Correlation of Plasma Renin Activity Values and Resistive Index on Ultrasound Doppler with Findings of Renal Dynamic Scan in Patients with the Society of Fetal Ultrasound grades 3 and 4 Unilateral Hydronephrosis

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Background: Renal dynamic scans (RDS) despite being considered the gold standard for the diagnosis of pelvic ureteric junction obstruction (PUJO), fail to help resolve the dilemma about management issues in many patients. Multiple invasive and noninvasive methods are being studied to help the decision-making in these patients. We did this study to find correlation of plasma renin activity (PRA) values and resistive index (RI) on Doppler ultrasound with findings of RDS in patients with the Society for Fetal Urology (SFU) Grades 3 and 4 unilateral hydronephrosis (HDN) and also to determine the cut-off values of PRA and RI that could categorically acknowledge the success of pyeloplasty.

Methodology: Twenty patients with SFU Grades 3 and 4 unilateral HDN due to PUJO were enrolled. Demographic details were recorded. All underwent Anderson-Hynes dismembered pyeloplasty. Based on the follow-up RDS scans, these patients could fall into one of three categories- improved (successful), status quo, or deteriorated (unsuccessful). Outcomes were compared based on RDS (split renal function [SRF]), ultrasonography, and Doppler findings were done at 3 months of postoperative period.

Results: Follow up period was 3 months after Pyeloplasty. Seventeen patients had successful outcomes based on RDS findings, 12 had improvement in SRF (>5%), and 6 had normal drainage curves (t-t1/2 < 10 min). Three patients had indeterminate curves (t-t1/2 between 10 to 20 min). Four had improvement on both the criteria, i.e., SRF and drainage curves. Among the three patients who showed no improvement in RDS, two were in “status quo” category and one patient showed deterioration. Seventeen patients also showed improvement in PRA and RI. No significant correlation between PRA and RI with SRF could be established. However, PRA was found to have good concordance with RDS (90%).

Conclusion: No significant correlation could be demonstrated between SRF and the respective values of PRA and RI. However, PRA could act as an adjunct to
predict the early success of pyeloplasty in view of good concordance with RDS. A larger trial with bigger cohort of patients is required to confirm our contention.

**KEYWORDS:** Anderson-Hyne pyeloplasty, Doppler ultrasound, plasma renin activity, pelvic ureteric junction obstruction, resistive index, society of fetal ultrasound, unilateral hydronephrosis

resolve over time. SFU Grades 3 and 4 are likely to have a significant obstruction at pelvic ureteric junction obstruction (PUJO) and need timely work up to decide for surgery, as most of these are asymptomatic. This subgroup of renal units has been known for the loss of nephrons and the irreversible functional loss if surgery is delayed. Rarely, other complications such as secondary hypertension, infection, renal stones may also arise. 

Having undergone an early pyeloplasty, an improvement in the renal dilatation and excretion pattern is expected in up to 95% of renal units. The key issue, therefore, is to identify markers of significant obstruction that could conclusively identify those renal units that need timely treatment; i.e., those who, if left untreated, will develop renal damage. There are no accepted antenatal markers, and hence the decision to operate for HDN must be based on a postnatal assessment.

**METHODOLOGY**

After obtaining Institutional Ethics Committee approval, a prospective longitudinal study was done from October 2016 to March 2018. Children up to 12 years of age with SFU Grades 3 and 4 unilateral HDN on ultrasound were included in the study. Children with solitary kidney or bilateral HDN, syndromic patients, patients having secondary PUJO, for example, due to urolithiasis, vesicoureteric reflux, patients with a history of previous surgery on kidneys were excluded from the study. A convenience sample size of 20 patients was taken. Informed consent was obtained from all parents and assent was obtained from all children >7 years of age. Pro forma was maintained for each patient, including the demographic details, clinical history, and relevant clinical findings. The indications for pyeloplasty were set as: patients having obstructed renal scan drainage curves (defined as t-t1/2 >20 min) AND the patients having indeterminate renal scan drainage curves (defined as t-t1/2 10–20 min) with ipsilateral SRF <40%. t-t1/2 is the time taken in minutes for the nuclear activity in the area of interest on renal dynamic scans (RDS) to reduce from its maximum to its half. SRF is a relative contribution of each of the two kidneys to total renal function.

In this study, we also studied anteroposterior pelvic diameter (APPD), parenchymal thickness (PT), pelvis cortex (P/C) ratio, resistive index (RI), ΔR (difference between RI of affected kidney and normal contralateral kidney), RI ratio (RIR), i.e., ratio between RI of affected kidney and normal contralateral kidney) both preoperatively and postoperatively. Doppler study (RI) was done at the level of arcuate arteries.

All the patients in the study group (both managed surgically or conservatively) had repeat follow-up RDS scan, Doppler Ultrasound (DUS), and plasma renin activity (PRA) after 3 months. Based on the follow-up RDS scan, these patients could fall into one of three categories- improved (successful), Status quo, or deteriorated (unsuccessful). The patients were known to improve if:

1. Change of obstructed curve to normal (t-t1/2 <10 min) or equivocal (t-t1/2 10–20 min) and/or improvement of ipsilateral SRF of >5%
2. Change of indeterminate to normal drainage curve (t-t1/2 less <10 min) and/or improvement of ipsilateral SRF of >5%.

The patients were known to deteriorate if:

1. Change of indeterminate to obstructed drainage curve
2. No change in drainage curve and ipsilateral SRF deteriorates or improvement ≤5%.

All others not falling in any of the two above categories would be labeled to have “status quo.” Similarly, success was also defined based on postoperative data on PRA and RI values by taking cut-off values based on receiver operating characteristic (ROC) curves analysis. Accordingly, success was considered if postoperative values fall below the cut-off values.

The correlation of PRA and RI was studied to RDS scans at presentation and that at follow-up.

ROC analysis [Table 1] has been done based on pre- and post-operative values to find the cut-off values of various imaging and biochemical parameters to predict the outcome of surgery in comparison with RDS, which is considered the gold standard. The concordance of each parameter (PRA, RI) with RDS was determined by statistical analysis.

**Statistical analysis**

Data were analyzed and statistically evaluated using the SPSS software version 17 (Chicago II, USA), manufactured by IBM. Quantitative data were expressed...
in mean, standard deviation, and differences between pre–post groups were tested by paired “t”-test or Wilcoxon signed-rank test, while qualitative data were expressed in percentage. Differences between the proportions were tested by the MacNemar test. The Pearson or Spearman correlation coefficient was used to study the correlation between different quantitative parameters. ROC curves were used to know the cut-off values to predict the success of the pyeloplasty. The “P” < 0.05 was considered statistically significant. Cohen’s kappa was used as a statistical method for assessing the concordance between two techniques.

RESULTS

Twenty children aged between 2 to 144 months with SFU Grade 3 and 4 HDN were included in the study; half of the patients were infants. All were males except one. In 14 (70%) children, the left kidney was affected.

In our study, 50% had antenatal diagnosis. Seventeen patients (85%) were symptomatic. The symptoms included abdominal pain (n = 9), lump (n = 5), fever (n = 2), and vomiting (n = 1); few of the patients had more than one symptom. Abdominal pain was the chief complaint in children >36 months of age. Painless lump was seen only in infancy.

Comparison of preoperative and postoperative findings of the affected kidney

Statistically significant difference was found between the pre- and postoperative mean values based on ultrasonography (USG) parameters (APPD, PT, P/C ratio), renal Doppler (RI, Δ R, RIR), and PRA values [Table 2].

After 3 months follow-up of pyeloplasty, 17 had improved status. Twelve patients had improvement in SRF (>5%) and six patients had normal drainage curves (t-t1/2 <10 min). Three patients had indeterminate curves (t-t1/2 between 10 and 20 min). Few patients (n = 4) improved on both the criteria, i.e., SRF and drainage curve. Preoperatively, peak (t) was reached in only five patients and t-t1/2 inconclusive in all 20 patients. Postoperatively, t-t1/2 could be determined in eight patients ranging from 5 to 13 min. Even though 12 patients had significant improvement in SRF as per predefined criteria, but no statistically significant difference could be demonstrated for the mean preoperative and postoperative SRF values (P = 0.08). The postoperative cut-off values of PRA and RI for successful pyeloplasty were 7.68 ng/ml/h and 0.71, respectively. Using these cut-off values, both the parameters showed improvement in 17 out of 20 (85%) patients each. However, only 14 out of 20 (70%) patients displayed postpyeloplasty fall in both these parameters. This was in total agreement with the success of pyeloplasty on RDS parameters in the same patients; 13 had successful pyeloplasty by RDS parameters, whereas one patient had “status quo” on RDS based on predecided criteria.

Among the three patients who showed no improvement in RDS, two were in “status quo” category and one patient showed deterioration. Among two patients in “status quo,” one presented with pain and palpable lump at previously operated site 4 months after pyeloplasty. USG showed gross HDN. Hence, percutaneous nephrostomy tube was placed under USG guidance. Nephrostogram showed nonclearance of contrast beyond the pelviocalyceal system. Therefore, the patient underwent redo pyeloplasty. After redo pyeloplasty, the patient was followed up for 3 to 6 months and found asymptomatic with follow-up USG showing improvement in the degree of HDN and RDS showed improvement in drainage curves and SRF.

Other patient in “status quo” category was asymptomatic during follow-up period with gradual improvement in USG parameters. Subsequent RDS could not be done as patient was lost to follow-up. One patient, who showed deterioration, was ordered micturating cystourethrogram and found normal. The patient was asymptomatic, hence decided to follow-up with USG and RDS. Repeat RDS showed improvement in SRF from 30% to 35% and the repeat USG showed mild HDN.

Preoperative correlations

No statistically significant correlation was found between SRF and PRA (P = 0.800) and between SRF and RI (P = 0.528). However, significant correlation was found between RI and Δ R (P = 0.03); RI and RIR (P = 0.011) and between Δ R and RIR (P < 0.001). Statistically significant correlation was found between SRF and APPD (P = 0.001) and SRF and P/C ratio (P = 0.001). Furthermore, statistically significant correlation was found between APPD and P/C ratio (P < 0.001) and P/C ratio and mid pole PT (P < 0.001) [Table 3].

Table 1: Cut off values for plasma renin activity and resistive index drawn from receiver operating characteristic curves

| Variable | Area under the curve | SD | P  | 95% CI (lower bound–upper bound) | Cut off values drawn from ROC curves (value) |
|----------|----------------------|----|----|---------------------------------|---------------------------------------------|
| RI       | 0.700                | 0.086 | 0.030 | 0.531-0.869                       | 0.71                                        |
| PRA      | 0.495                | 0.101 | 0.957 | 0.297-0.693                       | 7.68 (ng/ml/h)                              |

CI: Confidence interval, SD: Standard deviation, RI: Resistive index, PRA: Plasma renin activity, ROC: receiver operating characteristic curves

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Postoperative correlation

No statistically significant correlation was found between SRF and PRA ($P = 0.70$) and between SRF and RI ($P = 0.66$). However, significant correlation was found between RI and $\triangle R$ ($P = 0.002$); RI and RIR ($P = 0.011$) and between $\triangle R$ and RIR ($P < 0.001$) [Table 4].

**Determination of cut-off values for plasma renin activity and resistive index from receiver operating characteristic curves based on preoperative and postoperative values**

There is poor correlation between PRA and RI with SRF on RDS. However, cut-off values have been derived for PRA and RI from ROC analysis [Figures 1 and 2] to predict the success of the surgery and to find the concordance between the predictive values of gold standard RDS with PRA and RI.

**Concordance of plasma renin activity and resistive index with Renal dynamic scans (Gold standard)**

The success of pyeloplasty was determined based on PRA and RI individually by using the above cut-off values, and concordance was derived using kappa analysis statistically.

Based on PRA, 17 were successful. Among them, 16 matched with successful patients defined by RDS. Hence, concordance was found to be 90%.

Similarly, based on RI, 17 were successful, with 14 matching with RDS. Accordingly, concordance was found to be 70%.

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**Table 2: Preoperative and postoperative findings of affected side on ultrasonography, plasma renin activity, and renal dynamic scans in study participants**

| Parameter          | Preoperative | Postoperative | $P$  |
|--------------------|--------------|---------------|------|
|                    | Mean±SD      | Median (IQR)  | Range| Mean±SD      | Median (IQR)  | Range|
| APPD (mm)          | 33.2±16.9    | 27.5 (18.0‑51.8) | 12‑60 | 14.5±8.1    | 13.0 (8.5‑17.6) | 6.0‑36.0 | $<$0.001 |
| Mid pole PT (mm)   | 5.1±2.1      | 5.0 (3.6‑7.4)  | 2.0‑9.0| 8.8±4.0     | 8.0 (6.1‑10.6) | 4.0‑20.0 | $<$0.001 |
| P/C ratio          | 8.5±7.6      | 5.8 (3.1‑10.9) | 1.8‑29.0| 2.2±2.2     | 1.2 (1.0‑2.8)  | 0.4‑9.0  | $<$0.001 |
| SRF (%)            | 37.2±16.0    | 42.0 (25.8‑49.8) | 4.0‑55.0| 39.7±14.0   | 46.3 (33.5‑49.0) | 8.0‑55.0 | 0.08   |
| RI                 | 0.71±0.08    | 0.72 (0.64‑0.76) | 0.50‑0.85| 0.66±0.07   | 0.66 (0.60‑0.70) | 0.55‑0.85 | 0.04   |
| R1‑R2 ($\triangle R$) | 0.09±0.08    | 0.08 (0.02‑0.15) | −0.03‑0.29| 0.06±0.02   | 0.0 (−0.02‑0.10) | −0.1‑1.0  | 0.02   |
| R1/R2 (RIR)        | 1.16±0.14    | 1.12 (1.03‑1.25) | 0.95‑1.51| 1.05±0.13   | 1.0 (0.96‑1.16) | 0.85‑1.33 | 0.01   |
| PRA (ng/ml/h)      | 7.5±5.4      | 6.9 (3.2‑8.7)  | 1.3‑20.6| 3.9±4.8     | 3.9 (0.9‑6.2)  | −8.0‑14.44 | $<$0.01 |

APPD: Anteroposterior pelvic diameter, PT: Parenchymal thickness, IQR: Interquartile range, SD: Standard deviation, PRA: Plasma renin activity, RIR: Resistive index ratio, i.e., Ratio between the resistive index of the affected kidney (R1) and normal contralateral kidney (R2), $\triangle R$: Difference between the resistive index of the affected kidney (R1) and normal contralateral kidney (R2), RI: Resistive index, SRF: Split renal function, P/C: Pelvic diameter‑to‑cortical thickness ratio

**Table 3: Correlation between split renal function, plasma renin activity, and resistive index of the affected kidney (preoperative)**

| Parameter          | SRF of affected kidney | RI of affected kidney | R1‑R2 ($\triangle R$) | R1/R2 (RIR) | PRA |
|--------------------|------------------------|-----------------------|-----------------------|--------------|-----|
|                    | $r$                     | $P$                   | $r$                   | $P$           |     |
| SRF of the affected kidney | −0.15                  | 0.53                  | 0.6**                 | 0.5*          | 0.35|
| RI of affected kidney       | −0.15                  | 0.5                   | 0.003                 | 0.01          | 0.1 |
| R1‑R2 ($\triangle R$)      | −0.33                  | 0.62**                | 0.99**                | 0.08          |     |
| R1/R2 (RIR)               | 0.1                    | 0.003                 | 0.000                 | 0.00          | 0.8 |
| PRA                       | −0.32                  | 0.55*                 | 0.99**                | 0.03          |     |

*Correlation is significant at the 0.05 level (two‑tailed). **Correlation is significant at the 0.01 level (two‑tailed). RI: Resistive index, SRF: Split renal function, PRA: Plasma renin activity, RIR: Resistive index ratio, i.e., Ratio between the resistive index of the affected kidney (R1) and normal contralateral kidney (R2), $\triangle R$: Difference between the resistive index of the affected kidney (R1) and normal contralateral kidney (R2), RI: Resistive index, SRF: Split renal function, P/C: Pelvic diameter‑to‑cortical thickness ratio
**DISCUSSION**

PUJO is the most common congenital urinary obstruction. RDS remains a gold standard in the evaluation of these patients with loss of SRF in repeat renal scan being the criterion for significant PUJO deserving surgery. However, the lost SRF does not always recover following pyeloplasty, underscoring the need to select such patients earlier by alternative methods.\(^5\) An impaired SRF (<40%) is generally accepted as an indication for pyeloplasty in asymptomatic HDN.\(^6\) Similarly, the slope excretion curves and t-\(t_{1/2}\) are also considered important, though recently, their significance has been questioned.\(^7\) The other downside is the limited availability of RDS in public hospitals in India. Further, a recent study revealed that RDS findings in almost 1/3\(^{rd}\) such renal units had inconclusive results.\(^6\) In our present study, RDS scans did not provide excretion values of radionucleotide retained in kidneys beyond 16 min. Keeping in mind the fact that obstruction being present if t-\(t_{1/2}\) is more than 20 min, ideally, at least values up to 25 min should be provided on the x-axis of the graph. Hence, we could not correlate RI and PRA with t-\(t_{1/2}\).

Even if we overlook these limitations, the decision of performing pyeloplasty is simple if the results of USG (SFU Grade 3–4) and RDS (SRF and nature of curve) are in sync. In patients of SFU Grade 3–4 HDN with RDS showing obstructive curve and SRF <40%, early pyeloplasty is recommended, whereas in patients of SFU Grade 3–4 HDN with RDS showing nonobstructive curve and SRF >40%, conservative management is recommended.\(^7\) However, controversy appears when in patients of SFU Grade 3–4 HDN with RDS having mismatch of the two criteria of curve pattern and SRF, for example, obstructive or equivocal curve with SRF >40% or nonobstructive or equivocal curve with SRF <40%.\(^8,9\) In the present study, 10 out of 20 showed SRF >40% with inconclusive t-\(t_{1/2}\).

In our study, we compared values of PRA and RI with RDS for all 20 patients, both preoperatively and postoperatively. Poor correlation was found between PRA and SRF (\(P = 0.8\)) and also between RI and SRF (\(P = 0.528\)) both preoperatively and postoperatively. No study has been done to find the correlation between RI with SRF hitherto.

Gilbert *et al.*, Ordorica *et al.*, and Shokeir *et al.* showed a good positive correlation between RI and t-\(t_{1/2}\).\(^{10-12}\) In

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**Table 4: Correlation between split renal function, plasma renin activity, and resistive index of the affected kidney after the operation**

|              | SRF | RI  | R1_R2 (\(\Delta R\)) | R1/R2 (RIR) | PRA |
|--------------|-----|-----|----------------------|-------------|-----|
| **SRF**      |     |     |                      |             |     |
| r            | 0.1 | −0.02| 0.02                 | 0.09        |     |
| P            | 0.6 | 0.9  | 0.9                  | 0.7         |     |
| **RI**       |     |     |                      |             |     |
| r            | 0.1 | 0.7**| 0.6*                 | −0.01       |     |
| P            | 0.7 | 0.002| 0.01                 | 0.9         |     |
| **R1_R2 (\(\Delta R\))** |     |     |                      |             |     |
| r            | −0.02| 0.7**| 0.72**               | 0.001       |     |
| P            | 0.9 | 0.002| 0.00                 | 0.9         |     |
| **R1/R2 (RIR)** |     |     |                      |             |     |
| r            | 0.02| 0.5* | 0.72**               | 0.005       |     |
| P            | 0.9 | 0.01 | 0.00                 | 0.9         |     |
| **PRA**      |     |     |                      |             |     |
| r            | 0.09| −0.01| 0.001                | 0.005       |     |
| P            | 0.7 | 0.9  | 0.9                  | 0.9         |     |

**Correlation is significant at the 0.01 level (two-tailed),**

**Correlation is significant at the 0.05 level (two-tailed).**

RI: Resistive index, SRF: Split renal function, PRA: Plasma renin activity, RIR: Resistive index ratio, i.e., Ratio between the resistive index of the affected kidney (R1) and normal contralateral kidney (R2), \(\Delta R\): Difference between the resistive index of the affected kidney (R1) and normal contralateral kidney (R2)
the present study, we did not have excretion values of radionucleotide retained in kidneys beyond 16 min, so this correlation could not be studied. However, no statistically significant difference was observed between mean values of SRF before and after surgery ($P = 0.08$). Our results correlate well with the similar study reported earlier.\(^{[13]}\)

The difference in the mean values of APPD, mid-pole PT, P/C ratio before and after pyeloplasty was statistically significant ($P < 0.001$). Hence, these USG parameters may be used for predicting early success after pyeloplasty. Therefore, USG could probably preclude the need for RDS during follow-up after pyeloplasty.

The mean RI before surgery and after surgery were 0.71 ± 0.08 and 0.66 ± 0.22, respectively, which was statistically significant ($P = 0.04$). Similar findings were reported in the study done earlier by Kessler et al.\(^{[14]}\) mean RI before and after surgery was 0.75 ± 0.03 and 0.65 ± 0.05, respectively. Kessler et al. defined RI ≥0.7 and RIR ≥0.08 as surgical indications.\(^{[14]}\)

The preoperative and postoperative mean ΔR values in the present study were 0.09 ± 0.08 and 0.06 ± 0.22, respectively, which is statistically significant ($P = 0.02$). Our results correlate with the study done earlier in which the mean ΔR of the obstructive kidney was 0.08 ± 0.06 and nonobstructive kidney was 0.02 ± 0.02 ($P < 0.001$).\(^{[15]}\)

Similarly, the mean RIR decreased from the preoperative value of 1.16 ± 0.14 to the postoperative value of (1.05 ± 0.13) ($P = 0.01$). Our results are in agreement with the study done earlier in which the mean RIR of the obstructive kidney was 1.11 ± 0.125 and nonobstructive kidney was 1 ± 0.07 ($P = 0.05$).\(^{[15]}\)

In the present study, the mean PRA significantly reduced from preoperative value of 7.51 ± 5.36 ng/ml/h to postoperative value of 3.9 ± 4.75 ng/ml/h ($P < 0.01$). Singh and Bajpai also showed similar findings whose mean preoperative and postoperative PRA values of 7.3 ± 1.6 ng/ml/h and 4.4 ± 1.2 ng/ml/h, respectively.\(^{[16]}\)

Another study by the same group also showed significant difference in mean PRA values between preoperative (15.9 ± 6.4) and postoperative (4.2 ± 2.2) values ($P = 0.001$).\(^{[17]}\) However, the preoperative mean PRA value in our patients was lower than that of Bajpai et al.\(^{[17]}\) This could probably be due to difference in the age distribution, as PRA is age dependent. Bajpai et al. showed good correlation between PRA and SRF, but in our study it was not statistically significant. Their mean age at presentation was 12.5 ± 7.3 months, whereas in our study mean age at presentation was 42.6 ± 45.6 months. The PRA values are age dependent; they are inversely correlated with age.

PRA was found to have good concordance with RDS (90%), followed by RI (70%), APPD (70%). Hence, PRA, RI, and APPD can be used in follow-up of patients after surgery instead of RDS. One of the studies done by Faure et al.\(^{[18]}\) found no agreement between gold standard RDS and USG. According to this study, improvement in HDN on USG is slow and often takes >12 months. However, in the present study, fair agreement is found between USG parameters (APPD and RI) and RDS. However, to the best of our knowledge, this is the first study assessing the concordance of PRA with RDS. No similar study was done earlier.

In an obstructed kidney, function improves within 6–8 weeks following free drainage\(^{[19]}\) provided renal parenchyma retains a potential of reversibility. In one of the studies by Chatterjee et al., it was inferred that if diuretic renogram at 8th week did not show improvement despite free drainage with DJ stent following pyeloplasty, the renal parenchyma is likely to be irreversibly damaged.\(^{[20]}\)

**CONCLUSIONS**

1. RDS, which is considered as gold standard for the diagnosis of PUJO globally displays two very important parameters, namely, SRF and $t \cdot t_{1/2}$. In our study, $t \cdot t_{1/2}$ could not be derived in most of the patients preoperatively. Even peak (t) was not reached in many patients. Hence, correlations of PRA and RI, if any, could be derived against only SRF. It also refutes our primary assumption that RDS is a gold standard investigation for diagnosis of PUJO, at least in cases with SFU Grade 3 and 4 HDN.

2. No significant correlation could be demonstrated between SRF and the respective values of PRA and RI.

3. PRA was found to have good concordance with RDS (90%). Hence, PRA could act as an adjunct to predict the early success of pyeloplasty. A larger trial with bigger cohort of patients is required to confirm our contention.

4. PRA, RI can be used in follow-up of patients after surgery.

5. The use of RIR and ΔR significantly improves the diagnostic accuracy to identify obstruction compared to RI alone, as both are age independent.

**Limitations of the study**

1. Small sample size.
2. RDS curves drawn for inadequate period, i.e., 16 min.
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Conflicts of interest
There are no conflicts of interest.

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