

Impact of transurethral resection on urinary flow rate in children with posterior urethral valve in short term follow-up

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ABSTRACT

الأهداف: تقييم معدل تصحيح معدل الجريان البولي بعد استئصال الصمام الاحليلي الخلفي (PUV) لتنبؤ عن مدى نجاح العملية.

الطريقة: أجريت دراسة استعدادية خلال الفترة من مارس 2006م حتى فبراير 2013م في قسم المسالك البولية للأطفال، كلية الطب، جامعة أكدينيز، أنطاليا، تركيا. من بين 67 مريض أجري لهم صمام احليلي خلفي شارك 52 مريض. تم تسجيل كلا من الفحوصات الطبية، وتحليل الدم والبول، وقياس تدفق البول، والحد الأقصى لمعدل التدفق ومتوسط معدل التدفق، وحجم البول الشمالي بعد الإفراغ. وتم تسجيل كلا من UFM و PVR وتصوير المثانة والاحليل الافراغي ومستويات الكرياتينين في مصل الدم في الزيارات الإكلينيكية. وقد تم إجراء عمليات إضافية إذا كانت هنالك أعراض قصور بولية. كما تم إجراء تحليل إحصائي.

النتائج: كان متوسط العمر 9 ± 2.9 عام. ومعدل المتابعة 10.6 ± 4.2 شهر. ظهر اختلاف إحصائي في مستويات الكرياتينين لمصل الدم قبل وبعد العملية $p=0.028$ ، و Q_{max} ($p=0.001$)، و Q_{avg} ($p=0.002$) و PVR ($p=0.001$). وارتبطت مستويات الكرياتينين في مصل الدم بشكل إيجابي ومهم إحصائي مع PVR بعد إجراء العملية $p=0.024$. في تحليل الانحدار اللوجستي، ارتبط النجاح في استئصال PUV مع Q_{avg} قبل الجراحة ($p=0.016$) و PVR ($p=0.004$) و Q_{avg} بعد العملية ($p=0.039$) و PVR ($p=0.030$). ومن بين 42 مريض (80.7%) كان هنالك تحسن ملحوظ في UFM و PVR ومستويات الكرياتينين لمصل الدم في الأداء. وفي 10 من المرضى أعدت العملية لهم مرة أخرى.

الخلاصة: أن الفعالية القصيرة المدى لاستئصال الصمام الاحليلي الخلفي قد يتم التنبؤ به بواسطة تغيرات مؤشرات UFM و PVR لدى المرضى المختارين.

Objectives: To evaluate the correction rate of urinary flow rate after posterior urethral valve (PUV) resection for predicting success after operation.

Methods: This retrospective study was performed between March 2006 and February 2013 at the Department of Pediatric Urology, Akdeniz University School of Medicine, Antalya, Turkey. Of the 67 patients with PUV, 52 patients were enrolled. Physical examinations, urine and blood analyses, uroflowmetry (UFM) including maximum flow rate (Q_{max}) and average flow rate (Q_{avg}), and post voiding residual urine volume (PVR) were recorded. The UFM, PVR, voiding cystourethrography, serum creatinine levels were recorded in clinical visits. Additional operations were performed if there were symptoms of urinary obstruction. Statistical analyses were carried out.

Results: The mean age was 9 ± 2.9 years. The mean follow-up was 10.6 ± 4.2 months. There was a significant difference between preoperative and postoperative serum creatinine ($p=0.028$), Q_{max} ($p=0.001$), Q_{avg} ($p=0.002$), and PVR ($p=0.001$). Postoperative serum creatinine was significantly positively correlated with postoperative PVR ($p=0.024$). In logistic regression analysis, success on PUV resection was associated with preoperative Q_{avg} ($p=0.016$) and PVR ($p=0.004$), and postoperative Q_{avg} ($p=0.039$) and PVR ($p=0.030$). Of the 42 (80.7%) patients, significant improvements in UFM, PVR, and serum creatinine levels were obtained after first operation. In 10 patients, re-operations were performed.

Conclusion: Short-term effectiveness of PUV resection may be predicted by changes in UFM and PVR parameters in selected patients.

Saudi Med J 2014; Vol. 35 (5): 460-465

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Received 28th December 2013. Accepted 7th April 2014.

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Posterior urethral valve (PUV) occurs in 1:4000 to 1:25000 of live births, and clinical presentation of PUV considerably varies.¹ Posterior urethral valves are the most common cause of bladder outlet obstruction in children.¹ Despite medical managements, PUV may lead to serious inabilities, such as renal insufficiency and incontinence. Therefore, rapid diagnosis and treatment are essential. Endoscopic resection, which has been accepted as a definitive surgical treatment still maintained its importance in the treatment of PUV.² After surgical treatment, follow-up can be performed by voiding cystourethrography (VCUG), uroflowmetry (UFM), post voiding residual urine volume (PVR), the other clinical and endoscopic findings.³ However, VCUG leads to exposure to x-ray, and endoscopy requires anesthesia in children. Additionally, to evaluate and predict the course of PUV from clinical findings needs long-term follow-up. Therefore, UFM may come to the forefront for prediction of success in surgical treatment of PUV resection with its non-invasive and easy applicable methods. Moreover, importance of UFM parameters has not been reported for continuum and prediction of PUV's success during short term follow-up in the literature before. The present study aimed to investigate prediction of success in PUV resection according to UFM parameters, in short-term follow-up. Our aim was to show that resection of PUV improves UFM parameters. Additionally, if UFM does not improve, there may be residual valves, and additional ablations may improve UFM parameters.

Methods. The data from PUV patients was retrospectively evaluated. Between March 2006 and February 2013, children who underwent surgical treatment for PUV at the Department of Pediatric Urology, Akdeniz University School of Medicine, Antalya, Turkey was investigated. Our institutional board approved the study. Informed consent was obtained and signed by the parents of all children. Additionally, our study was performed according to principles of Helsinki Declaration. Exclusion criteria were previous endoscopic PUV, missing data, detrusor instability in urodynamic examinations, children younger than 5 years old, children who were not toilet-trained, and upper urinary tract dilatation on ultrasonography (US). Patients who were diagnosed as PUV, or referred to our clinic were evaluated from our

PUV database. The files of patients were investigated. Of the 67 patients, 52 patients whose age was between 5-17 years were enrolled in the study. Detailed physical examination, medical history, laboratory analyses including serum creatinine, urine analyses, UFM including maximum flow rate (Q_{max}), average flow rate (Q_{avg}) (Solar Uroflow, Medical Measurement Systems Inc, Dover, NH, USA), PVR (The BioCon 500, Medline LA, CA, USA), and US of the urinary tract were performed. These parameters were recorded before PUV resection as a baseline. Additionally, these parameters were recoded after the first month of operation. Changes in parameters were evaluated. Delta Q_{max} (postoperative-preoperative), and delta PVR (preoperative-postoperative) were analyzed.

Surgical technique. All operations were performed by the same surgeon with an endoscopic route under general anesthesia using Young's classification.⁴ According to this classification, all patients that underwent surgery were of PUV type 1. We used a pediatric resectoscope with 0° optical lens (Richard Wolf, Chicago, IL, USA). Cold knives were used in all procedures. Resection of valves was performed at the 5, 7, and 12 o'clock position. Additional endoscopic controls were performed during surgery for checking residual valves after resection. These were decided by the surgeon. Urethral catheter was indwelled after the operation. All operations were performed in the day-case surgery center of our institution. All patients were discharged on the day of surgery with urethral catheter. Urethral catheter were removed on the first day after operation in the Urology Outpatient Clinic. In the follow-up period, all patients underwent voiding diary, renal function tests, urinary US, UFM, PVR, and VCUG every 3 months. These were also recorded. Further endoscopic assessment and possible interventions (ablation of residual valve) were carried out when there was no improvement in UFM, PVR, and VCUG parameters in the first month of operation. The same devices were used in additional operations.

Statistical analysis. The independent-samples t test was used to compare measurable values. Pearson's correlation test was used to identify correlations between parameters. A receiver operating characteristic (ROC) curve was used to identify cutoff points for determining UFM parameters in the success of PUV resection. Logistic regression analysis was performed to identify factors predicting reasons for increased urinary flow rate. Statistical significance was considered as $p < 0.05$, and all p -values were 2-sided. All statistical analyses were performed with the Statistical Package for Social Sciences for Windows version 16.0 (SPSS Inc., Chicago, IL, USA), and graphs were plotted using the same software.

Disclosure. Authors declare no conflict of interests, and the work was not supported or funded by any drug company.

Results. The mean age was 9 ± 2.98 years. The mean follow-up was 10.6 ± 4.2 months. There was a significant decrease in serum creatinine ($p=0.028$), decrease in PVR ($p=0.001$), and increase in Qmax ($p=0.001$), Qavg ($p=0.002$) in the postoperative follow-up when compared with the preoperative period (baseline) (Table 1). In the Pearson correlation table, postoperative serum creatinine was statistically significantly positively correlated with age ($p=0.006$), baseline serum creatinine ($p=0.001$), and postoperative PVR ($p=0.024$).

Table 1 - Comparison of preoperative and postoperative parameters.

Parameters	Baseline \pm standard deviation	Postoperative \pm standard deviation	P-value
Serum creatinine (mg/dl)	1.68 \pm 2.97	0.94 \pm 1.69	0.028*
Qmax	12.99 \pm 5.81	17.11 \pm 6.54	0.001*
Qavg	7.30 \pm 3.02	8.91 \pm 3.36	0.002*
PVR	32.30 \pm 19.18	22.48 \pm 18.32	0.001*

Qmax - maximum flow rate, Qavg - average flow rate, PVR - post-voiding residual urine volume. *statistically significant

Table 2 - Correlations table of studied parameters in the present series conducted in the Department of Pediatric Urology, Akdeniz University School of Medicine, Antalya, Turkey.

Parameters	Age (year)	Baseline serum creatinine (mg/dl)	Baseline Qmax (ml/sec)	Baseline Qavg (ml/sec)	Baseline PVR (ml)	Postoperative serum creatinine (mg/dl)	Postoperative Qmax (ml/sec)	Postoperative Qavg (ml/sec)	Postoperative PVR (ml)	Delta Qmax	Delta Qavg	Delta PVR
<i>Age (year)</i>												
R	1	0.201	0.044	-0.004	-0.021	0.375	0.043	-0.050	0.112	0.003	-0.044	0.139
P		0.153	0.757	0.979	0.883	0.006*	0.763	0.725	0.430	0.981	0.757	0.325
<i>Baseline serum creatinine (mg/dl)</i>												
R		1	-0.343	-0.262	0.183	0.618	0.069	0.083	0.122	0.333	0.300	-0.073
P			0.013*	0.061	0.194	0.001*	0.628	0.561	0.390	0.016*	0.031*	0.609
<i>Baseline Qmax (ml/sec)</i>												
R			1	0.821	-0.065	-0.079	0.299	0.135	0.107	-0.526	-0.570	0.182
P				0.001*	0.649	0.577	0.032*	0.340	0.450	0.001*	0.001*	0.198
<i>Baseline Qavg (ml/sec)</i>												
R				1	-0.139	-0.112	0.302	0.381	0.049	-0.382	-0.489	0.202
P					0.324	0.429	0.03*	0.005*	0.733	0.005*	0.001*	0.151
<i>Baseline PVR (ml)</i>												
R					1	0.152	0.032	-0.075	0.559	0.080	0.048	-0.507
P						0.282	0.822	0.599	0.001*	0.574	0.736	0.001*
<i>Postoperative serum creatinine (mg/dl)</i>												
R						1	-0.121	-0.150	0.313	-0.045	-0.047	0.160
P							0.394	0.288	0.024*	0.753	0.743	0.256
<i>Postoperative Qmax (ml/sec)</i>												
R							1	0.791	-0.349	0.654	0.490	-0.398
P								0.001*	0.011*	0.001*	0.001*	0.004*
<i>Postoperative Qavg (ml/sec)</i>												
R								1	-0.400	0.598	0.620	-0.334
P									0.003*	0.001*	0.001*	0.015*
<i>Postoperative PVR (ml)</i>												
R									1	-0.396	-0.418	0.431
P										0.004*	0.002*	0.001*
<i>Delta Qmax</i>												
R										1	0.888**	-0.498
P											0.001*	0.001*
<i>Delta Qavg</i>												
R											1	-0.487
P												0.001*
<i>Delta PVR</i>												
R												1

Qmax - maximum flow rate, Qavg - average flow rate, PVR - post-voiding residual urine volume, R - rank according to Pearson Correlation, P - p-value. *statistically significant

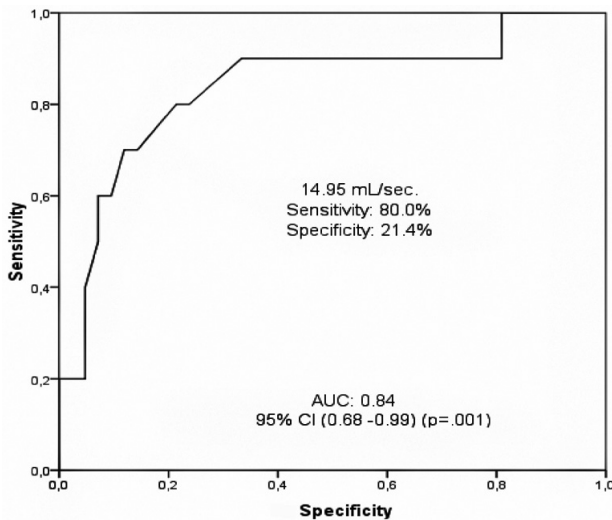


Figure 1 - The cutoff maximum urinary flow rate as determined (14.95 ml/sec) using the receiver operating characteristic curves. AUC - area under the curve, CI - confidence interval

Table 3 - Logistic regression analyses of associated factors with increasing maximum flow rate after operation.

Parameters	P-value
Age	0.9
Preoperative serum creatinine	0.249
Preoperative Qmax	0.92
Preoperative Qavg	0.016*
Preoperative PVR	0.004
Postoperative serum creatinine	0.441
Postoperative Qmax	0.897
Postoperative Qavg	0.039*
Postoperative PVR	0.03

Qmax - maximum urinary flow rate, Qavg - average urinary flow rate, PVR - post voiding residual urinary volume. *statistically significant

Additionally, postoperative PVR was statistically significant positively correlated with preoperative PVR ($p=0.001$), postoperative creatinine levels ($p=0.024$), and delta PVR ($p=0.001$) (Table 2). However, 42 (80.7%) children had significant improvement in UFM, PVR, and serum creatinine levels, and 10 (19.3%) children needed additional PUV operations. There were residual valves in 7 (13.4%) children, and one child had urethral stricture. This was associated with Clavien Grade 3 complications. The urethra seemed normal, and there were no residual valves in 2 (7.6%) children. The cutoff Qmax was 14.95 ml/sec for determining success in the first PUV resection according to ROC curves (area under the curve [AUC] was 0.839, $p=0.001$) (Figure 1). In logistic regression analysis, preoperative ($p=0.16$), and postoperative parameters of Qavg ($p=0.039$) and

PVR ($p=0.03$) were statistically significant associated factors on increasing urinary flow rate. Age ($p=0.9$), preoperative serum creatinine ($p=0.249$) and Qmax ($p=0.92$), and postoperative serum creatinine ($p=0.441$) and Qmax was not associated with increasing urinary flow rate ($p=0.897$). The results of logistic regression analyses are shown in Table 3. Of the 4 children that had urinary retention after operation, the urethral catheter was indwelled again, and oral anti-inflammatory drugs were recommended for one week. These were related with Clavien Grade 2 complications. After one week, the urethral catheter were removed, and micturition of children was observed. In follow-up, there was an increase in UFM parameters, and decrease in PVR in these children. They did not need further operations.

Discussion. In the present study, we investigated the effects of PUV resection on UFM and PVR parameters in children with PUV. Additionally, further resections of residual PUV developed UFM and decreased PVR. However, primary PUV resection is essential; effectiveness of resections may not be predicted accurately in short-term follow-up. It is for this reason that we designed this study. Outcomes of our study may enable us to predict adequate drainage, and give us an opinion on the continuum of PUV resection, in short-term follow-up.

We used the same classification as Young⁴ reported previously. All patients underwent endoscopic PUV resection. de Jong et al⁵ reported that the method of obtaining the best outcome on UFM could be provided by cutting at the 5 and 7 o'clock positions. We performed the same surgical methods like de Jong et al.⁵ After resections, the urethra was checked for residual PUV in all procedures. John et al⁵ also reported an endoscopic view of resected valves may not predict residual PUV, or stringency. The results of our study were parallel to the study of John et al.⁵ Of the 10 (19.3%) children needing re-operation, there was residual PUV in 7 (13.4%) patients, and one child had urethral stricture. The urethra of 2 children were normal. Additionally, Qmax did not increase significantly after the operation in these patients. Seven patients underwent additional valve ablations. In follow-up, a statistical significant increase in Qmax and decrease in PVR were obtained. Furthermore, the mean serum creatinine levels significantly decreased after the first resection in all procedures in short-term follow-up ($p=0.039$). Caione and Nappo⁶ reported recovery of serum creatinine and bladder functions after primary resection of PUV in long term follow-up. Our results were parallel to their study.⁶ However, this present study included short-term outcomes, and decreased serum creatinine was obtained at the first month of PUV resection. Additionally,

these were significantly positively correlated with postoperative PVR in correlation tables ($p=0.024$). Decreased postoperative PVR may be an indicator of success in PUV resection in short-term follow-up. Thus, development in UFM and PVR parameters may be a reflection of better kidney functions in this series.

On the other hand, postoperative PVR was significantly correlated negatively with delta Qmax in the correlations table ($p=0.004$). In addition, delta Qmax was negatively correlated with postoperative serum creatinine without statistical significance ($p=0.753$). Sarin and Sinha⁷ reported urodynamic investigations that might help clinicians for proper treatments according to bladder functions. Outcomes of our series were parallel to their studies.⁷ One of the indicator of success may be a postoperative increase in Qmax, as well as decrease in PVR in follow-up after PUV resection, in short-term follow-up. If UFM and PVR parameters have not developed after PUV resection, clinicians should be aware of failure in surgery.

The serum creatinine may be an indicator of better outcomes, in long term follow-up. Capitanucci⁸ reported better results in kidney functions, in short-term follow-up after PUV resection. Our results were parallel to the study of Capitanucci.⁸ There was a significant decrease in the mean serum creatinine after the first operation when compared with preoperative levels ($p=0.028$). These may be a proof of better kidney functions in follow-up. As mentioned above, and shown in correlations tables, postoperative serum creatinine was associated with postoperative PVR, and indirectly with other UFM parameters ($p=0.024$).

Follow-up methods may still be a subject of debate after PUV resection.⁹ Smeulders et al¹⁰ reported that they used routine cystoscopy and VCUG in diagnosis, as well as in follow-up. When VCUG is used to confirm success in PUV resection, exposure to x-ray comes into question. Additionally, VCUG needs urinary catheterization. Moreover, the accuracy of VCUG is still being debated.⁹ Despite all of these disadvantages, VCUG is used for diagnosis and follow-up for PUV.⁹ Cystoscopy needs anesthesia in children. On the other hand, we investigated usage of UFM and PVR, as additional follow-up criteria, in short-term follow-up. As we pointed above, these parameters may be used for prediction of success in PUV resection, in short-term follow-up. Thus, children may not undergo cystoscopy, and/or VCUG. This was one of the goal of the present study. However, our surgeon had long fellowship training on pediatric urology, and we confirmed urethral opening in all cases, 19.3% need re-operations.

The UFM and PVR were non-invasive methods for follow-up. In our opinion, these may be useful in clinical practise after PUV resection, in short-term

follow-up. To be non-invasive, without risk of exposure to radiation, easy to applicable are some of the advantages of UFM and PVR. Moreover, these examinations may be an indicator of success, when they would not be improved after PUV resection.^{10,11} According to the outcomes of this study, the cutoff Qmax was 14.95 ml/sec for predicting success after resection (Figure 1). Besides these, cutoff value in Qmax should be considered. Nevertheless, these values and comments are not precise results. They may be used for obtaining ideas on continuum of PUV resection, in short-term follow-up.

In the correlation tables, delta PVR was significantly negatively correlated with postoperative Qmax ($p=0.004$). This may be an indicator of better bladder functions after PUV resection. Lopez Pereira et al¹² reported better bladder functions were associated with kidney functions in their series. Outcomes of this series were parallel to them. However, we did not provide results of urodynamic studies; correlation in PVR and UFM parameters may help to predict better outcomes. Hennis et al¹³ reported a wide range of bladder and kidney function outcomes after PUV resection. We had limited numbers of patients, and the exclusion criteria had a wide range. Nevertheless, our series was comparable to the literature.^{9,12,13} The UFM and PVR parameters may help us to consider regarding bladder functions after PUV resection, in short-term follow-up.

Sudarsanan et al¹⁴ reported better bladder functions with early surgical management of PUV. However, our series included 5-17 year old boys, and outcomes of this series were parallel to their study.¹⁴ Additionally, according to our PUV protocols, urodynamic studies are performed only when needed. As a part of urodynamic studies, development in UFM and PVR parameters may be used for prediction of better bladder functions after PUV resection. Sarhan et al¹⁵ reported the urethral stricture after PUV resection with a range of 2-50%, in long term follow-up. However, our results included short-term data; and outcomes of our series were parallel to them Sarhan et al.¹⁵ Urethral stricture occurred in one child in our study. Babu and Kumar reported urethral stricture according to diathermy.¹⁶ Our surgical technique was not similar with them as we used cold knives in all procedures. Moreover, 4 children had acute-urinary retention after urethral catheter removal. In our clinical aspect, these may be related with urethral edema, which may be caused by urethral intervention. After anti-inflammatory drugs were used for one week, urethral catheters were removed, and there were no complications in the follow-up.

We know that there were some limitations, such as the retrospective pattern, selection bias with low numbers of patients with a short-term follow-up

period, and without prenatal diagnosis in this study. We included children older than 5 years old. We aimed to overcome cooperation problem in children for using UFM and PVR accurately. Moreover, late presentations of PUV are rare nowadays, but scattered cases have been reported in the past 2 decades.¹⁷ Additionally, PUV is the cause of renal insufficiency in approximately 10-15% of children undergoing renal transplant, and approximately one-third of patients born with PUV progress to end stage renal disease.¹⁸

In our study, the mean age was 9 years, and thereby, it may be also possible that some of the patients had a "mild grade" PUV, without permanent renal damage; in "true" PUV patients the renal damage is congenital, and it is not quite influenced by a late treatment. Therefore, outcomes of our series may be a reflection of selected patients. Therefore, we enlarged exclusion criteria for having accurate changing results of UFM, PVR, and serum creatinine levels. Besides all of these above, in our community, patients with PUV may be followed-up in peripheral hospitals after PUV resection. The findings of cystoscopy, VCUG, and the importance of urodynamics were not assessed in this series. These can be all a new subject of future studies.

The goals of our study were including predictable success on PUV resection according to UFM and PVR parameters, in selected patients, in short-term follow-up. Thus, some of the children may be free from cystoscopy and/or VCUG. All of these were the reasons for being unique in the present present series.

In conclusion, primary PUV resection with cold knives is the first choice in the surgical treatment of children with PUV. Changes in UFM and PVR parameters may provide to predict success in selected patients, in short-term follow-up after PUV resection. The PUV resection increase Qmax and decrease PVR. If Qmax was under 14.95 ml/sec after PUV resection in selected population, there might be residual valves, and thereby, further resections may increase Qmax. These findings should be confirmed by performance of controlled studies with large cohorts.

Acknowledgment. *The authors gratefully acknowledge all radiology doctors of our institute for ultrasonography examinations of our PUV patients.*

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