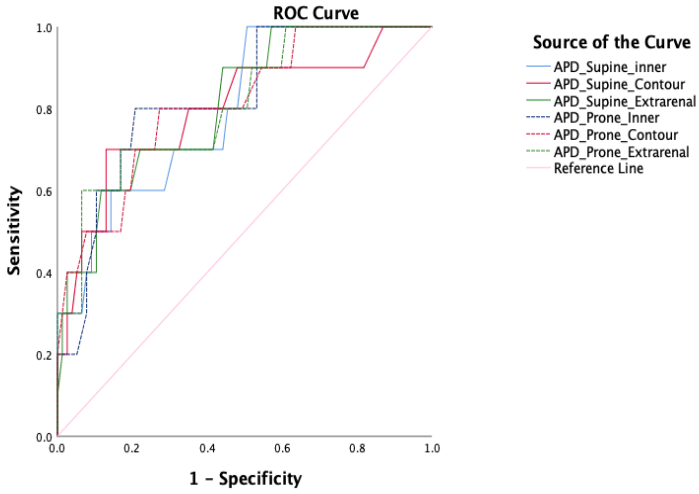


Measurement	Cutoff Point	Sensitivity	Specificity
APD Prone Inner AUC =0.91, 95%CI=0.85-0.96, p<0.001	>15	59.1%	96.7%
	>18	**34.1%**	**100%**
	>20	31.8.%	100%
APD Prone Contour AUC =0.9, 95%CI=0.83-0.97, p<0.001	>20	61.4%	98.9%
	>24	**40.6%**	**100%**
	>30	9.1%	100%
APD Prone Extra renal AUC =0.89, 95%CI=0.82-0.96, p<0.001	>20	63.6%	94.4%
	>27	**40.9%**	**100%**
	>30	25%	100%

Figure 2- The association of different supine and prone APD measurements with pyeloplasty, using an ROC Curve.



Measurement	Cutoff Point mm	Sensitivity	Specificity
APD Supine Inner AUC =0.9, 95%CI=0.82-0.97, p<0.001	>15	65.9%	97.8%
	>20	**32%**	**100%**
	>30	4.9%	100%
APD Supine Contour AUC =0.89, 95%CI=0.81-0.96, p<0.001	>15	80.5%	80.4%
	>21	**61 %**	**100%**
	>30	7.3%	100%
APD Supine Extra renal AUC =0.88, 95%CI=0.8-0.96, p<0.0001	>20	73.2%	93.5%
	>24	**48.8%**	**100%**
	>35	12.2%	100%
APD Prone Inner AUC =0.88, 95%CI=0.81-0.96, p<0.001	>15	61%	95.7%
	>18	39%	100%
	>25	7.3%	100%
APD Prone Contour AUC =0.89, 95%CI=0.82-0.96, p<0.001	>15	80.5%	82.6%
	>23	**48.8%**	**100%**
	>30	9.8%	100%
APD Prone Contour AUC =0.87, 95%CI=0.78-0.95, p<0.001	>20	68.3%	93.5%
	>24	**48.8%**	**100%**
	>35	12.2%	100%



Measurement	Cutoff Point mm	Sensitivity	Specificity
APD Supine Inner AUC =0.8, 95%CI=0.66-0.93, p=0.002	>20	50%	89.6%
	>25	**30%**	**100%**
	>35	20%	!00%
APD Supine Contour AUC =0.8, 95%CI=0.63-0.96, p=0.002	>20	70%	72.3%
	>35	**20%**	**100%**
	>40	10%	!00%
APD Supine Extra renal AUC =0.81, 95%CI=0.68-0.95, p=0.0001	>25	60%	83.1%
	>40	**30%**	**!00%**
	>50	10%	!00%
APD Prone Inner AUC =0.82, 95%CI=0.7-0.95, p=0.001	>20	50%	89.6%
	>26	**20%**	**100%**
	>35	10%	100%
APD Prone Contour AUC =0.81, 95%CI=0.67-95, p=0.001	>25	50%	88.3%
	>35	**20%**	**100%**
	>40	10%	100%
APD Prone Contour AUC =0.81, 95%CI=0.66-0.95, p=0.002	>25	60%	83.1%
	>40	30%	100%
	>50	20%	100%

Figure 3- ROC curves demonstrate the association of different supine and prone APD measurements with T1/2>20 minutes (upper diagram) and T1/2 >75 minutes (lower diagram).

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Measurement	Cut-off	Sensitivity % (95%CI)	Specificity % (95%CI)	PPV % (95%CI)	NPV % (95%CI)
All Units					
Supine inner APD	24 mm	9.1 (3-23)	100 (94.8-100)	100 (39.6 –100)	69 (60-77)
Supine contour APD	27 mm	18.2 (9.1-33.9)	100 (94.8-100)	100 (59.8-100)	71.5 (62.6-79.1)
Supine extrarenal APD	24 mm	47.4(32.5-63.3)	100 (94.8-100)	100 (80.8 – 100)	80 (71.1-86.8)
Prone inner APD	18 mm	34.1 (20-50.3)	100 (94.8-100)	100 (80-100)	77.2 (68.2-84.3)
Prone contour APD	24 mm	40.6 (26-56.7)	100 (94.8-100)	100 (77.1-100)	77.9 (68.9-84.9)
Prone extrarenal APD	27 mm	40.9 (26.7-56.7)	100 (94.8-100)	100 (78.1-100)	77.2 (68.2-84.3)
T1/2 >20 min					
Supine inner APD	20 mm	32 (18.2-47.2)	100 (90.1-100)	100 (71.1-100)	62.3 (50.5-73)
Supine contour APD	21 mm	61 (43.5-74)	100 (90.1-100)	100 (83.1-100)	73.8 (61.2-83.6)
Supine extrarenal APD	24 mm	48.8 (32.6-63.7)	100 (90.1-100)	100 (81.5-100)	70.6 (58.2-80.7)
Prone inner APD	18 mm	39 (24.6-55.5)	100 (90.1-100)	100 (76-100)	65.3 (53.1-75.6)
Prone contour APD	23 mm	48.8 (33.4-64)	100 (90.1-100)	100 (80-100)	69.1 (56.6-79.5)
Prone extrarenal APD	24 mm	48.8 (33.4-64)	100 (90.1-100)	100 (5.5-100)	69.1 (56.5-79.5)
T1/2 >75 min					
Supine inner APD	25 mm	30 (8.1-64.6)	100 (94.3-100)	100 (31-100)	92 (83.6-96.4)
Supine contour APD	35 mm	20 (3.5-55.8)	100 (94.3-100)	100 (19.8-100)	90.9 (82.3-95.7)
Supine extrarenal APD	40 mm	30 (8.1-64.6)	100 (94.3-100)	100 (31-100)	92 (83.6-96.4)
Prone inner APD	26 mm	20 (3.5-55.8)	100 (94.3-100)	100 (74.7-100)	90.9 (82.3-95.7)
Prone contour APD	35 mm	20 (3.5-55.8)	100 (94.3-100)	100 (74.7-100)	90.9 (82.3-95.7)
Prone extrarenal APD	40 mm	30 (8.1-64.6)	100 (94.3-100)	100 (31-100)	92 (83.6-96.4)

Appendix 2 Specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) of different APD measurement

VIII. Summary

Antero-posterior diameter of the renal pelvis is one of the most important predictors for surgical intervention in isolated hydronephrosis. There is no consensus regarding the best way to measure APD. In the literature, there are two common methods for how to measure APD. The first one represents measurement at the maximal diameter of renal pelvis in the transverse plane. The other one is at the renal contour. Moreover, despite the fact the APD is commonly measured in the supine position, the prone position is gaining more attention because the pelvi-calyceal dilatation is more prominent. Additionally, no studies in the literature adjusted the APD cuttoffs in terms of the grade of hydronephrosis.

In this thesis, we conducted a retrospective evaluation of six possible measurements of APD. APD was measured at the intrarenal pelvis, renal contour and extrarenal pelvis in prone and supine positions. To evaluate the reliability of all measurements, APD was measured by 2 investigators (a urologist and a radiologist). The inter-rater reliability and internal consistency of all techniques were excellent. In the current study, all APD measurements were similarly associated with pyeloplasty. Overall, the APD cutoffs associated with elevated half-times were higher than those seen with surgery.

The technique of APD measurement should be specified in publications on the subject, as well as in grading systems and should be consistent when comparing different ultrasound results over time for a patient. Measurements could be taken in the supine position only, thus simplifying the ultrasound examination of the child.