

Re-ablation of residual posterior urethral valves: a single-centre retrospective review

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Background: Residual posterior urethral valves (RPUV) after primary ablation can be responsible for the persistence of urinary symptoms and worsening of renal function in children. This study aims to determine the impact of repeat cystoscopy and subsequent re-ablation of RPUV using changes in serum creatinine and ultrasonographic renal pelvic diameter (RPD).

Methods: A retrospective review of 85 patients with posterior urethral valves (PUV) was conducted. Serial serum creatinine measurements (umol/L) and ultrasonographic RPD measurements (mm) were retrieved and recorded on three separate, dated occasions against the date of surgery as follows: M1: before primary valve ablation; M2: before repeat cystoscopy; and M3: after repeat cystoscopy. The changing trends in both the serum creatinine and the RPD were analysed for significance against time.

Results: The median age at primary valve ablation was seven weeks (IQR [interquartile range] 2.75–91.45). Repeat cystoscopy was performed in 94.7% of patients, detecting a 77.1% prevalence of residual valves. The initial mean creatinine before primary ablation was 150.8 umol/L, with 75% of patients having elevated creatinine levels before surgery. The serum creatinine showed a significant improvement after primary ablation (mean: M1: 150.8 umol/L to M2: 42.1 umol/L, $p = 0.0001$) but minimal improvement after re-ablation (M2: 42.1 umol/L to M3: 39.2 umol/L, $p = 0.68$). There was more dilatation in the left renal units (mean: M1: 13.4 mm, M2: 10.9 mm, M3: 8.3 mm) compared to the right (mean: M1: 11.9 mm, M2: 9.7 mm, M3: 8.5 mm). The left RPD showed significant improvement after both primary ablation ($p = 0.04$) and re-ablation ($p = 0.04$). Similarly, the right RPD showed improvement on both occasions, albeit not statistically significant ($p = 0.14$ and $p = 0.29$, respectively).

Conclusion: The prevalence of RPUV after primary ablation was 77%, with an improvement in the trend of hydronephrosis and serum creatinine after re-ablation of residual valves. Repeat cystoscopy is therefore effective in the detection of residual valves and has the added benefit of being both diagnostic and therapeutic.

Keywords: posterior urethral valves, residual posterior urethral valves, repeat cystoscopy, re-ablation

Introduction

PUV are the most common cause of lower urinary tract obstruction (LUTO) in newborn males, affecting one in every 5 000–8 000 births and accounting for roughly 60% of all LUTO cases.¹ Endoscopic valve ablation via a transurethral incision is the definitive treatment for PUV, failure of which can result in severe urological sequelae affecting both the upper and lower urinary tract.¹

The recommended follow-up measures after valve ablation include clinical evaluation using urinalysis and renal function tests, radiological evaluation using repeat kidney-ureter-bladder (KUB) ultrasonography and voiding cystourethrogram (VCUG), and cystoscopic evaluation.^{2,3} Routine follow-up is paramount to detecting voiding dysfunction, preventing progression to end-stage renal disease (ESRD), and managing the presence of urinary tract infections (UTIs).⁴

RPUV are defined as persistent PUV leaflets after the primary endoscopic ablation of valves. These RPUV are responsible for the persistence of symptoms and the progression of disease after PUV ablation.^{5,6} The incidence of RPUV in the literature varies from 12% to 78%.^{5–7} The diagnosis of such RPUV can be suspected based on clinical and radiological findings; however, detection can only be confirmed by cystoscopy.^{8–9} Whereas cystoscopy is considered a standard procedure after ablation, a significant proportion of

centres would only offer repeat cystoscopy when there were clinical or radiological signs of persistent obstruction.^{2–10}

This study aims to assess the magnitude of RPUV in children and the impact of repeat cystoscopy and subsequent re-ablation as a standard routine procedure in the management of PUV based on the changing trends of serum creatinine and sonographic measurements of the renal pelvis.

Materials and methods

A retrospective review of patients with PUV who underwent primary valve ablation at the Red Cross War Memorial Children's Hospital (RCWMCH) was conducted. The protocol for PUV ablation at the RCWMCH is an endoscopic transurethral ablation under general anaesthesia with the aid of a monopolar hook on an 11 Fr resectoscope or a cold knife on a 10 Fr optical urethrotomy set for smaller urethral lumens. Thereafter, routine repeat cystoscopy is scheduled six weeks after primary urethral valve ablation. During repeat cystoscopy, if RPUV are detected, re-ablation is carried out using the same endoscopic technique. At the end of both endoscopic interventions, an on-table Credé manoeuvre is performed as a measure of adequate resolution of obstruction. Bladder neck incisions are concomitantly offered to patients with gross hydronephrosis and poor renal function. Routinely, serum

creatinine and renal sonography are performed as part of the preoperative workup and follow-up protocol.

Serum creatinine measurements (umol/L) and ultrasonographic RPD measurements (mm) were retrieved and recorded on three separate, dated occasions against the date of surgery as follows:

- M1: before primary valve ablation (initial creatinine level);
- M2: before repeat cystoscopy (≥ six weeks after primary valve ablation); and
- M3: after repeat cystoscopy (≥ six weeks after repeat cystoscopy).

The values of serum creatinine and the RPD on both the left and right kidneys were plotted against the occasions listed above. The changing trends in both the serum creatinine and the RPD were analysed for significance against time.

Informed consent was obtained for all patients before undergoing the procedures under review. Institutional approval was sought before the study was conducted, and ethical clearance was given by the University of Cape Town Human Research Ethics Committee (Ref: HREC: 256/2023).

Results

The records of 85 male children with PUV were retrieved from the registry between August 2014 and March 2023. Among these, 22 patients were excluded as they had non-ablative procedures or diversion procedures such as ureterostomy and vesicostomy before definitive PUV ablation. Additionally, six patients were excluded based on PUV ablation performed at a separate facility from the RCWMCH.

Repeat cystoscopy and prevalence of RPUV

A total of 57 patients formed the subject population that underwent primary PUV ablation at the RCWMCH; the median age at primary ablation was seven weeks (IQR 2.75–91.45). A total of 54 patients (94.7%) underwent repeat cystoscopy after primary ablation. The mean duration interval at repeat cystoscopy was 9.82 weeks (standard deviation [SD] 6.2505). Notably, residual valves were detected in 44 patients (77.1%) who underwent repeat cystoscopy.

All children with residual valves were subsequently offered repeat ablation during the repeat cystoscopy session. Concomitantly, bladder neck incisions were offered to 16 patients during the same repeat ablative session. The descriptive flow and patient data are shown in Figure 1.

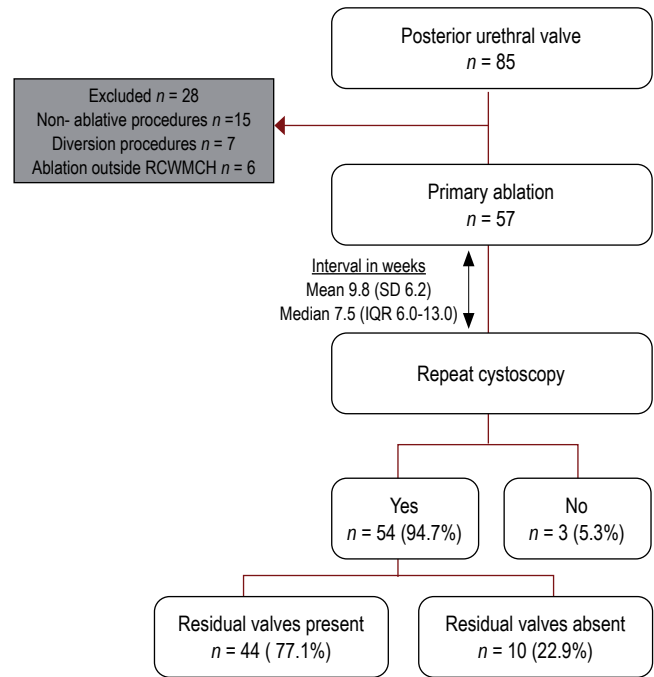


Figure 1: Descriptive flow and patient data

Follow-up measurement interval

The follow-up intervals for measurements taken during the study period for both serum creatinine and RPD are summarised in Table I. The first interval represents the period between the pre-ablative metric (M1) and post-ablative metric (M2), while the second interval represents the period between the post-ablative metric (M2) – which is the same as the pre-repeat cystoscopy metric (M2) – and the post-repeat cystoscopy metric (M3). For both serum creatinine and RPD measurements, the mean interval duration was 10 weeks for the first interval and 15 weeks for the second interval.

Serum creatinine trends

The mean creatinine before primary ablation was 151 umol/L (median 117, IQR 44–220). The proportion of patients presenting with elevated creatinine before primary ablation was 75%. Serum creatinine was analysed on three occasions based on the primary ablation and repeat cystoscopy timelines. The description of serum creatinine values against the time analysed is shown in the graphical trend in Figure 2.

A significant improvement was noted in the serum creatinine trend after primary ablation (p = 0.0001). There was minimal improvement in serum creatinine before and after repeat ablation (p = 0.6791).

Table I: Follow-up interval in weeks

Measurement timeframe	Serum creatinine (interval in weeks)		Renal ultrasound (interval in weeks)	
	First interval (M1–M2)	Second interval (M2–M3)	First interval (M1–M2)	Second interval (M2–M3)
Mean	10.0	15.4	10.6	14.7
SD	6.5	12.9	9.5	11.1
Median	8.0	11.2	7.4	13.7
IQR	6.0–14.0	4.6–24.0	5.1–13.8	7.2–19.0

SD – standard deviation, IQR – interquartile range, first interval – interval between pre-ablative metric (M1) and post-ablative metric (M2), second interval – interval between pre-repeat cystoscopy metric (M2) and post-repeat cystoscopy metric (M3)

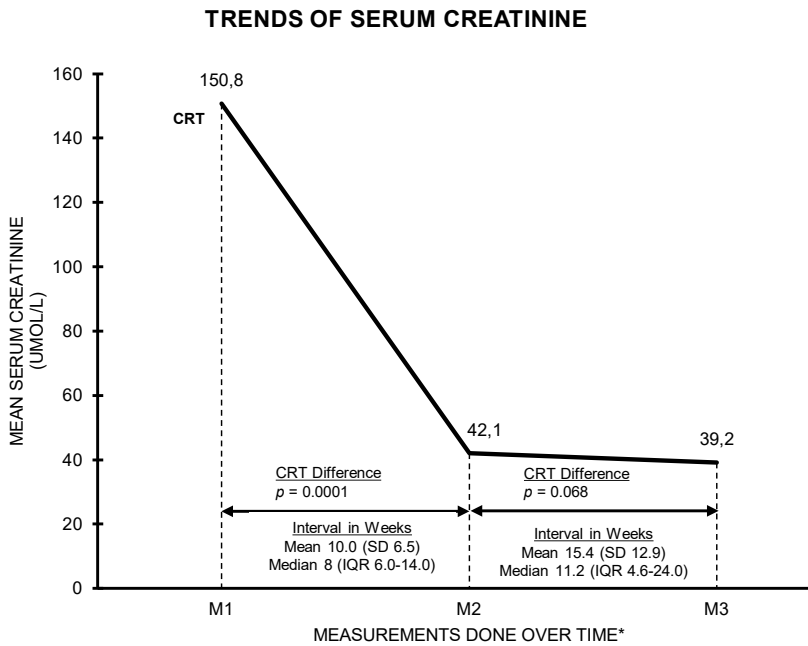


Figure 2: Trends of serum creatinine
 CRT – creatinine, SD – standard deviation, IQR – interquartile range
 * Measurements over time:
 • first pre-ablative metric (M1);
 • second pre-repeat cystoscopy metric (M2); and
 • third post-repeat cystoscopy metric (M3).

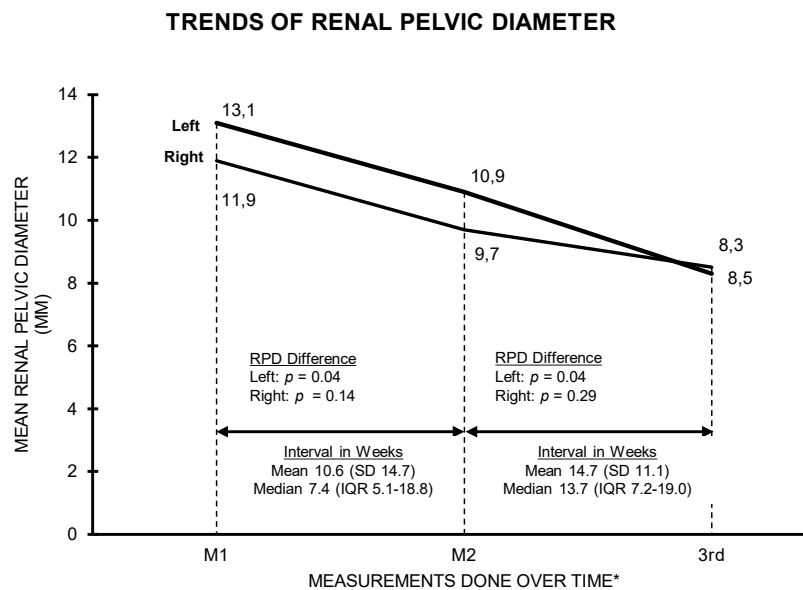


Figure 3: Trends of renal pelvic diameter
 RPD – renal pelvic diameter, SD – standard deviation, IQR – interquartile range
 * Measurements over time:
 • first pre-ablative metric (M1);
 • second pre-repeat cystoscopy metric (M2); and
 • third post-repeat cystoscopy metric (M3).

RPD trends

Sonographic RPD was analysed on three occasions based on the primary ablation and repeat cystoscopy timelines. The description of left and right RPDs against the time analysed is shown in the graphical trend in Figure 3.

A significant improvement was noted on the left RPD after primary ablation ($p = 0.04$). Similarly, there was a significant improvement

on the left RPD after re-ablation of RPUV ($p = 0.04$). Whereas the same improvement trend was noted on the right RPD after both primary ablation of PUV and re-ablation of RPUV, this difference was not statistically significant ($p = 0.14$ and $p = 0.29$, respectively).

Association of residual valves with hydronephrosis and serum creatinine

The means of both left and right RPDs as well as creatinine levels in patients with residual valves were compared to the means of patients without residual valves after primary valve ablation. There was no statistically detected significance in a univariate t-test model. This association is shown in Table II.

Discussion

Residual valves are defined as persistent PUV leaflets after primary endoscopic ablation of valves. These leaflets can be responsible for recurrent UTIs and the rapid progression to bladder dysfunction, chronic kidney disease, and end-stage renal failure.^{2,5} The diagnosis of such residual valves can be suspected clinically and radiologically; however, detection can only be confirmed by cystoscopy.^{7,8}

This study sought to determine the magnitude of RPUV and the impact of repeat cystoscopy and subsequent re-ablation as a standard routine procedure in the management of PUV based on the changing trends of serum creatinine and sonographic measurements of the renal pelvis. Significantly, the prevalence of residual valves was 77.1%, with an improvement in both serum creatinine and RPD after ablative and re-ablative procedures. Serum creatinine showed a statistically significant improvement after the primary ablation of valves, while the left RPD showed a statistically significant improvement after both the primary ablation of PUV and the re-ablation of RPUV.

The median age at surgery in our study was seven weeks, which is earlier than reported in other studies. In a systematic review by Hennus et al.,¹¹ the age range at surgery for PUV was 0–180 months, with the largest study in the review recording a mean age of 30 months. Early intervention is a direct result of early diagnosis, which is now well established with the advent of antenatal diagnosis.^{2,3}

The protocol at RCWMCH is to offer repeat cystoscopy after six weeks of primary ablation. This was performed in 94.7% of patients, detecting a 77.1% prevalence of residual valves. This finding compares well with the incidence of RPUV in the literature, which varies from 12% to 78%.⁵⁻⁷ In a systematic review, repeat cystoscopy

Table II: Association of residual valves with hydronephrosis and serum creatinine

Measure	Residual posterior urethral valves		p-value
	Present (n = 44)	Absent (n = 10)	
Left RPD	Mean	10.9	0.20
	SD	6.1	
	SEM	0.9	
Right RPD	Mean	9.7	0.55
	SD	5.3	
	SEM	0.7	
Serum creatinine	Mean	42.1	0.12
	SD	28.5	
	SEM	4.3	

SD – standard deviation, SEM – standard error of the mean, RPD – renal pelvic diameter

was found to be described as a standard procedure independent of clinical course in some studies, while in other studies, the decision to repeat cystoscopy was based on VCUG results.¹¹

A consensus statement from India recommends the performance of check cystoscopy and/or VCUG for patients who have persistent symptoms. In their statement, routine cystoscopy and/or VCUG are labelled as optional.² Conversely, Smeulders et al.¹⁰ found that repeat VCUG alone is not effective in detecting residual valves and recommended check cystoscopy for all patients.¹⁰ Consequently, the modality that should be used to detect RPUV is debated, as is highlighted in the literature, with no clear consensus.^{6,7}

In a retrospective study, Oktar et al.⁵ demonstrate that a combination of clinical, radiological, and endoscopic modalities is required to evaluate the presence of residual valves or strictures. Nawaz et al.⁷ go further to justify the use of check cystoscopy on all patients by stating that routine cystoscopy can identify more cases of residual valves as opposed to the performance of cystoscopy only after clinical or radiological suspicion.⁷

Since the protocol at RCWMCH is repeat cystoscopy for all patients, our study could not demonstrate a comparison between VCUG versus re-look cystoscopy. However, a 77% RPUV prevalence in our study supports the practice of routine repeat cystoscopy after primary ablation. In a quest to find an authoritative answer to the debate herein cited, the European Association of Urology (EAU) Paediatric Urology Guidelines, updated in 2023, recommend that the effectiveness of primary valve ablation should be demonstrated within three months, either by clinical improvement (sonogram and renal function), control VCUG, or a re-look cystoscopy, depending on the clinical course.³

Renal function is the most significant and reported outcome of PUV. The proportion of patients with elevated creatinine before ablation ranges from 17% to 57%, with a mean between 88 $\mu\text{mol/L}$ and 141 $\mu\text{mol/L}$.¹² Our study had a mean creatinine level of 150 $\mu\text{mol/L}$ before primary ablation, with 75.5% of patients having an elevated creatinine level before surgery. Nadir creatinine is defined as the lowest creatinine level during the first year following diagnosis.¹³ A serum nadir creatinine above 88.4 $\mu\text{mol/L}$ (1.0 mg/dL) is shown to be the most significant and independent risk factor for poor renal outcomes. A local study by Nimako et al.¹² at RCWMCH confirmed

this finding, with moderate to severe renal impairment occurring in patients with a serum nadir creatinine above 89 $\mu\text{mol/L}$.

Serial serum creatinine measurements, usually within three months after ablation, are a significant component of follow-up for patients with PUV and have been used to monitor renal function post-PUV ablation.³ Additionally, a rise in serum creatinine and/or persistence of high serum creatinine is seen in residual valves, necessitating the need for a re-look cystoscopy.¹⁴ In our study, a significant improvement was noted in the serum creatinine trend after primary ablation, with a drop in the mean creatinine value of more than 50%. However, there was minimal change in serum creatinine before and after repeat ablation in patients with RPUV. There was also no statistical difference in the mean serum creatinine of patients with residual valves and those without after primary ablation. These findings underscore the clinical significance of initial bladder drainage and primary ablation in the treatment of PUV.^{2,3}

Ultrasonography is recommended within three months after ablation and is particularly favourable as it is readily available, affordable, non-invasive, and lacks radiation exposure.^{2,3,15} The anteroposterior RPD is an objective ultrasonographic parameter of the renal pelvis that is used to grade the degree of hydronephrosis.¹⁶ Persistent hydronephrosis should warrant evaluation of the lower urinary tract for dysfunction or obstruction.¹⁷ Conversely, resolution of hydronephrosis is seen within three months after valve ablation in the absence of vesicoureteral reflux and residual LUTO.^{18,19}

Our study determined a significant resolution in the degree of hydronephrosis across the follow-up period. Both left and right RPDs showed an improvement trend after ablation and after re-ablative procedures within an average of 10 weeks to 14.7 weeks, respectively. These findings compare well with a prospective study by Priti et al.²⁰ where significant resolution of hydronephrosis was demonstrated on two ultrasonographic assessments taken three months apart in patients after PUV ablation.

Notably, there was more dilatation in the left renal units compared to the right. Likewise, the resolution of hydronephrosis across time was statistically significant for the left RPD compared to the right RPD. In a large prospective cohort study by Arora et al.,²¹ left hydronephrosis was 1.3 times more common than right hydronephrosis in patients with antenatally detected hydronephrosis, inclusive of those with PUV. Similarly, in those with transient hydronephrosis, the left renal units showed higher resolution rates than the right.²¹

Resolution of upper tract dilatation and improvement of renal function may be considered indirect signs of urinary tract decompression.⁵ However, the persistence of renal dysfunction and hydronephrosis in the absence of mechanical blockage is a well-considered sequelae of PUV and has been linked to renal polyuria, vesicoureteral reflux, and bladder dysfunction. This underscores the likelihood of persistent upper tract dilatation and elevated serum creatinine in patients without residual valves.²²

Study limitations

This study is not without limitations. Due to the study's retrospective nature, missing data, incomplete data, and errors of omission in

data recording may impact the study findings. Specifically, data not collected includes records on bladder anatomy, vesicoureteral reflux, and the degree of urethral abnormality both on imaging and endoscopically.

Additionally, the sample size is considered statistically small to make comparative inferences, and future prospective studies with larger sample populations and a higher level of evidence will be required to further test the hypothesis generated from our findings. Despite an improving trend in both serum creatinine and hydronephrosis, it is difficult to determine whether the re-ablation of residual valves makes a definite difference in these parameters or a perceived difference due to the overlapping impact of primary ablation. Finally, we acknowledge that glomerular filtration rate (GFR), which is not reported in our findings, is a more reliable marker of renal dysfunction than crude creatinine level.

Conclusion

The study shows a significant prevalence of RPUV of 77%, with a significant improvement in the trend of hydronephrosis and serum creatinine in the follow-up period. Notably, a significant improvement in the left RPD was found after the re-ablation of residual valves. Therefore, repeat cystoscopy is effective in the detection of residual valves and has the added benefit of being both diagnostic and therapeutic. Protocol-based vigilance after primary ablation is key to promoting early detection and re-ablation of RPUV.

Conflict of interest

The authors declare no conflict of interest.

Funding source

The study received no funding.

Ethical approval

Institutional approval was sought before the study was conducted, and ethical clearance was given by the University of Cape Town Human Research Ethics Committee (Ref: HREC: 256/2023).

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