The Whitaker Test in the Follow-up of Complex Upper Urinary Tract Reconstruction: Is It Clinical Useful or Not

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ABSTRACT

Purpose: To evaluate the feasibility and guiding significance in postoperative management of the Whitaker test after complex reconstruction of the upper urinary tract.

Materials and Methods: Patients who underwent complex ureteral reconstruction and received the Whitaker test after surgery between December 2018 and December 2019 were included. We judged it abnormal that the renal pelvis pressure was higher than 22 cmH_2O or the pressure difference was greater than 15 cmH_2O. The results were used as a reference for removing the nephrostomy tube. Based on whether the renal pelvic pressure was higher than 22 cmH_2O, the patients were divided into the elevated pelvis pressure group and the normal group. Follow ups at 1 month and every 3 months were collected.

Results: A total of 19 patients were included. Fifteen patients did not present obvious abnormalities. One patient suffered from contrast infiltrating into the renal parenchyma, and the pressure was higher than 15 cmH_2O. Ureteral stent implantation was performed. The other 3 patients had either elevated pelvis pressure or insufficient image, 2 of which prolonged the duration of nephrostomy tubes. The median follow-up time was 12.6 months. CTU/MRU after removing nephrostomy tubes indicated improved/stable hydronephrosis in all patients. The creatinine in the elevated pelvis pressure group was higher than that in the normal group (91.4 ± 27.6 vs 86.7 ± 16.5 μmol/L, P = .782), and the eGFR was lower (76.0 ± 14.0 vs 81.8 ± 24.1 mL/min/1.73m^2, P = .695), but without significant difference. The change in creatinine during follow-up in the elevated renal pelvic pressure group was significantly different from that in the normal group (-13.6 ± 1.0 vs -0.2 ± 10.6 umol/L, P = .047).

Conclusions: Postoperative Whitaker test can help judge whether nephrostomy could be removed. Elevated pressure in upper urinary tract after reconstruction suggests the need to prolong the time of the nephrostomy tube or even re-intervene. Proper management for patients with elevated renal pelvis pressure can help restore the renal function.

Key Words: dilation; ureteral reconstruction; diagnostic techniques; urodynamic study; renal function; the Whitaker test

INTRODUCTION

Complex ureteral stricture can lead to severe dilation and hydrops of the urinary tract. Upper urinary tract reconstructive surgery aims to restore the continuity of the urinary tract and protect renal function.[1] The main reconstructive strategies included Boari flap, appendix, oral mucisa, ileal ureter replacement and autotransplantation,[2-4] However, patients often receive ureteral stent or retain nephrostomy tube for the protection of the reconstructive upper urinary tract, and the majority need a relatively long time to recovery. Thus, the follow-ups are requisite.

Routinely, patients are suggested to underwent ultrasound, intravenous urography, diuretic renography, computed tomography urography (CTU) and magnetic resonance urography (MRU) at follow-up. The interpretation relies on the degree of hydrops and urinary tract lumen dilation to determine whether the urinary tract is unobstructed. Whereas, dilatation or hydrops does not always equate with obstruction.[5,6] More difficult to interpret is the dilatation that remains after relief of obstruction. Different from imaging examination, renogram utilized radioisotopes to assess the excretory function through radioisotopes and has been widely used since it was proposed. However, in a kidney with impaired function or associated with an extremely large system the test may be invalid, and the response to a diuretic is in doubt and different according to whether the damage mainly is glomerular or tubular. Moreover, with a renogram no information is achieved about compliance.[7] Since radionuclide imaging presents a blurred image of anatomical structure, the result of diuresis renogram cannot reflect the changes in the shape of the upper urinary tract and the degree of difficulty of deformation during urine transportation. More importantly, all the present examinations are affected by an ureteral stent and a nephrostomy tube. The uncertain outcome after removing protective ureteral stents or nephrostomy tubes is a concern.

In 1973, Whitaker advocated the use of a constant perfusion flow study to distinguish whether urinary tract dilatation is caused by obstruction.[8] Currently, there are seldom articles discussing the role of the Whitaker test in the postoperative evaluation of complex upper urinary tract reconstruction. In addition, previous studies investigating the relationship between the Whitaker test and renal function focused almost on the pelvis-bladder pressure difference, and the result is still controversial. This study presents the postoperative results of the Whitaker test in reconstructive upper urinary tract. We also explore the renal function after the Whitaker test guided management, aiming to evaluate the instructional significance of the Whitaker test in complex reconstructive upper urinary tract.

MATERIALS AND METHODS

Study population

A retrospective study of complex upper urinary tract reconstruction in 19 patients was conducted from December 2018 to December 2019. All patients were indicated to a surgical management by severe hydronephrosis, flank pain, and/or poor renal function. Complex reconstruction was defined as (1) long ureter defects longer than 5 cm that cannot be managed with simple resection and anastomosis, (2) secondary reconstruction and (3) severe ureteral injuries such as avulsion or rupture. Data on patient characteristics, etiology, laboratory data, imaging studies, surgery information and perioperative data were collected from our

Reconstruction of Urinary Tract: Technology, Epidemiology and Result (RECUTTER) database. The present study was approved by the Institutional Ethics Committee of our hospital. Informed consent was obtained from all individual participants included in the study.

Whitaker test

All patients had a nephrostomy tube before surgery. In order to protect the reconstructed upper urinary tract, the nephrostomy tube was intermittently clipped after surgery instead of being removed immediately. Patients were followed up at 1 and 3 months after surgery to determine whether to remove the nephrostomy tube. The process of perfusion was the same as the method Whitaker described in 1973. Patients took a prone position. A urinary catheter was placed before the examination. Nephrostomy tubes and urinary catheters were connected to the pressure transducer respectively. The contrast medium was diluted at 50 % with saline. The initial perfusion rate was 10 mL/min (decreasing to 5 mL/min in 3 equivocal cases). The perfusion was continued until a steady state was reached at which the pressure did not change. The pressure was recorded simultaneously from the renal pelvis and the bladder. If the patient had a bladder distention or the elevated pressure did not ease, the perfusion should be suspended or terminated.

We judged it abnormal that the renal pelvis pressure was higher than 22 cmH_2O or the pressure difference was greater than 15 cmH_2O.[8-10] At the same time, X-ray was used to evaluate the morphology of the upper urinary tract. Hold-up of contrast medium at anywhere in the ureter may be suspected. A significant rise in the pressure difference across the suspected obstruction allows the diagnosis, whereas free drainage of contrast at low pressure excludes obstruction. Based on whether the renal pelvic pressure was higher than 22 cmH_2O, the patients were divided into 2 groups for further comparison. namely the elevated pelvis pressure group and the normal group.

Follow-up

After removing the nephrostomy tubes, patients came to the clinic every three months. Physical examination, blood serum creatinine tests, urine routine tests and urinary ultrasound were performed at each visit. CTU/MRU was performed to evaluate the morphology of the reconstructive urinary tract. Based on the anteroposterior diameter of the pelvis in B-ultrasound, hydronephrosis is defined as normal (<5 mm), mild (5-9 mm), moderate (10-14 mm) and severe (≥15 mm). The estimated glomerular filtration rate (eGFR) is calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Successful nephrostomy removal was defined as no symptoms and improved or stable hydronephrosis.

Data analysis

All analyses were performed with SPSS® Statistics (version 20.0). The Kolmogorov-Smirnov test was used to check whether the data (age, BMI, pre- and postoperative creatinine, pre- and postoperative eGFR, changes in the creatinine and eGFR, pressure difference, follow-up time) were normally distributed. Independent-sample t-test was used to compare the difference of average value (creatinine and eGFR) between the elevated renal pelvic pressure group and the normal pressure group. Pearson's analysis was used to test the correlation of perfusion volume and pressure difference with the creatinine and eGFR. A two-sided $p < .05$ was taken to indicate statistical significance.

RESULTS

The clinical characteristic and surgical information were shown in Table 1. All patients received a nephrostomy preoperatively. All patients completed the Whitaker test successfully. No one experienced perfusion-related symptoms. The median perfusion volume at the end of the test was 227 mL (range 24 to 366 mL). 15 patients did not present obvious abnormalities (**Fig 1**). Among them, 4 patients showed a negative pressure difference that was lower than 0 cmH_2O. One patient had only insufficient image at lower ureter. One patient showed elevated pelvis pressure without abnormal pressure difference or poor imaging. An unusual rise in renal pelvis pressure during perfusion together with poor imaging at the ureterovesical junction was observed in 1 patient. In detail, perfusion fluid did not appear in the bladder until perfusion to 86 mL. Particularly, one patient showed obvious elevated pelvis pressure and suffered from contrast penetrating into the renal parenchyma (**Fig 2**). Consequently, the perfusion was temporarily suspended. After the pressure dropped, the perfusion was continued, and the pelvis-bladder pressure was higher than 15 cmH_2O (**Table 2**). The results of B-ultrasound and perfusion test were consistent negative in 5 patients. In contrast, 14 patients had remained different degree of dilation in ultrasound after surgery, but the Whitaker test showed a velocity of 10 mL/min perfusion could be tolerated in 11 of 14 patients (**Table 3**).

16 patients removed the nephrostomy tube after the confirmation of the Whitaker test. Two patients with elevated pressure prolonged the duration of the nephrostomy tube. One patient with obvious abnormality during perfusion underwent ureteral stent implantation, and the tube was removed after 3 months.

The median follow-up time was 12.6 months (range 8.6 to 17.3 months). All the patients were free of symptoms. The mean postoperative serum creatinine was 90.6 ± 25.3 μmol/L, and the mean eGFR was 80.9 ± 22.6 mL/min/1.73m^2. Urine routine tests showed positive white blood cells in 8 patients. There were no obvious abnormalities in the urine routine of the other patients. Ultrasound showed that hydrops was improved in 5 patients, meanwhile, the degree of dilation remained stable in the other 14 patients. CTU/MRU confirmed no dilation or mild dilation of the collecting system that were improved than before. For 3 patients with abnormal imaging urodynamic results, ultrasound found that hydrops disappeared in one patient and remained stable in the other 2 cases. CTU/MRU showed only mild dilation in these 3 patients (**Fig 3**).

The creatinine in the elevated pelvis pressure group was higher than that in the normal group (86.7 ± 16.5 vs 91.4 ± 27.6 μmol/L, *P* = .782), and the eGFR was lower (76.0 ± 14.0 vs 81.8 ± 24.1 mL/min/1.73m^2, *P* = .695), but without significant difference. **Figure 4** presented the changing trend of the creatinine and eGFR in the normal and elevated renal pelvis pressure group, respectively. The change in creatinine during follow-up in the elevated renal pelvic pressure group was significantly different from that in the normal group (-13.6 ± 1.0 vs -0.2 ± 10.6 umol/L, *P* = .047), but there was no difference in the change in eGFR (12.7 ± 4.2 vs -0.4 ± 12.7, *P* = .101). Neither The pressure difference didn't show correlation with creatinine (*r* = -.056, *P* = .819) or eGFR (*r* = -.109, *P* = .657). Nor did the perfusion volume showed correlation with creatinine (*r* = .205, *P* = .401)) or eGFR (*r* = -.040, *P* = .870).

DISCUSSION

Ureters are slender ducts that drainage urine from the kidney to the bladder. Urine transport relies on two major mechanisms: the active contraction of the smooth muscles, and passive flow driven by hydrostatic pressure. An obstruction that results in a decrease in urine output can cause dilation. Relaxed smooth muscle of the collecting system owing to long term hydronephrosis can also lead to dilation. Therefore, it is not enough to observe the dilation of the urinary tract, which is the shortcoming of the existing imaging examinations. The reasons behind the dilation also need to be brought to the forefront.

While investigating the dilation of upper urinary tract after reconstruction, whether the obstruction still exists is the focus of attention. The renogram not only judges how well the isotope can pass through the urinary system but also gives information on split renal function. However, dilated renal pelvic and ureter, particularly if associated with a poorly functioning kidney, can cause stasis to give a false impression of obstruction.(7) In addition, protective ureteral stent or nephrostomy tube may lead to better imaging results than it really is. The Whitaker test uses a constant perfusion flow study to evaluate the function of the upper urinary tract.(8) The Whitaker test provides a quantitative assessment of outflow resistance, and it has the advantage that it does not rely on renal function or a diuretic response.

During the past decade, researchers have passed different judgments on the Whitaker test. Djurhuus et al. have shown that the resting pelvis pressure may show a considerable overlap in a hydronephrotic or in a normal one.(11) Wahlin et al. also agreed the specificity of the method was limited.(12) However, proponents of the Whitaker test have approved its values for the diagnosis of obstruction and exclusion of unobstructed dilatation. Johnston proposed the Whitaker test was useful in evaluating patients with skeptical ureteropelvic or ureterovesical junction obstruction.(13) Lupton and George concluded that the Whitaker test contributed to the clinical management in 84% of the suspected upper urinary tract obstruction.(9) Except for these arguments, there are seldom articles reporting the use of the Whitaker test for postoperative evaluation of complex urinary tract reconstruction.

The Whitaker test can help clarify whether the urinary tract is still obstructed and determine when percutaneous nephrostomy tubes could be safely removed, especially for those patients who showed no improvement in radiographic appearances. Previous studies underlined that about 60% of the patients showed no clear improvement in ultrasound after reconstruction.(14) In the present study, we found 14 patients remained urinary tract dilation in ultrasound, while the negative Whitaker test in 11 of 14 patients provided evidence for nephrostomy removal. CTU or MRU prompted satisfactory imaging results of the reconstructive upper urinary tract after removing the nephrostomy tube. No patients suffered from renal function deterioration. Therefore, with normal results of the Whitaker test, no need to worry too much that ultrasound changes recovered slowly.(15)

The obstructive results often indicated a prolonged time of nephrostomy and even the possibility of reintervention. In our study, 3 cases with abnormal results were treated accordingly. In detail, 1 case who underwent ureteroneocystostomy had high pelvis pressure, high pressure difference and poor imaging, which together indicated the existence of obstruction. Marshall et al. reported a similar patient with left megaureter that was reimplanted into the bladder showed a pressure of 19 cmH_2O in the Whitaker test. A transureteroureterostomy and temporary left nephrostomy ensued. The pressure again was less than 8 cmH_2O, and the patient was free of symptoms and deterioration.(16) For our patient, the renal pelvis pressure increased with the progress of perfusion, and the perfusion was temporarily suspended twice. After a brief stop and position change, the renal pelvis pressure decreased to a stable level. But the pressure was still higher than the initial basic pressure, and the final pressure difference was greater than 15 cmH_2O. This patient subsequently underwent ureteral stent implantation. The other 2 patients showed high renal pelvis pressure with or without poor imaging. The pressure gradually decreased and remained stable as the perfusion went on. The reason may be the poor pelvic compliance. The Whitaker test simulates a high urine flow actually to evaluate the ability of the reconstructive upper urinary tract to convey urine. Under physiological conditions, the urine production rate is 1-3 mL/min,(17) but it can increase up to 20 mL/min after diuresis.(9) Accompanied by moderate dilation in ultrasound, these 2 patients were treated by prolonging the time of nephrostomy. The CTU/MRU during follow-up showed improved dilation in the collecting system.

Negative pressure difference reminds urologists to be vigilant against reflux, but for patients undergoing ileal ureter replacement, it may be a normal phenomenon. The ureter is contracted to close when transporting urine downward without reflux.(6) In this study, 4 patients had negative pressure difference, and 3 of them underwent ileal ureter replacement. The wide intestine was difficult to be completely closed during peristalsis, allowing reflux confined to the bowel segment. These 3 patients were not given special treatment, and there were no recurrent urinary tract infections, aggravated hydronephrosis, or deterioration of renal function during the follow-up. Another patient underwent Boari flap surgery. The negative pressure difference was due to the displacement of the transducer, and the measured bladder pressure was lower than the actual pressure.

Renal pelvis pressure was an informative factor. We found the creatinine in the elevated pelvis pressure group was higher than that in the normal group, and the eGFR was lower, but without significant difference. The changes of the creatinine and eGFR during follow-up were related to whether the renal pelvis pressure was elevated. The reason was that increased renal pelvic pressure indicated that the upper urinary tract had poor tolerance to hydrops, and the renal function could be impaired easily. However, the consequences were still reversible, so timely treatment helped restore the renal function. In the past, most researchers considered that abnormal results of the Whitaker test did not predict worse renal function. Djurhuus et al. pointed out the renal function in the high pressure group were the same as those in the low pressure group.(11.18) Identical with previous literature reports, pressure difference had no predictive value for postoperative renal function in our patients. However, few articles involved the pressure of the renal pelvis, which indicated the compliance of the upper urinary tract. Koff et al. thought renal pelvis pressure was a indicator determinant to progression.(19) In general, it was necessary to deal with when the renal pelvis pressure was abnormal, and the outcome was not different from the normal group after timely treatment.

There are still some limitations in our study. Firstly, contrast media have a greater viscosity than urine or saline and will produce higher pressure at a given flow rate. Moreover, with the high infusion rates used that are not physiological, the urinary tract may be overstretched. Thus, follow-up needs to perfect 1-3 mL/min physiological velocity perfusion or even individualize the infusion rates, so that some of the measurement bias could be avoided. Secondly, we didn’t perform a diuresis renogram for reference because the nephrostomy tube would affect the result of diuretic renogram. At last, large samples and long term follow-up result are necessary.

CONCLUSIONS

Despite the concerns and debates over its relative value, the Whitaker test can help judge whether nephrostomy tube could be removed. Abnormal results during perfusion prompts reintervention or longer duration of nephrostomy tube. Proper management for patients with elevated renal pelvis pressure can help restore the renal function.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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Table 1. Clinical characteristics and surgical information

Variables	**N (%)**
Gender	
Male	7 (36.8%)
Female	12 (63.2%)
Age, years, mean ± SD	41.6±9.8
BMI, kg/m^2, mean ± SD	24.2±3.2
Side	
Left	6 (31.6%)
Right	10 (52.6%)
Bilateral	3 (15.8%)
Lesion	
Upper	5 (26.3%)
Middle	3 (15.8%)
Lower	11 (57.9%)
Etiology	
Ureteroscopic holmium laser lithotripsy	9 (47.4%)
Radiotherapy	4 (21.1%)
Cervical cancer surgery	4 (21.1%)
Idiopathy	2 (10.5%)
Surgery	
Ileal ureter	11 (57.9%)
Boari flap	3 (15.8%)
Ureteroneocystostomy	2 (10.5%)
Appendiceal onlay flap	2 (10.5%)
Lingual mucosal	1 (5.3%)
Mean preoperative serum creatinine (μmol/L)	92.9±27.0
Mean preoperative eGFR (mL/min/1.73m^2)	79.2±23.7

Abbreviations: eGFR, estimated glomerular filtration rate.

Table 2. The detailed information of the Whitaker test in patients with abnormal results

Patients	**Surgery**	**Perfusion speed (mL/min)**	**Perfusion volume (mL)**	**Pelvis pressure (cmH_2O)**	**Final perfusion volume (mL)**	**Pressure difference (cmH_2O)**	**Imaging**
1	Ileal ureter	20	113	54	211	-6	Clear
2	Ileal ureter	10	71	46	205	-5	(1) Poor imaging at ureterovesical junction; (2) No contrast in the bladder until 86 ml; (3) Lower ureter was not visualized.
3	Ureteroneocystostomy	5	21	155	24	49	(1) Contrast penetrated into the renal parenchyma; (2) Lower ureter was not visualized.

4	Ureteroneocystostomy	5→10	/	Stable	366	0	Lower ureter and ureterovesical junction was visualized insufficiently

Table 3. Comparative analysis between Whitaker test and ultrasound

the Whitaker test / Ultrasound	No	Mild	Moderate	Severe	Total	*P*
Normal	5	5	2	4	16	.225
Abnormal	0	1	2	0	3	
Total	5	6	4	4	19	

Table 4. The comparative results of creatinine and eGFR between the elevated pelvic pressure group and the normal pressure group

Variables	**Elevated pelvis pressure group**	**Normal pressure group**	***P***
Serum creatinine, μmol/L	91.4±27.6	86.7±16.5	.782
eGFR, ml/min 1.73m^2	76.0±14.0	81.8±24.1	.695
ΔCreatinine, μmol/L	-13.6±1.0	-0.2±10.6	.047
ΔeGFR, ml/min 1.73m^2	12.7±4.2	-0.4±12.7	.101

Abbreviations: Δ, change; eGFR, estimated glomerular filtration rate.

LEGENDS TO FIGURES

Fig. 1 Normal postoperative result of the Whitaker test (lingual mucosal graft). Figure 1A &1B. Imaging of renal pelvis, upper urinary tract and bladder. Figure 1C. The record of pressure during perfusion. Co: Cough, Fi: First time feeling of urination, UU: Urgency of urination; P: Point of imaging time.

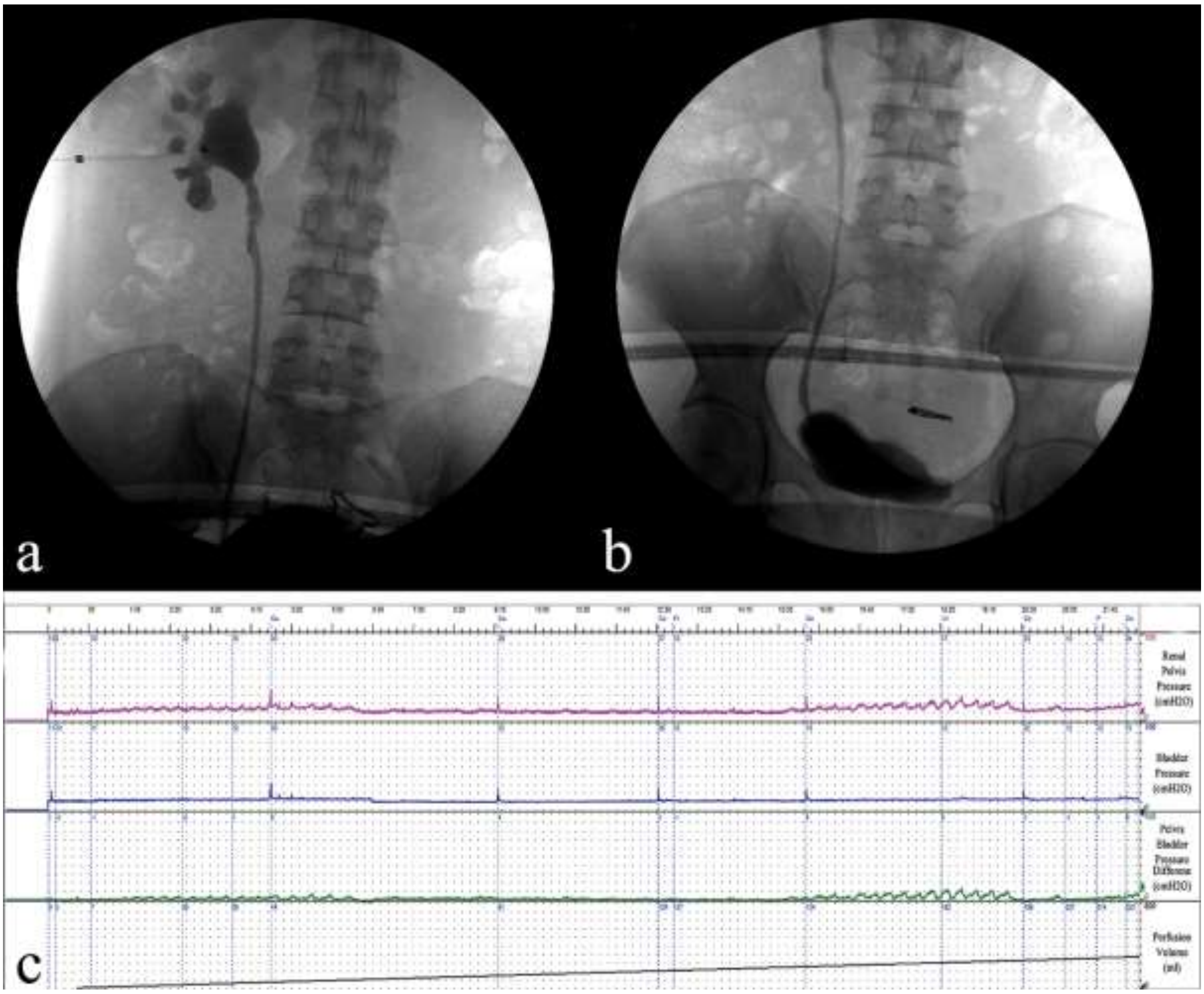


Fig. 2 Obstructive result of the Whitaker test. A. Contrast penetrating into renal parenchyma. B. Lower ureter was not visualized. C. The record of pressure during perfusion, the elevated renal pelvis pressure decreased when the perfusion was suspended, but it was still higher than the initial basic pressure. The final pressure difference was 49 cmH_2O. SP: Supine position, S:

Suspension, LP: Lithotomy position.

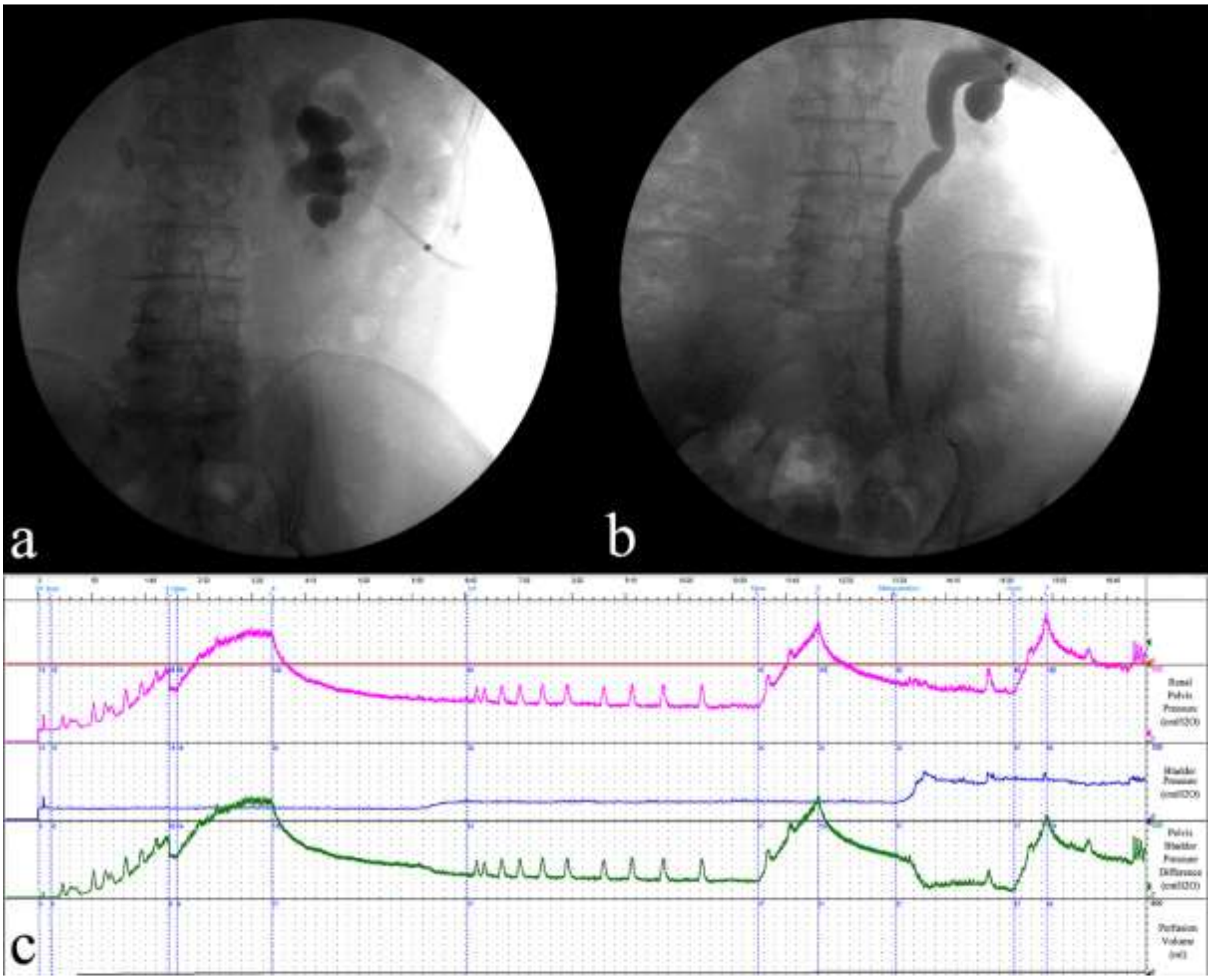


Fig 3. Pre- and postoperative CTU of the patient with elevated renal pelvis pressure and abnormal pressure difference. a. Preoperative cross section CTU; b. Preoperative coronary section CTU; c. Cross section CTU after removing the percutaneous nephrostomy tube; d. Coronary section CTU after removing the percutaneous nephrostomy tube.

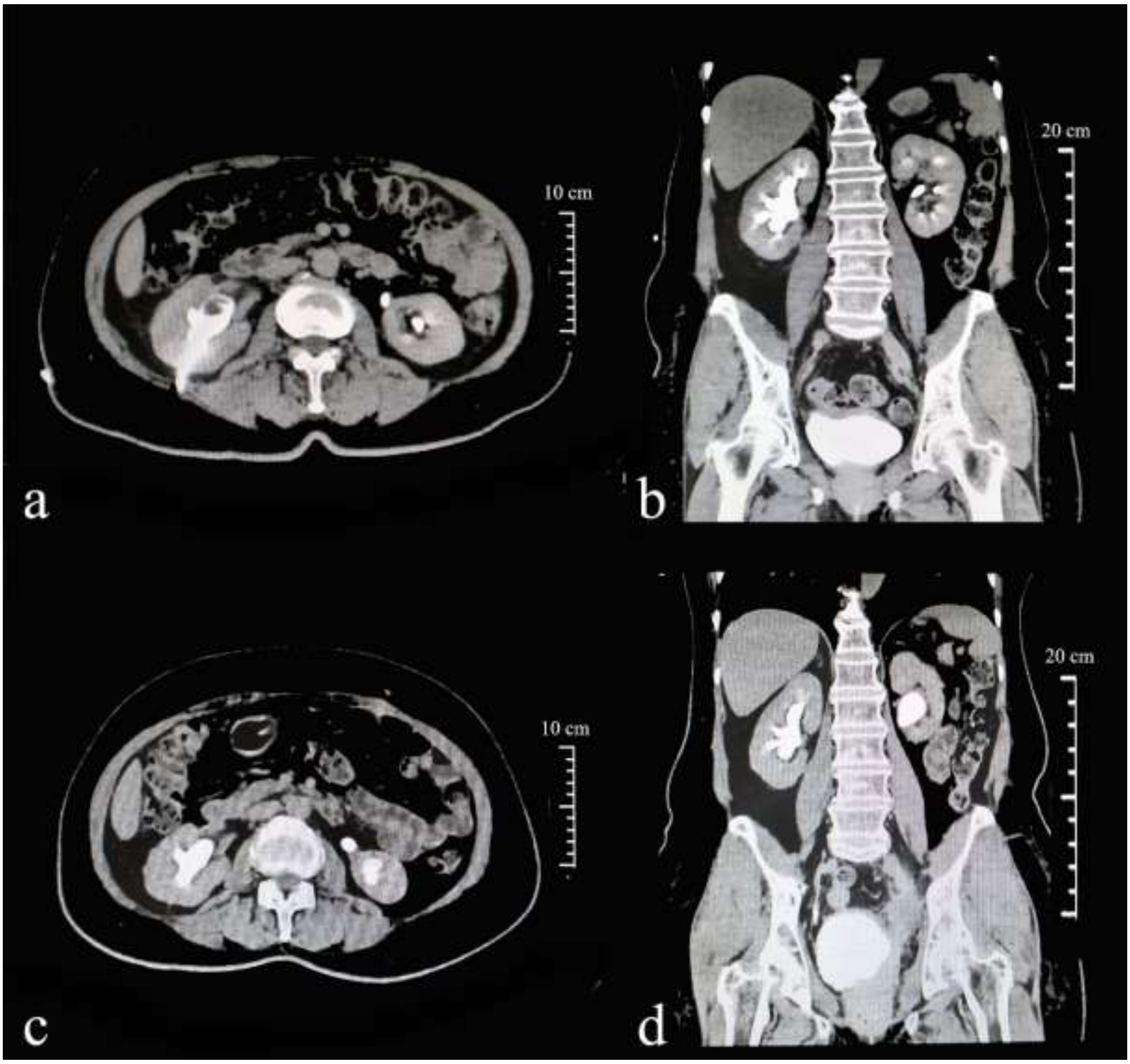
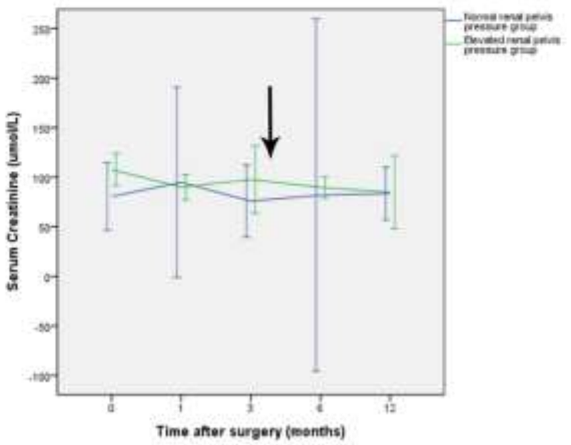
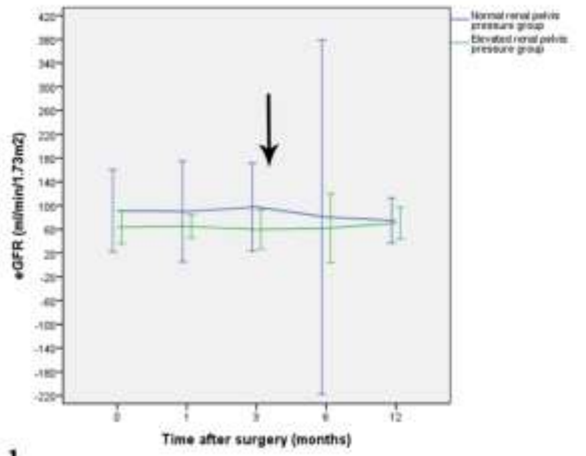


Fig 4. The changing trend of the renal function during follow-up. A. the trend of the creatinine in the normal and elevated renal pelvis pressure group. B. the trend of the eGFR in the normal and elevated renal pelvis pressure group. black arrow: the time of the Whitaker test and corresponding management.


Normal renal pelvis pressure group
Elevated renal pelvis pressure group
Serum Creatinine (umol/L)
Time after surgery (months)

a


Normal renal pelvis pressure group
Elevated renal pelvis pressure group
eGFR (ml/min/1.73m2)
Time after surgery (months)

b