

## Can We Predict Which Pelvi-Ureteric Junction Obstruction Need Surgical Correction?: A Literature Review

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### ABSTRACT

Pelvi-ureteric junction obstruction (PUJO) is a condition in which an obstruction occurs at the junction where the ureter attaches to the kidney. Correct diagnosis and appropriate treatment plan for PUJO are required. However, to date, research on tools or indicators to assess which PUJO cases require a surgical approach is still very limited. This study aims to predict which pelvi-ureteric junction obstruction need surgical consideration. Literature obtained from the search results of Pubmed, Medscape, Science Direct, and Google Scholar electronic databases with some keyword used. From the beginning of 2018, 74 articles were collected through the electronic database of NCBI, OVID (Medline), Elsevier, and Pubmed. Following all the inclusion and exclusion criteria mentioned earlier, the final selection considered 10 literatures were eligible to be included in this literature review. The results of the literature review showed that 4 studies reported the need of surgery in PUJO can be predicted by urinary marker. 3 Studies reported GFR/DFR as predictor for need of surgery. The most reported parameter as predictor for need of surgery was APD that was reported by 5 studies. 2 studies reported nuclear imaging as predictor: 1 studies reported T1/2 washout, and the other study reported MAG-3 in combination with other parameter to form MAG-SOS score. Other ultrasonography parameters were reported by 3 studies: 1 study reported renal pyramidal thickness, and 2 studies showed a predictive value of scoring system using ultrasonography parameters (Pyeloplasty Predictive Score and obstructive index). Several parameters could predict the need of surgery in PUJO, however we could not conclude which parameter have the higher predictive value. It may be better to use multiple parameters.

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**Keywords:** *anteroposterior diameter, ureteropelvic, ureteral obstruction, congenital UPJO/PUJO, pyeloplasty.*

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### 1. INTRODUCTION

The kidneys are organ with many important functions in the human body. They are the main body to maintain the balance between liquid and electrolyte. In addition, kidney also have an important role in the acid base balance in the body, the kidney plays an important role in suppressing the secretion of blood pressure and erythropoietin.<sup>1</sup> During the life of the fetus, the kidneys grow from metanephros mesoderm for distal tubules. Collecting duct, main and minor calix, kidney pelvis and ureter originate from mesonephric duct, resulting in the fifth week of the intrauterine phase. This explains why the ureteral pelvic junction is entirely composed of ureteral buds rather than a fusion of two different mesenchymal tissues.<sup>1,2</sup>

Pelvi-ureteric junction obstruction (PUJO) is a condition in which an obstruction occurs at the junction where the ureter attaches to the kidney.<sup>3,4</sup> The obstruction impedes the flow of urine from the renal pelvis to the ureter and increases fluid pressure in the ureter. Increased pressure in the kidneys can impair kidney function over time. Obstruction can be congenital or develop over time as a result of trauma or age-related changes in body shape.<sup>5</sup> Cases of PUJO have increased in recent years as prenatal scans have become more common. PUJO is more common in children than in adults, more common in boys, and up to 23 times more cases in boys than in girls. The incidence of PUJO is estimated at 1000-1500 to 1000-1500. PUJO is the most common cause of hydronephrosis. One of the seven newborns with acceptable hydronephrosis has PUJO.<sup>4-6</sup>

The surgical procedure is Gold Standard of PUJO treatment.<sup>6</sup> Indications for interventions include severe or chronic and troublesome low back pain or nausea, pyelonephritis, concomitant renal stones, or decreased renal function. In addition, surgery considers the potential risks and benefits of this approach, success rates, and in some cases the consequences of long-term delays. In children, two- thirds of PUJO do not develop kidney damage or do not require surgery

Hydronephrosis resolves spontaneously.<sup>7,8</sup> This makes it a major challenge for clinicians to determine which of these children, who are mostly asymptomatic, require renal pyeloplasty to remove the obstruction.<sup>7</sup>

Correct diagnosis and appropriate treatment plan for PUJO are required. However, to date, research on tools or indicators to assess which PUJO cases require a surgical approach is still very limited. We need a surveillance algorithm aimed at identifying early candidates for surgery.

## 2. MATERIAL AND METHODS

### *Literature search strategy*

Literature obtained from the search results of NCBI, Elsevier, OVID (Medline), and Pubmed electronic databases with the keywords used are “urinary system”, “ureteropelvic junction”, “pelvi-ureteric junction”, “obstruction of ureteropelvic junction”, “treatment of UPJO”, “surgical indication of UPJO”, “congenital UPJO/PUJO”, and “pyeloplasty” with year publication of 2018 to 2022. References cited in the relevant literature are taken manually and only from full articles, case reports and editorial letter were being excluded.

### *Inclusion and exclusion criteria*

According to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines, the literature turned into based with the aid of using reviewing PICOS (Population, Intervention, Comparator, Outcome, and Study design) to decide the feasibility of the study. Studies have been taken into consideration viable once they met the inclusion standards as followings; 1) Research articles which have been posted in national, worldwide journals, and court cases associated to investigate issues with sure key phrases at the NCBI, OVID (Medline), Elsevier, and Pubmed databases the use of the key phrases: urinary system, ureteropelvic junction, pelvi-ureteric junction, obstruction of ureteropelvic junction, treatment of UPJO, and surgical indication of UPJO; 2) The article turned into being put up throughout 2018-2022 3) The sort of article turned into unique article (RCT, medical trial, or cross sectional), 4) Article turned into completely accessible, 5) Article turned into written in Indonesian or English language, 6) the article included patients with PUJO, 7) the article compare patients between those who need surgery and those who do not need surgery or treated conservatively, 8) The article mention at least 1 clinical/laboratory/imaging parameter that is measured before surgery and describe its ability to predict the need for surgery in PUJO patients.

Literature in the form of case reports, best abstracts, file meetings, conferences, editorial comments, evaluations (systematic literature evaluations and meta-analyses), inappropriate results, inaccessible literature, duplications from preceding literature publications, and now no longer the use of English have been positioned into exclusion standards.

## 3. RESULTS

Throughout 2018-2022, 104 articles were collected through the electronic database of NCBI, OVID (Medline), Elsevier, and Pubmed. After the exclusion of multiple literatures, 51 relevant literatures were obtained for the evaluation of abstracts and titles. From the results of the evaluation of abstracts and titles, 18 literatures were eligible for a full evaluation. Following all the inclusion and exclusion criteria mentioned earlier, the final selection considered 10 literatures were eligible to be included in this literature review (**Figure 1.**).

Study by Killi et al 2018, involved 44 patients with antenatal hydronephrosis. They investigated the effective predictors for surgical decision in antenatal hydronephrosis. They divided patients into surgery and follow up group, then they evaluated longitudinal diameter of the kidney, parenchymal thickness of the kidney, AP diameter of renal pelvis, AP diameter of middle calyces on ultrasonography, and differential renal function, (DRF) 20<sup>th</sup> minute clearance, half- life of radionuclide tracer (T1/2), Tmax, Tmax-T1/2, and normalised residual activity (NORA) on diuretic renography. They conducted serial measurement of ultrasonography from the first week until 3 months post-natal. Patients with increase in AP diameter of renal pelvis, and decrease in parenchymal thickness with obstructive pattern on DRG curve and/or differential renal function detected on repeat US were operated. Patients with low degree of suspicion and persistent hydronephrosis were followed up at 6 month-intervals. They found that AP diameter of renal pelvis and differential renal function were the most effective parameters for surgical decision. Each 1 mm increase in AP diameter of renal pelvis was found to increase the risk of surgery for 1.37-fold (odds ratio) (95% CI 1.13-1.66). Each one unit drop of DRF increased the risk of being operated for 1.14-fold (odds ratio). (95% CI 1.01-1.29).

Study by Li et al, evaluate the Pyeloplasty Prediction Score (PPS) [**Figure 2.**] to predict the likelihood of pyeloplasty in infants with UPJO-like. Pyeloplasty Prediction Score was based on three parameters: society of fetal urology (SFU) grade of the ultrasound, transverse anteroposterior diameter (APD) measurement, and the absolute percentage difference between the lengths of the ipsilateral and contralateral kidneys. They included 353 eligible patients and concluded that Overall, PPS could detect patients more likely to undergo pyeloplasty using baseline ultrasound measurements. Those with a PPS of  $\geq 8$  were eight times more likely to undergo pyeloplasty.

Study by Rathod et al, study the role of urinary enzymes N-acetyl- $\beta$ - glucosaminidase (NAG), alkaline phosphatase (AKP)

and gamma glutamyl transferase (GGT) in the diagnosis and follow-up of patients with suspected pelviureteric junction obstruction (PUJO). Determination of conservative and surgery group was based on split renal function (SRF) with cutoff of 40%. The level of urinary enzymes NAG, AKP and GGT are significantly high in the patients with HDN requiring pyeloplasty when compared with the patients managed conservatively, thus they can be used to predict the need for surgery.

Hodhod et al, 2018 evaluated the feasibility and value of renal pyramidal thickness (PT) as a predictor of pyeloplasty in high-grade postnatal hydronephrosis. The study showed that PT is a good predictor for deciding surgery in patients with hydronephrosis. A cut-off value of  $\leq 3$  mm had 98.1% sensitivity and 89.7% specificity regarding the need for surgery (positive predictive value (PPV) = 0.82.8 and negative predictive value (NPV) = 0.99).

Study by Oktar et al 2022 aimed to determine the level of urinary heat shock protein 70 (HSP70) in children who required surgery for PUJO. They divided patients into 3 groups (pyeloplasty vs conservative with non-obstructive dilation vs healthy group). They found that using the cutoff value of 94.7 pg/mgCr, the sensitivity and specificity of urinary HSP70 for predicting the risk of surgical intervention were 69.7% and 68%, respectively (AUC = 0.689).

Jena et al 2021 included 135 patients with antenatal PUJO and aimed to evaluate the impact of obstructive index (OI) as a predictor of management in antenatal pelviureteric junction obstruction (PUJO). They also analyzed whether APD and DRF could also predict the need for surgery. OI was defined as  $\{\text{PAPD(A)} \times \text{T1/2 (A)}\} / \{\text{PAPD(N)} \times \text{T1/2 (N)}\}$ ; where [PAPD(A)] and PAPD(N) refer to Pelvic anteroposterior diameters of the affected and the normal kidney respectively, T1/2 (A) and T1/2 (N) refers to T1/2 of the affected and normal kidney respectively. Using ROC analysis, area under curve for OI was 0.95. A value of 12.2 could predict failure of conservative management with a sensitivity of 93.3% and a specificity of 92.4%.

Hodhod et al 2021 evaluated the role of Mercaptoacetyltriglycine (MAG-3) renogram as indication for surgery in PUJO patients. They divided patients into pyeloplasty group and control group that include non-operatively managed SFU grade 3 and 4. They combine MAG-3 with other parameters (DRF and T1/2) to build a scoring system (MAG-SOS score) that may be used as predictor for surgery. They found that the score was significantly associated with need for surgery and a score of 5 has 100% specificity for patients having a pyeloplasty performed.

Fendereski et al, 2020 aimed to evaluate and compare the efficacy of urinary carbohydrate antigen 19-9 (CA19-9), NGAL, and kidney injury molecule-1 (KIM-1) biomarkers as predictive factors to determine the surgery requirement in patients with PUJO. The outcomes were indicative of higher efficacy of CA19-9 level with a sensitivity and specificity of 84.2% and 73.2% at the cutoff point of 59.09 U/ml. Furthermore, they found negative correlation was detected between the kidney function and the concentrations of CA19-9 and NGAL.

Nabavizadeh et al, 2018 assessed the role of urinary CA19-9 measurement in determining optimal management of PUJO. The study divided 112 patients into 3 groups (non-operative treatment with improvement of condition vs pyeloplasty group after initial observation vs immediate observation group). ROC curve analysis revealed that urinary CA19-9 level at cut off value of 52.6U/mL had sensitivity of 92.0% and specificity of 70.9% in predicting failure of non-operative management.

The results of the literature review (**Table 1.**)

Author (Year)	Title	Design Study	Total of Subject	Age (Year)	Urinary Marker	Result of Review			Other Ultrasound Parameter
						GFR/DRF	Nuclear - imaging	APD	
Kili et al. 2018 <sup>9</sup>	Effective predictors for surgical decision in antenatal hydronephrosis: A prospective multiparametric study	Prospective study	44	<1	-	Differential renal function was the most effective parameters	-	AP diameter of renal pelvis ( $>2.5$ cm) was the most effective parameters	-

Li <i>et al.</i> 2020 <sup>10</sup>	Ultrasound-Based Scoring System for Indication of Pyeloplasty in Patients With UPJO-Like Hydronephrosis	Prospective study	353	Prenatal	-	-	-	APD	Pyeloplasty Prediction Score (PPS)
Rathod <i>et al.</i> 2021 <sup>11</sup>	Hydronephrosis due to pelviureteric junction narrowing: Utility of urinary enzymes to predict the need for surgical management and follow-up	Prospective study	70	<1 years	NAG, AKP, and GGT	-	-	-	-
Hodhod <i>et al.</i> 2018 <sup>12</sup>	Is the renal pyramidal thickness a good predictor for pyeloplasty in postnatal hydronephrosis?	Retrospective study	155	Neonates	-	-	-	-	Renal pyramidal thickness is a good predictor for pyeloplasty
Oktar <i>et al.</i>	Urinary HSP70 can predict the	Prospective study	43	-	Urinary HSP70	-	-	-	-

2022 13	indication of surgery in unilateral ureteropelvic junction obstruction								
Jena <i>et al.</i> 2021 14	Obstructive Index In Antenatal Unilateral Pelviureteric Junction Obstruction: A Novel Predictor Of Failure Of Conservative Management	Retrospective study	135	-	-	-	T1/2 washout	APD	Obstructive index Cortical thickness
Hod <i>et al.</i> 2021 15	MP44-20 Introduction Of Mercaptoacetyltriglycine-Suspected Obstruction Scoring System (Mag-Sos) As A Diagnostic Tool For Ureteropelvic Junction Obstruction	Retrospective study	97	-	-	-	Mercaptoacetyltriglycine (MAG-3) renogram in MAG-SOS score	-	-
Fenders	Comparing predictive	Prospective study	161	-	CA19-9 and	DRF	-	APD	-

ki <i>et al.</i> 2020 <sup>16</sup>	values of carbohydrate antigen 19-9, neutrophil gelatinase-associated lipocalin, and kidney injury molecule-1 in 161 patients with Ureteropelvic junction obstruction				NGAL				
Nabavizadeh <i>et al.</i> 2018 <sup>17</sup>	Value of Urinary Carbohydrate Antigen 19-9 to Predict Failure of Conservative Management in Children with Ureteropelvic Junction Obstruction	Retrospective study	112	-	High urinary CA19-9	DRF	-	APD	-

showed that of the 9 studies, 4 studies reported the need of surgery in PUJO can be predicted by urinary marker. 2 studies reported urinary CA19-9, while other studies reported different urinary marker. 3 Studies reported GFR/DFR as predictor for need of surgery. The most reported parameter as predictor for need of surgery was APD that was reported by 5 studies. 2 studies reported nuclear imaging as predictor: 1 studies reported T1/2 washout, and the other study reported MAG-3 in combination with other parameter to form MAG-SOS score. Other ultrasonography parameters were reported by 3 studies: 1 study reported renal pyramidal thickness, and 2 studies showed a predictive value of scoring system using ultrasonography parameters (PPS score and obstructive index).

#### 4. DISCUSSION

Pelvi-ureteric junction obstruction (PUJO) is a partial blockage of urine flow that occurs where the ureter enters the kidneys. PUJO if not properly identified and treated, can lead to loss of the affected kidney. PUJO is primarily a congenital condition and can be detected by prenatal ultrasonography in late pregnancy. Surgical intervention is the definitive in the treatment of PUJO as needed. However, not all PUJO conditions are operated on. Treatment is at improving renal drainage and function and managing clinical symptoms.

After vigorous searching of literature, we collected 9 most eligible article in this review. However, meta-analysis could not be conducted in this study due to difference in methods across studies. First, not all article included only patients with PUJO. 3 articles included patients with hydronephrosis which meant that patients with diagnosis other than PUJO were also included. Furthermore, the methods of diagnosis of PUJO were not the same across study. Second, the parameters that were evaluated were different across study; and if the study evaluated the same parameters; the timing of measurement and the protocols were different. Third, all studies defined group differently, some articles divided patients into 3 groups, and also the indication for surgery was different across study.

The most reported parameter as predictor for need of surgery was APD that was reported by 5 studies. Study by Killi et al showed that Each 1 mm increase in AP diameter of renal pelvis was found to increase the risk of surgery for 1.37-fold (odds ratio).<sup>9</sup> Studies that reported APD were studies with the highest number of sample. One of them, study by Li et al, involved 353 patients, however the study the inclusion criteria of the study was patients with diagnosis of PUJO-like hydronephrosis, not exclusively patients with PUJO. They also combined APD with other ultrasonographic parameters to build a scoring system to predict need of surgery. PPS scoring was calculated by addition of several parameters below:<sup>10</sup>

Based on the sensitivity and specificity calculations, clinicians can expect a 90% probability that those with a score  $\geq 8$  will end up having a pyeloplasty in the future. Those with a PPS of  $\geq 8$  were eight times more likely to undergo pyeloplasty.<sup>10</sup>

Study by Jena et al. involved 135 patients with PUJO and found significant correlation between APD and need for surgery on univariate analysis, however on multivariate analysis, they did not find any significant association. Similar to Li et al, Jena et al, also combined APD with other parameters to build scoring system called obstructive index. OI was calculated by formula  $\{PAPD(A) \times T1/2 (A)\} / \{PAPD(N) \times T1/2 (N)\}$ . Using ROC analysis, area under curve for OI was 0.95. A value of 12.2 could predict failure of conservative management with a sensitivity of 93.3% and a specificity of 92.4%.<sup>11</sup> Study by Fendereski et al, evaluated the predictive value of APD and they revealed that the evaluation of the receiver operating characteristic (ROC) APD in patients with PUJO to determine the optimized level for prediction of surgical intervention requirement illustrated a sensitivity of 73.3% and specificity of 76.5% at the cutoff point of 26 mm (area under the curve: 81.2%; 0.741–0.870;  $P < 0.0001$ ).<sup>12</sup>

DRF/GFR of the affected kidney was the second most reported predictor (reported by 3 studies). PUJO cases are generally partial where there is an increase in the production of vasoactive peptides and cytokines as interleukin (IL)-5 and eotaxin-2. By changing the eicosanoid elaboration in the kidney, the monocytic infiltration is believed to affect the renal blood supply and decrease the total GFR in the affected kidney, however, single nephron GFR will be increased. The decrease in GFR is an indication for corrective surgery. In general, a decrease of differential renal function (DRF)  $<40\%$  is considered an indication.<sup>7</sup>

4 studies reported the need of surgery in PUJO can be predicted by urinary marker. 2 studies reported urinary CA19-9, while other studies reported different urinary marker. Fenderesky et al, found that CA19-9 level had a sensitivity and specificity of 84.2% and 73.2% at the cutoff point of 59.09 U/ml,<sup>12</sup> while Nabavizadeh et al. found that CA19-9 level at cut off value of 52.6U/mL had sensitivity of 92.0% and specificity of 70.9%.<sup>13</sup> Urinary HSP70 with the cutoff value of 94.7 pg/mgCr, had the sensitivity and specificity for predicting the risk of surgical intervention were 69.7% and 68%, respectively.<sup>14</sup> A cut-off value of 5.73 mU/mg cr of NAG yielded a sensitivity of 82.5% and a specificity of 82.1% to identify the patients who were included in group B and underwent operative management. NGAL sensitivity of 64.3%, and specificity of 69.6% at the cutoff point of 11 ng/ml.<sup>15</sup> Based on the sensitivity, specificity and number of study, we can concluded that CA 19-9 was the most reliable urinary marker for predicting the need of surgery in PUJO patients.

We could not conclude which parameter is the best options for making surgical decision in PUJO patients since we could not conduct meta-analysis. However, it could be a better option to manage patients individually based on multiple parameters. 3 studies employed scoring systems to predict the need of surgery, they are PPS score, obstructive index, and MAG-SOS score. However, the PPS score by Li et al, was designated for hydronephrosis patients with PUJO-like diagnosis. And MAG-SOS score was designated for patients with antenatal hydronephrosis (not only PUJO patients). Obstructive index had higher sensitivity and specificity for predicting the need of surgery than PPS score . We could not find the sensitivity of the MAG-SOS score in articles by Hodhod et al. Thus if scoring system be used as predictor for need of surgery in PUJO patients, obstructive index can be a good tool.

#### *Limitation*

The limitation of this article was the high heterogeneity of the study that made it impossible to conduct quantitative analysis on which parameters had the best predictive value of need for surgery in patients with PUJO. We found no study with clinical trial design. Surgery in PUJO is very essentials for patient's safety, thus conducting a clinical trial with limited previous study would put the patients in obvious danger.

## **5. CONCLUSION**

Study have shown that we can predict which PUJO need surgical correction. APD, DFR, urinary marker, and other ultrasonography parameter could be used as predictor. However, the use of multiple parameters, such as using scoring system may be a better option for predicting the need of surgery in PUJO patients. Further study with a standardized method in the similar population is required to evaluate which parameter is have the highest predictive value.

#### **Conflicting interests**

The authors declare no conflict of interest

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#### **Informed consent**

Written informed consent was not required for this study because only published data were used

#### **Ethical approval**

Ethical approval was not required for this study because only published data were used

#### **Guarantor**

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#### **Contributorship**

PLW contributed in conceptualization, data curation, methodology, formal analysis, and software. PLW and JS reviewed and edited the manuscript and approved the final version of the manuscript.

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#### **Figure Legends**

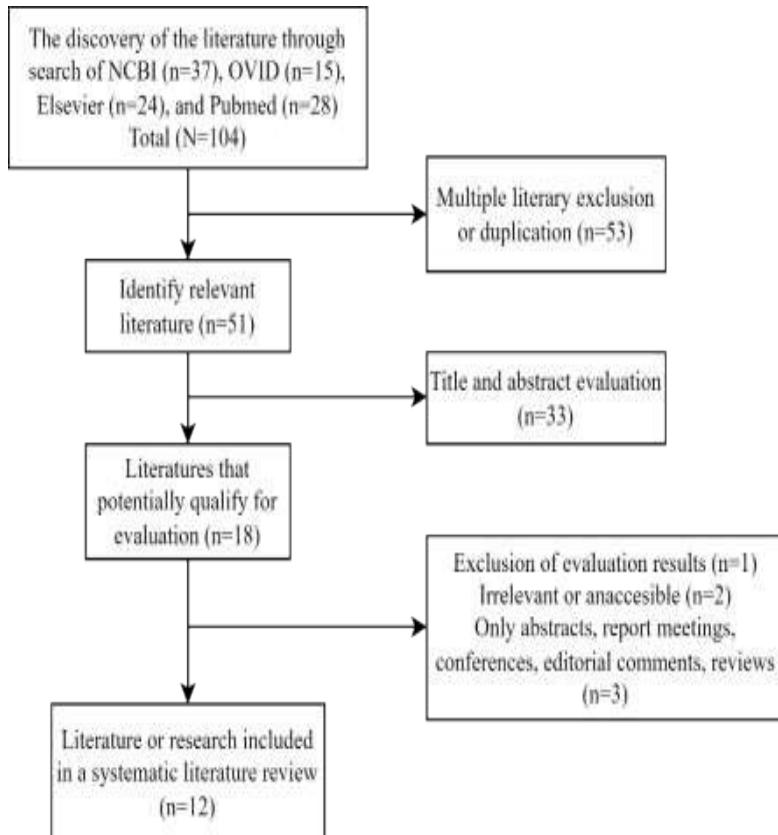


Figure 1. PRISMA diagram that describes the search process for literature review and literature selection

<b>A. SFU grading of affected kidney on ultrasound</b>	
0	Normal
1	SFU Grade 1
2	SFU Grade 2
3	SFU Grade 3
4	SFU Grade 4

<b>B. APD measurement of affected kidney on ultrasound</b>	
0	<5 mm
1	5–10 mm
2	11–15 mm
3	16–19 mm
4	≥20 mm

<b>C. Absolute percentage difference between the ipsilateral and contralateral renal lengths [[100% * (Ipsilateral Renal Length- Contralateral Renal Length)/Ipsilateral Renal Length]]</b>	
0	<5%
1	5%–10%
2	11%–15%
3	16%–19%
4	≥20%

PPS = A + B + C

Each parameter is assigned a score from 0 to 4, 0 being least severe and 4 being most.

Figure 2. PPS score

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