Endoscopic Treatment for Post-Transplant Vesicoureteral Reflux

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ABSTRACT

Introduction. Vesicoureteral reflux (VUR) is one of the most common ureteric complications after kidney transplantation that might cause symptomatic infections which deteriorate graft function. Surgical reimplantation has been the standard treatment; recently, endoscopic injection has been an alternative approach. We report our endoscopic treatment results and analyze the long-term outcome, even in patients with less optimal graft function.

Materials and methods. A total of 16 patients and 19 symptomatic VUR were diagnosed at mean time of 88.3 months after their transplantation. The distribution of VUR grade was 1, 2, 8, 6, and 2 for grade I to V, respectively, with a mean VUR grade of 3.26 according to their voiding cystourethrogram images. Endoscopic Deflux injections were performed by a single urologist via rigid cystoscope with a beveled needle system. They were followed monthly thereafter.

Result. The average number of admissions due to symptomatic urinary tract infection was 2.68/person, and the mean creatinine level before endoscopic treatment was 1.63 mg/dL. The amount of Deflux injection was 0.7 to 1.2 mL per affected ureter; the mean creatinine level after endoscopic treatment was 1.41 mg/dL. The eGFR remained stationary in both eGFR $>$ 60 and eGFR $<$ 60 mL/min groups with a clinical success rate of 75% in both groups.

Conclusion. Endoscopic dextranomer-hyaluronic acid injection is a safe and feasible treatment option for VUR after kidney transplantation. Our data showed its efficacy in recipients whose eGFR is less than 60 mL/min.

VESICOURETERAL reflux (VUR) has been one of the ureteric complications following kidney transplantation; varied incidence between 3% to 50% has been reported [1,2]. Although the majority are asymptomatic and do not require intervention [3], some may result in graft pyelonephritis and even sepsis, causing deterioration of graft function; therefore, proper management should be carried out. Surgical reimplantation has been the standard treatment [4]; alternatively, endoscopic management provides a minimal invasive choice [5,6]. The aim of this study is to summarize the experience of endoscopic management of VUR at our center.

MATERIALS AND METHODS

A total of 16 patients (14 women and 2 men) developed symptomatic VUR after kidney transplantation between 2014 and 2018, and they were treated endoscopically. All patients received extravesical Lich-Gregoir ureterovesical anastomosis with temporary double-J stenting during the kidney transplant surgery. The standard immunosuppressive regimen in our center was perioperative methylprednisolone 500 to 1000 mg without routine antibody induction, followed by 3-combined maintenance immunosuppression (consisting of trough-level monitored calcineurin inhibitor, mycophenolate mofetil, and prednisolone) as described earlier [7]. Most recipients convert to mTORi-based regimen after 3 months if proteinuria is less than 1 g/day [8]. All VUR were confirmed by

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Table 1. Demographic Data

No.	Age	Sex	Original Diagnosis	Preop Urologic Disorder/Infection	DM	Postop 3 Months SCr	Postop 3 Months eGFR	Postop 6 Months SCr	Postop 6 Months eGFR	Alb/Cr Ratio (mg/g)	Organisms in Urine	Symptoms Requiring Intervention
1	56	F	SLE	recurrent UTI	-	1.53	39.488	4.06	15.897	621.7	*E coli*	urosepsis, recurrent UTI
2	65	F	unknown	recurrent UTI	-	1.02	54.911	1.31	50.166	45.1	*E coli*	deteriorate Cr
3	57	F	CGN	recurrent UTI	-	1.72	31.018	1.67	32.092	121.6	*E coli, P aeruginosa*	febrile UTI
4	35	F	unknown	febrile UTI	-	1.1	56.587	1.03	61.339	165.7	*E coli*	febrile UTI
5	66	F	unknown	febrile UTI	-	2.87	16.483	2.63	18.23	1755.8	*E coli*	febrile UTI
6	65	F	unknown	febrile UTI	-	2.44	20.07	2.67	18.088	4206.1	*E coli*	urosepsis
7	68	F	unknown	recurrent UTI	+	1.19	44.975	-	-	2395.2	-	deteriorate Cr
8	70	F	primary GN	recurrent UTI	-	0.49	124.854	-	-	227.3	Proteus, *E coli*	deteriorate Cr
9	46	F	drug*	recurrent UTI	-	-	-	-	-	2403	*E coli*	deteriorate Cr
10	63	F	unknown	recurrent UTI	+	1.08	37.979	0.95	59.413	82.6	*En faecium*	deteriorate Cr
11	61	F	unknown	febrile UTI	-	1.01	55.91	1.1	50.496	69.6	*E coli*	urosepsis
12	65	F	unknown	recurrent UTI	+	3.31	13.891	-	-	-	*K pneumoniae*	dysuria with recurrent UTI
13	25	F	unknown	recurrent UTI	-	0.87	79.993	1.01	67.34	72.2	*K pneumoniae*	deteriorate Cr
14	42	M	unknown	febrile UTI	-	7.84	7.575	7.2	8.358	113.9	*E coli*	febrile UTI
15	62	M	unknown	febrile UTI	+	0.97	78.683	0.93	82.601	-	*E coli*	dysuria, febrile UTI
16	17	F	FSGS	recurrent UTI	-	0.92	75.67	1.01	15.897	24	-	urosepsis, recurrent UTI

Abbreviations: Alb, albumin; CGN, chronic glomerulonephritis; Cr, creatinine; DM, diabetes mellitus; *E coli*, *Escherichia coli*; eGFR, estimated glomerular filtration rate; *En faecium*, *Enterococcus faecium*; F, female; FSGS, focal segmental glomerulosclerosis; M, male; *P aeruginosa*, *Pseudomonas aeruginosa;* SCr, serum creatinine; SLE, systemic lupus erythematosus; UTI, urinary tract infection.

*Drug-related end-stage renal disease.

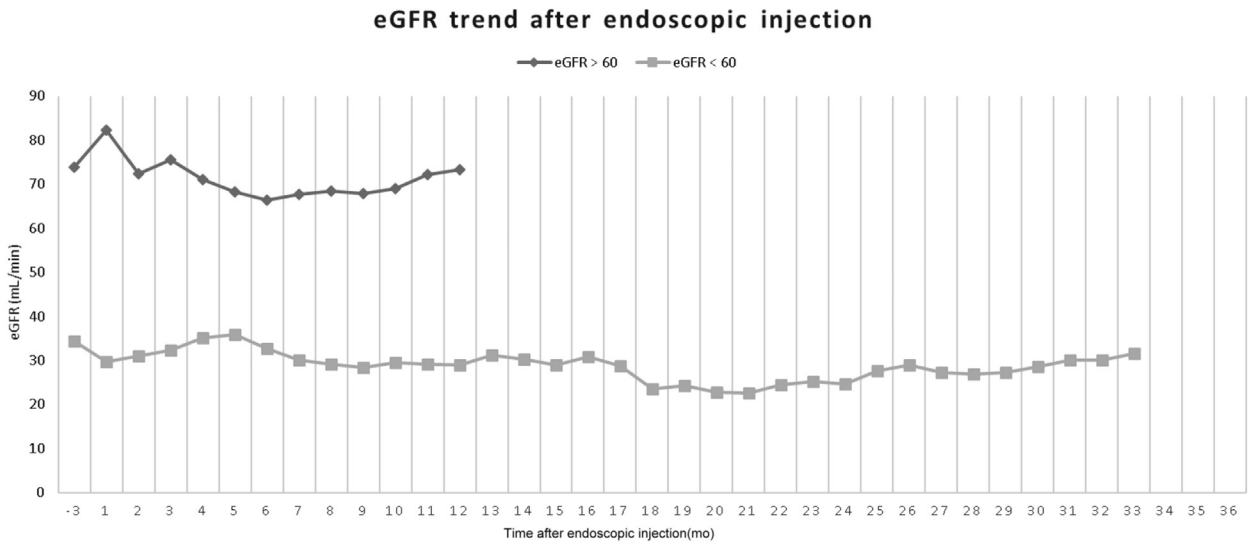

Fig 1. eGFR trend after endoscopic injection. eGFR, estimated glomerular filtration rate.

voiding cystourethrogram (VCUG), and proper antibiotics treatment was given prior to endoscopic treatment. The endoscopic procedures were performed by a single urologist (W.T.M.) under satisfactory general anesthesia. Dextranomer-hyaluronic acid (Deflux) was injected to affected ureter openings via rigid cystoscope with a beveled needle system. A Foley catheter was placed after the procedure to monitor urine color and amount; it was removed later if no infection or obstruction sign.

RESULTS

The mean age of these 16 patients was 47.4 years (ranging from 13 to 63), with their symptomatic VUR diagnosed at an average of 88.3 months after kidney transplantation (Table 1). One woman was found to have bilateral native ureter VUR, and 1 man had right native ureter VUR in addition to their graft VUR; therefore, a total of 19 ureters were affected. The distribution of VUR grade was 1, 2, 8, 6, and 2 for grade I to V, respectively, with a mean VUR grade of 3.26 according to their VCUG images. The average number of admissions due to symptomatic urinary tract infection (UTI) was 2.68/person, and the mean creatinine level before endoscopic treatment was 1.63 mg/dL.

The amount of Deflux injection was 0.7 to 1.2 mL per affected ureter. All injections were performed smoothly, except the first injection attempt in the first male recipient failed due to not being able to identify the ureter opening under cystoscopy. A percutaneous antegrade double-J stenting was performed by an intervention radiologist to identify the opening in the bladder, and then Deflux was injected successfully at the second attempt. None of the patients developed fever or sepsis after injection, and the mean creatinine level after endoscopic treatment was 1.41 mg/dL. Two patients developed transient oliguria, which improved spontaneously after 3 days.

These 16 patients were followed monthly with a mean follow-up period of 18.9 months. Four developed symptomatic graft pyelonephritis, indicating a clinical success rate of 75% (12 out of 16). The average number of admissions due to symptomatic UTI reduced to 0.31/person after Deflux injection. The woman with graft and bilateral native VUR had second VCUG 3 years later, which showed grade III VUR on her graft and right ureters (there was no more left native VUR); although asymptomatic, s second Deflux injection was performed for her remaining VUR and she was free of UTI thereafter. All graft remained functional; only 1 patient died of sepsis (intra-abdominal origin, not related to UTI) at 12 months after injection.

DISCUSSION

Surgical reimplantation of the affected ureter has been the standard treatment for VUR after kidney transplantation; the average success rate ranged from 83% to 100% [9,10], but the procedure may be difficult and significant morbidity of 16% to 53% has been reported [4,9–11]. As a result, alternative minimal invasive endoscopic management were applied [5,6]; with the accumulation of experience, a low morbidity of 10% and success rate of 60% to 86% have been described [5,12–15]. The success rate in our series was 75%, which is compatible with the reports from large series.

The mean diagnosis time of VUR in our series is more than 7 years after transplantation, with 5 patients at more than 10 years. If we divide our patients with the eGFR = 60 mL/min at the time of endoscopic treatment, there are 8 patients in both groups. We plot their mean eGFR according to time after Deflux injection, as seen in Fig 1. The demographics data were similar between the 2 groups,

except the mean follow-up time was 8.8 months in the eGFR $>$ 60 group and 29.0 months in the eGFR $<$ 60 group. We observe that in the eGFR $>$ 60 group, mean eGFR improved from preoperative 73.86 mL/min to postoperative 82.26 mL/min (which might have related to the absence of VUR-related graft inflammation after injection), then maintained around 70 mL/min, and finally ended at 73.27 mL/min. In the eGFR $<$ 60 group, the eGFR was 34.41 mL/min preoperatively, decreased to 29.74 mL/min postoperatively (due to the 2 patients with transient oliguria), then remained around 30 mL/min throughout the time course, ending with 31.53 mL/min at 33 months after injection. There were 2 patients in each group who had symptomatic UTI and required admission after injection (clinical failure rate of 75%). The eGFR remained stationary following Deflux injection, suggesting that endoscopic treatment of VUR after kidney transplantation is a feasible and safe option, suitable for recipients of both eGFR $>$ 60 and eGFR $<$ 60 groups.

CONCLUSION

Endoscopic dextranomer-hyaluronic acid injection is a safe and feasible treatment option for VUR after kidney transplantation. Our data showed its efficacy in recipients whose eGFR is less than 60 mL/min.

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