Original Article

Supranormal differential renal function in adults with ureteropelvic junction obstruction: Does it really exist?

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ABSTRACT

Introduction: Some patients with ureteropelvic junction obstruction (UPJO) have supranormal differential renal function (snDRF). We aimed to study the outcomes of pyeloplasty in adult patients with UPJO and either snDRF or normal differential renal function (nDRF) and to identify preoperative factors responsible for the snDRF phenomenon.
Materials and Methods: We retrospectively retrieved data for all patients who underwent pyeloplasty and had snDRF (differential renal function [DRF] ≥55%) and nDRF (DRF between 45 and 55%) preoperatively. Preoperative radiological data using computed tomography or magnetic resonance imaging were correlated with the presence of snDRF phenomenon. In addition, scintigraphic findings pre- and post-operatively were also assessed to evaluate the functional outcomes.
Results: Of a total of 856 patients, 31 had snDRF (group 1) and 42 had nDRF (group 2). After a mean of 37 months' follow-up in Group 1, 22 patients developed DRF reduction with non-obstructive pattern. Mean DRF % decreased from 59 ± 2.8 to 48 ± 13 ($P < 0.0001$). However, in Group 2, five patients had DRF decrease. Four patients developed snDRF phenomenon postoperatively. Increased renal pelvis volume ≥50 mm^3 and increased anteroposterior pelvic diameter (APD) ≥37 mm were found to predict snDRF phenomenon. The same findings, in addition to preoperative snDRF, correlated with postoperative DRF decrease.
Conclusion: SnDRF function could be expected in patients with increased renal pelvis volume and APD. The absolute value or changes in DRF are not reliable to judge treatment failure.

INTRODUCTION

Pyeloplasty is the most common surgical procedure to manage ureteropelvic junction obstruction (UPJO) with a high success rates.[1] Indications for surgery include worsening of hydronephrosis, persistent pain, reduced differential renal function (DRF) <40%, or prolonged drainage time on diuretic renogram.[2] DRF refers to the relative ability of a kidney to eliminate a radiotracer from the blood using ^{99m}Tc-MAG3 scan.[3]

Most patients with UPJO have lower DRF except in 9%–21% of the patients who have a higher DRF than the normal contralateral kidney, referred to as "supranormal" function.[4,5] Supranormal differential function (snDRF) is considered to exist when DRF in the affected kidney is more than 55% of the total renal function and normal DRF (nDRF) is considered as ranging between 45% and 55%.

The pathophysiology of snDRF remains unclear. Some theories suggest that snDRF is an artifact with the use of different radioisotopes, in addition to the reservoir effect of the dilated renal pelvis.[6,7] Additional theories included renal parenchymal hypertrophy; contralateral hypofunction

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and hyperfiltration in the presence of obstruction had been suggested to play a role in the hydronephrotic kidney.[8-10]

Salle *et al*.[11] experimentally documented that the geometrical configuration of the kidney and the relative distribution of activity in the parenchyma would alter the detection of scintillations and overestimate the function, especially in hydronephrotic kidney. The nature, causes, and fate of snDRF have been studied in pediatric age groups.[3,4,12] However, this topic was rarely discussed in the adult population. Hence, we intended to evaluate functional outcomes and predictors for snDRF phenomenon occurrence in adult patients with UPJO.

MATERIALS AND METHODS

We retrospectively retrieved the records of all patients who underwent pyeloplasty for UPJO at a tertiary center from January 2005 to December 2017. Patients with snDRF and nDRF) were identified. Patients were considered to have snDRF when DRF was more than 55%. While nDRF was considered when DRF was between 45% and 55% in comparison to the contralateral renal unit. Patients with recurrent UPJO, congenital renal malformations, missing preoperative or follow-up data, age <18 years, bilateral UPJO and patients with solitary kidney, either anatomical or functional, were also excluded from the study.

Investigation and intervention

Renogram technique was standardized and carried out by the same team of radiologists throughout the study. The patients were well hydrated with 2 L of fluid within 2 h before the study. Diuretic medications were stopped 72 h before the examination. Evacuation of the urinary bladder was done just before image acquisition. The patient was placed supine on the table with detectors beneath, using a bright view dual-head gamma camera. Image acquisition was done using one frame/s for 60 s (Perfusion phase) followed by one frame/20 s for 19 min (uptake and excretion phases). Complete urinary tract including both kidneys and bladder needed to be in the field of view. Intravenous bolus injection of TC_{99}-MAG_3 dose (1.6–2 MBq/kg) was given through a two-way cannula. F-15 min diuretic renography was done by injection of furosemide 15 min, before radiographic material injection. Regions of interest (ROIs) were manually drawn on a summed image. The entire kidney and the pelvis were included. Lateral or perirenal background correction was performed using a surrounding background ROI. DRF was calculated as the percentage of the sum of right and left kidneys during the first 1–2 min of the study. Visual interpretation of the vascular phase (Perfusion) of renogram was routinely used in the evaluation of the kidney function as well as the shape of curves. T½ was estimated (normal <10 min, equivocal 10–20, obstructed >20 min).

Non-contrast computed tomography (NCCT), contrast-enhanced computed tomography (CE-CT) (Philips brilliance 64, Netherlands) or magnetic resonance imaging (Philips Ingenia 3T, Netherlands) were used to evaluate renal morphology. Preoperative radiological data including anteroposterior pelvic diameter (APD) in mm, parenchymal thickness in mm, renal pelvis volume (Pelvic volume was calculated from the equation of a sphere: $4/3\ \pi r^3$ (where r is the radius of the pelvis, calculated as APD/2), and renal parenchymal volume in both kidneys were estimated by means of CT.[13] Grades of hydronephrosis were classified according to the Society of Fetal Urology (SFU).[14]

Open or laparoscopic Anderson-Hynes dismembered pyeloplasty were performed for all the patients included in the study, according to the surgeon's preference. After excision of the ureteropelvic junction segment and reduction (if the renal pelvis was hugely dilated according to surgeon's view), the anastomosis was performed in an interrupted, continuous or mixed manner using 4–0 or 5–0 Vicryl sutures. Antegrade double-J stent was placed for 4–6 weeks (median 4 weeks).

Follow-up and measurements

According to our protocol, all patients were followed up by abdominal ultrasound (US) and diuretic renography 6 months after the procedure, a biannual US and annual renography for 3 years subsequently. Preoperative demographics, radiological data, operative notes, renogram findings including DRF, glomerular filtration rate (GFR), and T½ preoperatively and postoperatively at last follow-up were assessed.

Outcomes

The primary outcome was to investigate which preoperative correlated with snDRF in hydronephrotic kidneys. For that, we selected patients with nDRF as comparative group. We also compared our results with patients with DRF <45% (Group 3). The secondary outcome was to analyze the long-term functional outcomes of both snDRF and nDRF patients after pyeloplasty. We considered a renogram DRF change of 5% as the definition of 'renal function change'.[2] Based on this, patients were categorized into two groups; static/improved DRF and decreased DRF.

Statistical analysis

Continuous data were expressed as mean ± standard deviation or median (range) according to the pattern of distribution. Comparison of functional outcomes was done using paired sample *t*-test. Univariate analysis for preoperative factors affecting snDRF detection was done using one-way ANOVA, Kruskal–Wallis test, independent sample *t*-test, Chi-square, and Mann–Whitney *U*-tests. The receiver operating characteristics (ROCs) curve was used to identify cutoff values for significant continuous variables in univariate analysis. Multivariate analysis was performed by logistic regression analysis. All statistical tests were carried out using IBM "SPSS" statistics version 21 (Somers NY, USA), with a $P < 0.05$ was considered statistically significant.

Ethical consideration

The study was approved by the institutional review board (IRB no. 21.09.46-9/2018). All subjects provided written informed consent for inclusion in the study/for undergoing the procedures described. The procedures adhered to the ethical guidelines of Declaration of Helsinki. The authors confirmed the availability and access to all original data reported in this study.

RESULTS

Out of 856 patients who underwent pyeloplasty in our center in the period between 2005 and 2017, the study initially included 79 patients with snDRF and nDRF. 6 cases had incomplete follow up data and hence, the final data included 73 patients (47 males and 26 females) with a mean age of 34 ± 14 years. Patients were allocated into two groups according to DRF to snDRF ≥55% (31 patients) and nDRF <55 and ≥45% (42 patients). The demographics of both groups were illustrated in Table 1.

On univariate analysis to identify preoperative variables causing snDRF phenomenon, increased renal pelvis volume in mm^3, increased APD of the renal pelvis in mm and a higher degree of hydronephrosis according to SFU classification were significant ($P \leq 0.0001$, 0.001, and 0.005, respectively). In multivariate analysis, increased renal pelvis volume and increased APD were associated with increased the risk of snDRF detection by 6.9 and 1.7 times, respectively [Table 1].

To confirm our findings, we compared both previous groups with Group 3 (patients who underwent pyeloplasty with preoperative DRF <45% with available preoperative radiological data (n = 652 patients). We found that patients with snDRF presented at an older age than other groups (P = 0.001) and had significant increase in the renal pelvis APD and renal pelvis volume (P = 0.002 and 0.01, respectively) [Table 2]. In Group 3, the overall success of pyeloplasty was 90.2% (improved and static postoperative DRF).

ROC curve was generated to identify cutoff value of both renal pelvis volume in mm^3 and APD of the renal pelvis in mm. We found that renal pelvis volume of 50 mm^3 (area under the curve [AUC]: 0.74 and P = 0.002) and APD of 37 mm (AUC: 0.64 and P = 0.01) were the cutoff point showing highest sensitivity and specificity of 93%, 89% and 83%, 79%, respectively [Figure 1].

At a mean of 37 ± 12 months' follow-up, 71% of patients in snDRF (22 patients) developed a decrease in DRF and were non-symptomatic with non-obstructed T½ (T½ changed significantly from 23 (16–34) min to 6.8 (0–10.3) min) on renogram (P = <0.0001). Mean GFR and DRF in this group changed from 40 ± 10 ml/min and 59% ± 2.8% preoperatively to 41 ± 14 ml/min and 48% ± 13% postoperatively (P = 0.5 and <0.0001, respectively). Nine patients (29%) continued to have snDRF after surgery.

Evaluating DRF changes according to the renal pelvis reduction in snDRF group, the DRF changed from 58.9% ± 2.8% and 58.7% ± 2.6% preoperatively to 48.7% ± 14% and 49.5% ± 11% in groups of non- reduction versus those with reduction respectively with the

Table 1: Patient's demographics and univariate and multivariate analysis of preoperative data causing supranormal differential renal function

Variable	snDRF, (*n*=31)	nDRF, (*n*=42)	*P*	Multivariate analysis OR (95% CI), *P*
Age (years)*, mean±SD	36.7±16	35.2±12.8	0.08	
Gender** (male/female)	18/13	29/13	0.2	
Presenting symptoms (pain/infection)	29/2	41/1	0.4	
Side** (right/left)	16/15	20/22	0.5	
Culture** (+ve/−ve)	17/14	29/13	0.1	
Presence of stones** (no/yes)	21/10	33/9	0.2	
Renal pelvis volume (mm^3)***, median (range)	118 (30-679)	26 (14-287)	<0.0001	6.9 (1.9-8.2), <0.0001
Parenchymal thickness (mm)*, mean±SD	16±6	18±6	0.8	
Renal parenchymal volumetry (mm^3)*, mean±SD	62.9±28.9	66.7±26	0.7	
APD of renal pelvis (mm*), mean±SD	48±15	33±11	0.001	1.7 (1.1-4.34), 0.006
Grades of hydronephrosis**				
Low grade	8	17	0.005	0.2 (0.07-1.1), 0.9
High grade	23	25		
Preoperative GFR (ml/min)*, mean±SD	40±10	41±10.9	0.6	
Presence of crossing vessels (yes/no)	7/24	5/37	0.1	
Contralateral kidney parenchymal volume (mm^3), mean±SD	64±22	62±23	0.2	
Primary surgeon (number of patients)** (expert/general)	21/10	21/21	0.1	
Reduction of renal pelvis ** (yes/no)	17/14	8/32	0.08	
Approach** (open/laparoscopic)	26/5	34/8	0.4	

*Independent sampled *t*-test, **Chi-square test, ***Mann-Whitney test. OR=Odds ratio, CI=Confidence interval, SD=Standard deviation, APD=Anteroposterior pelvic diameter, DRF=Differential renal function, snDRF=Supranormal DRF, nDRF=Normal DRF, GFR=Glomerular filtration rate

Table 2: Comparison between patients with supranormal differential renal function, normal differential renal function and patients with differential renal function <45%

Variable	Patients with snDRF (*n*=31)	Patients with nDRF (*n*=42)	Patients with DRF <45% (*n*=652)	*P*
Age (years)*, mean±SD	36.7±16	35.2±12.8	33.7±9.3	0.01
Gender** (male/female)	18/13	29/13	443/209	0.6
Side** (right/left)	16/15	20/22	303/349	0.068
Culture** (+ve/−ve)	17/14	29/13	343/299	0.4
Presence of stones** (no/yes)	21/10	33/9	574/78	0.059
Renal pelvis volume (mm^3)***, median (range)	118 (30-679)	26 (14-287)	85 (23-453)	0.002
Parenchymal thickness (mm)*, mean±SD	16±6	18±6	16.9±7.1	0.4
APD of renal pelvis (mm*, mean±SD	48±15	33±11	40±15	0.01
Grades of hydronephrosis**				
Low grade	8	17	282	0.1
High grade	23	25	370	
Preoperative GFR* (ml/min), mean±SD	40±10	41±10.9	28.4±12.9	<0.0001
Primary surgeon (number of patients)** (expert/general)	21/10	21/21	407/245	0.1
Reduction of renal pelvis** (yes/no)	17/14	8/32	118/534	0.6
Approach** (open/laparoscopic)	26/5	34/8	568/84	0.8

*One-way ANOVA, **Chi-square test, ***Kruskal-Wallis test. SD=Standard deviation, APD=Anteroposterior pelvic diameter, DRF=Differential renal function, snDRF=Supranormal DRF, nDRF=Normal DRF, GFR=Glomerular filtration rate

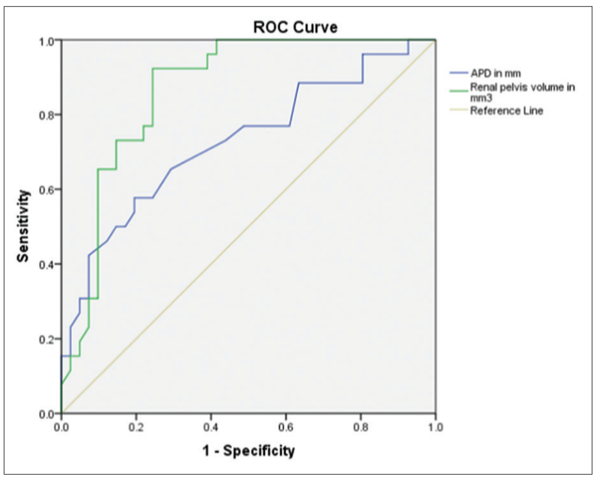

Figure 1: Receiver operating characteristic curve for anteroposterior pelvic diameter and volume of the renal pelvis affecting supranormal differential renal function

Table 3: Functional outcomes in supranormal differential renal function and normal differential renal function groups

Variable	snDRF (*n*=31)	nDRF (*n*=42)
Status of renal function post pyeloplasty, *n* (%)		
Decreased	22 (71)	5 (11.9)
Increased	4 (13)	10 (23.8)
Static	5 (16)	27 (64.3)
Supranormal phenomenon presence postpyeloplasty (yes/no)	9/22	4/38
GFR (ml/min)*		
Preoperative	40±10	41±10.9
Postoperative	41±14	43±15
P	0.5	0.2
DRF%*		
Preoperative	59±2.8	47.4±2.2
Postoperative	48±13	46±9
P	<0.0001	0.34

*Paired sampled *t*-test. DRF=Differential renal function, snDRF=Supranormal DRF, nDRF=Normal DRF, GFR=Glomerular filtration rate

difference in DRF change between both groups being non-significant ($P = 0.8$).

In contrast, in patients who underwent pyeloplasty in the nDRF group, 11.9% (5 patients) developed a decrease in DRF at the last follow-up; all of them were non-obstructed; T½ changed significantly from 25 (23–39) min to 5.4 (0–12.8) min ($P < 0.0001$) and were asymptomatic. Four (9.5%) patients developed snDRF phenomenon postoperatively. Mean GFR and DRF were nearly static at follow-up with $P = 0.2$ and 0.34, respectively [Table 3].

Comparison between patients with decreased DRF in both the groups ($n = 27$) and patients with static/improved DRF ($n = 46$) to identify predictors for DRF decrease postpyeloplasty was done. Increased renal pelvis volume >50 mm^3, APD >37 mm, and preoperative snDRF were independent risk factors for DRF decrease postoperatively at last follow-up [Table 4].

DISCUSSION

The occurrence of a supranormal function in our present study is 3.6%, which is lower than the previous reports in pediatric age groups which ranged from 9% to 21%.[3,4,7,10,12] This lower incidence may be attributed to the late diagnosis of UPJO at adulthood which affect the renal function of the affected kidney at the first presentation. Concerning renal function outcome after pyeloplasty, it was documented that children with snDRF who underwent pyeloplasty were found to have an obvious decrease in hydronephrosis, and 70% of them had a decrease in postoperative DRF, reaching a normal level of function (40%–55%).[3,4] These findings were detected in our study as we noticed that 71% of patients with snDRF had a decrease in the DRF reaching normal DRF at the last follow-up. Interestingly, we noticed that 9.5% of the patients with normal DRF had developed snDRF at last follow-up.

Table 4: Predictors for differential renal function change in both groups postpyeloplasty

Variable	Decreased DRF (*n*=27)	Static/increased DRF (*n*=46)	*P*	Multivariate analysis OR (95% CI), *P*
Age (years)*, mean±SD	33.3±14.2	35.4±13.6	0.4	
Gender** (male/female)	17/10	30/16	0.4	
Renal pelvis volume (mm^3)				
≤50	7	26	0.01	1.8 (1.1-4.6), 0.04
>50	20	20		
APD of renal pelvis (mm)**				
≤37	11	33	0.009	2.9 (1.4-8.2), 0.001
>37	16	13		
Grades of hydronephrosis**				
Low grade	6	19	0.03	0.9 (2.1-3), 0.1
High grade	21	27		
Pre-DRF category**				
SnDRF	22	9	<0.0001	3.2 (1.2-8.9), 0.001
nDRF	5	37		
Reduction of renal pelvis**				
Yes	4	13	0.1	
No	23	33		
Approach**				
Open	23	37	0.4	
Laparoscopic	4	9		

*Independent sampled *t*-test, **Chi-square test. OR=Odds ratio, SD=Standard deviation, DRF=Differential renal function, snDRF=Supranormal DRF, nDRF=Normal DRF

The impact of snDRF in the management of UPJO is still a matter of debate in terms of its nature, tsignificance and the need for intervention and their clinical outcomes. Some authors suggetsed that snDRF was a result of a technical artifact related to the type of the radiotracer, identification of the interest area, an error in the calculation method, or subtraction of background activity.[15-18] Notably in an experimental study, Salle *et al*. showed that supranormal function was not an artifact but a pathophysiological phenomenon affected by parenchymal thinning, degree of hydronephrosis, shape, and geometrical view of the renal pelvis and radioisotope distribution during renogram recommending conjugate view during renogram to eliminate this phenomenon.[11] This recommendation was supported by Wehbi *et al*. who demonstrated that for each 1 mm increase in APD, the odds of observing discrepancy between anterior and posterior views increased by 2%.[19] Alternatively, other authors tried to find other explanations for the snDRF phenomenon related to glomerular mass hyperfunction and increased the renal blood flow.[20] However, this explanation was encountered by Ham *et al*.[16] based on renal biopsy.

In a pediatric cohort, it has been shown that renal function could decrease in patients with snDRF and increased APD of the renal pelvis preoperatively when hydronephrosis improved after surgery.[12] They recommended close surveillance and early surgical treatment in those children if hydronephrosis or drainage time on renogram deteriorated.[12]

We support this concept in the adult population. We found that increase in both renal pelvis volume ≥50 mm^3 and APD of the renal pelvis ≥37 mm were associated with greater possibility of snDRF detection by 6.9 and 1.7 times. These results support the previous experimental hypothesis that the geometrical view of the renal pelvis affects calculation of snDRF. Furthermore, we noticed that a minority of patients had sustained factual snDRF while others with deceptive snDRF returned to normal DRF without significant clinical symptoms, radiological evidence of obstruction and nonsignificant decrease in GFR postoperatively. These factors not only predict the presence of snDRF phenomenon, but also predict the decrease of DRF in addition to preoperative snDRF postpyeloplasty at last follow-up.

In adults without snDRF who undergo pyeloplasty, renal function recoverability is unpredictable as 65% show improved renal function postoperatively, 30% remain the same, and 5% deteriorate.[2,21] Others have documented that improvement of renal function was likely to occur after the repair of adult UPJO.[22,23] In our study, we notably observed that the success rate in patients with nDRF was 88.1% (64% had static DRF and 23% had increased DRF, postoperatively). In patients with snDRF, only 29% preserved the same renal function postoperatively. Further, at last follow-up in patients with DRF <45%, we noticed that 9.8% developed renal function deterioration with overall success rate reaching 90.2%.

In patients with snDRF, we found that intraoperative renal pelvis reduction did not show significant difference in DRF change. However, we also noticed that more than 50% of the patients in snDRF group required renal pelvis reduction which was still higher in nDRF. This supports the findings that reduction or no reduction of the renal pelvis does not affect renal function.[24]

On the other hand, it was theorized that DRF >60% was the only independent risk factor associated with early postoperative complications (within the 1st year postoperatively), including pyeloplasty failure (which was defined as worsening of the hydronephrosis and symptomatic obstruction).[25] In our study, no patients in the snDRF or nDRF groups developed clinical failure or obstructed T½ requiring reintervention at a long-term follow-up period reaching nearly 3 years' period.

This study provides the incidence of snDRF in an exclusively adult population and reiterates the significance of clinical symptoms and T½ at follow-up and not only of DRF estimation. Being a single-center study, the study avoided the variability in both diagnosis (clinical and radiological), management and follow-up protocols which could affect the functional outcomes. However, it was limited by its retrospective nature with inherent selection bias with a low number of patients and the absence of standardized protocol for renal pelvis reduction intraoperatively. In addition, the lack of another control group on follow-up without intervention which could delineate the importance of follow-up in such cases of snDRF and nDRF.

CONCLUSION

In adult patients, snDRF function could be expected in patients with larger renal pelvis volume ≥50 mm^3 and APD of the renal pelvis ≥37 mm. These findings support the theory that snDRF is related to kidneys with large renal pelvis with severe obstruction. At long-term follow-up, 29% could preserve snDRF where others could develop asymptomatic decrease in DRF. Increased renal pelvis volume, APD of the renal pelvis and preoperative snDRF were predictors for DRF decrease after pyeloplasty. Long-term decisions for functional and clinical outcomes for snDRF patients should not be taken only by the net result of renal function but also symptoms and T½ values.

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