Antegrade Balloon Dilatation as a Treatment Option for Posttransplant Ureteral Strictures: Case Series of 50 Patients

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Abstract

Objectives: **The aim of this study was to investigate the effects of antegrade balloon dilatation on ureteral strictures that developed after kidney transplant.**

Materials and Methods: **The hospital databases of the Erasmus Medical Center (Rotterdam, The Netherlands) and the Academic Medical Center (Amsterdam, The Netherlands) were retrospectively screened for patients who underwent balloon dilatation after kidney transplant. Balloon dilatation was technically successful whenever it was able to pass the strictured segment with the guidewire followed by balloon inflation; the procedure was clinically successful if no further interventions (for example, surgical revision of the ureteroneocystostomy or prolonged double J placement) were necessary.**

Results: **Fifty patients (2.4%) of 2075 kidney transplant recipients underwent antegrade balloon dilatation because of urinary outflow obstruction. Median time between transplant and balloon dilatation was 3 months (range, 0-139 mo). In 43 patients (86%), balloon dilatation was technically successful. In the remaining 7 patients (14%), it was impossible to pass the strictured segment with the guidewire. In 20 of 43 patients (47%) having a technically successful procedure, the procedure was also clinically successful, with median follow-up after balloon dilatation of 35.5 months (range, 0-102 mo). We did not identify any patient or stricture characteristic that influenced the outcome of treatment.**

Conclusions: **Balloon dilatation is a good option for ureter stricture treatment after kidney transplant as it is minimal invasive and can prevent surgical exploration in almost 50% of cases.**

Key words: *Balloon dilatation, Kidney transplant, Urinary outflow obstruction, Urologic complications*

Introduction

Major urologic complications after kidney transplant, including urinary leakage and ureter strictures, are reported with an incidence between 2.3% and 20%.[1-3] Ureteral strictures are the most commonly reported urologic complication and can cause significant morbidity after kidney transplant with prolonged hospital stay and repetitive interventions.

A ureteral outflow obstruction is characterized by elevated serum creatinine in combination with hydronephrosis on ultrasonography examination and is generally treated with a percutaneous nehrostomy (PCN). In a number of cases, the obstruction will resolve spontaneously. However, in a few cases, additional treatment is necessary to guarantee adequate outflow.

Treatment options for ureteral strictures include long-term double J catheter insertion, balloon dilatation, or surgical revision of the ureteroneocystostomy. In the literature, only a few studies are available that report on the success rates of these treatments. Helfand and associates reported on their experience with surgical treatment of ureteral strictures after kidney transplant and proposed an algorithm for management of strictures.[4] The algorithm is based on size of the stricture (< 3 cm) and the time between transplant and diagnosis of the stricture (< 3 mo). However, the study population was small (n = 13).[4]

Balloon dilatation has proven its efficacy in the treatment of the ureterovesical junction for an obstructive megaureter and in ureteroileal strictures of 1 cm or less in patients after surgical urinary diversion.[5-7]

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The primary objective of this study was to present a case series of balloon dilation treatment for posttransplant ureteral strictures and to determine its success rate. The secondary objective was to determine which factors might be of influence on the outcomes of balloon dilatation.

Materials and Methods

Patients

The Medical Ethical Committee approved the trial protocol (MEC-2015-119). The hospital databases of the Erasmus Medical Center (Rotterdam, The Netherlands) and the Academic Medical Center (Amsterdam, The Netherlands) were screened for patients who underwent radiologic balloon dilatation of the ureter after kidney transplant. Baseline characteristics included recipient sex and age, type of donor (deceased vs living), second warm ischemic time, cold ischemic time, technique for ureteroneocystostomy (intravesical vs extravesical), number of prior transplant procedures, months between kidney transplant and balloon dilatation, stricture characteristics, readmissions within 1 month after balloon dilatation, and follow-up in months after balloon dilatation. Balloon dilatation was considered technically successful if the interventional radiologist was able to pass the strictured segment with the guidewire and the balloon could be inflated. Balloon dilatation was clinically successful if no further interventions (for instance, surgical revision of the ureteroneocystostomy or later prolonged double J placement) were necessary. Graft survival was based on the date a patient returned to hemodialysis or peritoneal dialysis or received a preemptive new transplant. All complications that occurred within 30 days after balloon dilatation and led to a readmission were documented.

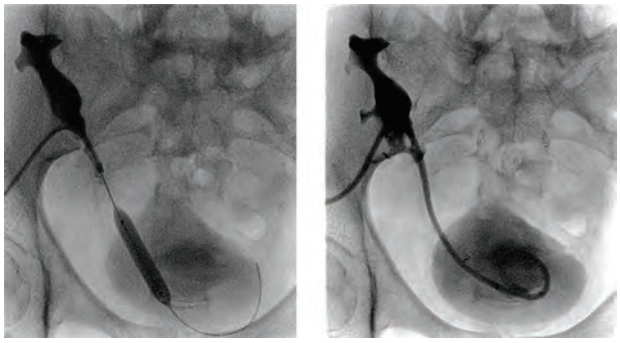
Diagnosing ureteral stricture

For all patients who presented with increased serum creatinine and hydronephrosis on ultrasonography examination, PCN placement was the first step in treatment. Ureteral stricture diagnosis was confirmed with anterograde pyelography. For this study, all pyelograms were analyzed retrospectively for location of the ureter stricture (proximal, midureteral, distal, total, or multiple) and length of the stricture by 1 interventional radiologist (AM) with over 8 years of experience in urogenital interventions. If the ureter had multiple strictured segments, the length of the longest stricture was documented.

Balloon dilatation procedure

The nephrostomy tube was replaced by an 8F vascular sheath, and a 4F catheter with a hydrophilic 0.035-inch guidewire (Terumo, Belgium) was introduced through the sheath into the renal pelvis and ureter in antegrade fashion. The guidewire was then passed through the strictured segment of the ureter into the bladder, and a 3- to 8-mm-diameter balloon was advanced over the guidewire and inflated over several minutes. In cases where traversing the stricture was difficult, smaller diameter wires (0.014 inch) and balloons could be used. The type of balloon varied over time between a regular and a cutting balloon, which was at the discretion of the treating interventional radiologist. The cutting balloon has 3 or 4 microsurgical blades. These blades are fixed longitudinally on the outer surface of the balloon, expand radially, and deliver longitudinal incisions in the strictured segment of the ureter. After deflation of the balloon, a PCN, a percutaneous nephroureterostomy (PCNU; Figure 1) catheter, or a double J catheter was placed.

Figure 1. Balloon Dilatation and Percutaneous Internal/External Nephroureteral Catheter



Statistical analyses

Categorical variables are presented as numbers (with percentages in parentheses). Continuous variables are presented as median (range) if not normally distributed; continuous variables with normal distribution are presented as means with standard deviation. Normality was based on the shape of the histogram plot and tested with the Shapiro-Wilks test. Categorical variables were analyzed using the chi-square test. Continuous variables were analyzed using the Mann-Whitney *U* test or an independent *t* test. Graft survival was analyzed using a log-rank

test and censored for death. For graft survival, we did not distinguish between technically or clinically successful balloon dilatations. All technically and clinically unsuccessful balloon dilatations were considered as unsuccessful. All analyses were conducted using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY, USA). $P < .05$ (2-sided) was considered statistically significant.

Results

Baseline characteristics

The database analyses showed 50 patients who underwent antegrade balloon dilatation (Table 1). This included 37 patients (2.5 %) of 1496 kidney transplants that were performed at Erasmus Medical Center between August 2007 and September 2015. At the Academic Medical Center, 13 of 579 kidney transplant patients (2.2%) patients underwent balloon dilatation. The Academic Medical Center database results included within a shorter period (from March 2011 to June 2015). Median time between kidney transplant and balloon dilatation treatment was 3 months (range, 0-139 mo). The median length of the total strictured segment was 2 cm (range, 0.5-5 cm), and median follow-up after balloon dilatation was 35.5 months (range, 0-102 mo).

Table 1. Baseline Characteristics of 50 Study Patients

Population Characteristic	
Number of male patients (%)	30 (60)
Mean age at kidney transplant ± SD, y	48 ± 16
Living donor, No. (%)	35 (70)
Median 2nd WIT, min (range)	26.5 (13-80)
Median CIT, min (range)	169 (96-2520)
Type of anastomose, No. (%)	
Intravesical	10 (20)
Extravesical	34 (68)
Not documented	6 (12)
Primary reason for PCN, No. (%)	
Hydronephrosis	43 (86)
Urinary leakage	7 (14)
Median number of transplants (range)	1 (1-4)
Median months between kidney transplant and BD (range)	3 (0-139)
Median length of longest stricture, cm (range)	1.5 (0.5-5)
Median length of total stricture, cm (range)	2 (0.5-5)
Location of stricture, No. (%)	
Distal	33 (66)
Proximal	3 (6)
Midureteral	2 (4)
Total	6 (12)
Multiple	6 (12)
Median number of BD (range)	1 (1-4)
Technically successful BD, No. (%)	43 (86)
Clinically successful (of technically successful) BD, No. (%)	20 (47)
Median follow-up after BD, mo (range)	35.5 (0-102)

Abbreviations: BD, balloon dilatation; CIT, cold ischemic time; SD, standard deviation; WIT, warm ischemic time

Balloon dilatation

In 43 of 50 patients (86%), balloon dilatation was performed successfully from a technical point of view. However, in 7 patients (14%), it was impossible to pass the strictured segment with the guidewire. Of these 7 patients, 2 patients had a second and even a third attempt for balloon dilatation. These all remained technically unsuccessful. In 20 of the 43 patients (47%) who underwent a technically successful balloon dilatation, the procedure was also clinically successful. Median follow-up after balloon dilatation was 35.5 months (range, 0-102 mo). In 12 patients, balloon dilatation was clinically successful after 1 attempt, 7 patients needed a second treatment, and 1 patient needed 4 balloon dilatation treatments before success was reached. These additional balloon dilatation procedures were during a repeat procedure and not in the same procedure.

One patient with a technically successful dilatation died from pneumosepsis (*Pneumocystis jiroveci*) 1 month after balloon dilatation. This was before stent removal; therefore, we were not able to determine whether balloon dilatation was successful. Another patient had a severe graft rejection after balloon dilatation and graft nephrectomy was necessary. In this case, we were also not able to determine the success of balloon dilatation. Therefore, in these 2 patients, the success was scored as missing. One patient had a kidney infarction after balloon dilatation, and this was scored as unsuccessful. This event will be discussed further below in the complications section.

Two patients underwent a surgical revision of the ureterocystostomy before a successful balloon dilatation. One of these patients received her transplant in 2003 and had a surgical revision of the ureteroneocystostomy in 2004. During this period, we did not yet carry out balloon dilatations in our hospital. In 2014, this patient had a recurrent stricture and underwent successful balloon dilatation. The other patient had urinary leakage that was primarily followed by a surgical ureteral reconstruction 2 days after transplant. This patient developed a stricture that was successfully treated with balloon dilatation.

Of the 43 patients who underwent technically successful balloon dilatation, a regular balloon was used in 36 patients and a cutting balloon in 7 patients. In 40 patients, the strictured segment was stented after the balloon dilatation with a PCNU catheter or a

double J catheter; in the other 3 patients, a regular PCN was placed and therefore scored as nonstented.

Twenty-six patients underwent surgical repair after a balloon dilatation attempt. In 16 patients, the strictured segment was resected and a new ureteroneocystostomy was made. In 4 patients, the native ureter was attached to the transplant renal pelvis: 3 patients had a pyelocystostomy and 1 patient had the native ureter attached to the transplanted ureter. During surgical exploration in 1 patient, the total ureter was strictured; therefore, no further surgical options were available. This patient remained nephrostomy dependent. In the last patient, no ureteral obstruction was objectified during surgical exploration; however, a limited bladder capacity was detected and this patient was treated with a suprapubic catheter.

Complications

In 1 patient, a kidney infarction was diagnosed 22 days after balloon dilatation treatment and 13 days after PCN replacement. As kidney function deteriorated, a biopsy was performed to exclude rejection. Renal failure was attributed to loss of parenchymal tissue secondary to infarction due to vascular damage. The complication was not attributed to balloon dilatation as such. However, the intervention procedure was scored as clinically unsuccessful in this case series.

One patient developed a ureter stricture of 1.5 cm in the distal part of the ureter 3 months after transplant. A PCN was placed, and a pyelogram was made to visualize the pyeloureteral anastomosis. During this procedure, a fistula between the renal pelvis and iliac vein was visualized (Figure 2). It is unknown whether it was present before or caused by the intervention. The antegrade balloon dilatation procedure was ended prematurely, ie, before entering the bladder with the guidewire, and no ureteral dilatation was performed. In the hours after the procedure, the patient developed septic shock and died despite antibiotic treatment. The cause of death was explained by bacteremia due to direct circulatory contamination with a multiresistant *Escherichia coli* in an immunocompromised patient.

There were 23 patients without complications who required readmission. Eighteen patients were readmitted within 1 month because of urosepsis. These readmissions could also be in conjunction with chronic contamination due to continued PCNU or PCN placement requiring a replacement of the PCNU catheter or PCN. One patient was readmitted because of the previously mentioned kidney infarction, 1 patient was readmitted because of hematuria with creatinine rise caused by an obstructive blood clot, 1 patient was readmitted with deep venous thrombosis, 2 patients were readmitted for treatment of additional rejection, 3 patients were readmitted because of PCN-related complications (urinary leakage or dislocation), and 1 patient was readmitted for diarrhea followed by urosepsis and surgical revision of the ureteroneocystostomy. All of these occurred within the first 30 days after the procedure. In the patient with diarrhea, a perforation of the ureter occurred while the radiologist tried to pass the strictured segment with the guidewire. It was impossible to pass the strictured segment, and the procedure was ended prematurely.

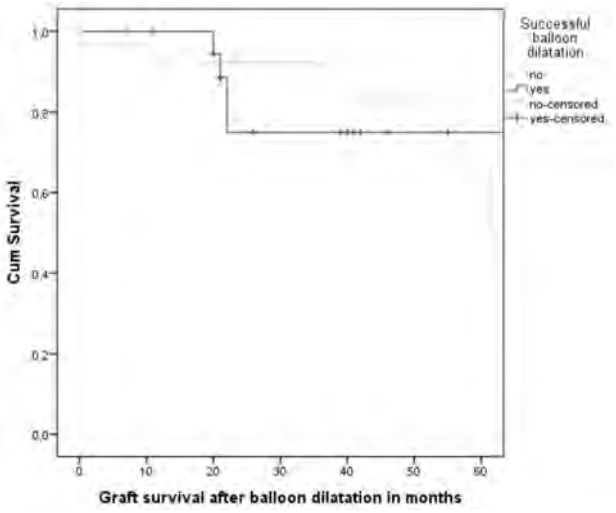
Figure 2. Pyelovenous Fistula

Graft survival

Graft survival was 100% at 12 months and 75% at 24 months after successful balloon dilatation. For the unsuccessful procedures, graft survival was 92% at 12 and 24 months after attempting the balloon dilatation ($P = .937$; Figure 3). Grafts failed due to several causes, including 3 chronic failures followed by preemptive retransplant in 2 patients, 2 acute rejections, the previously mentioned kidney infarc-

tion, 1 recurrent primary disease (focal segmental glomerulosclerosis), 1 case of glomerulosclerosis and interstitial fibrosis, 1 case of cardiac shock with subsequent contrast overload leading to acute tubulus necrosis, and 1 case of urosepsis.

Figure 3. Graft Survival After Balloon Dilatation



Risk factor analyses

In univariate analysis, we found that donor characteristics (type of donor, warm ischemic time, cold ischemic time), type of ureteroneocystostomy technique, recipient sex, months between kidney transplant and balloon dilatation, type and diameter of the balloon used, stricture length, stricture location, and the use of a stent after balloon dilatation were not factors that could influence the outcome of the treatment (Table 2).

Table 2. Factors That May Contribute to Clinical Success of Technically Successful Balloon Dilatation

Factor	Unsuccessful Clinical Balloon Dilatation (n = 21)	Successful Clinical Balloon Dilatation (n = 20)	*P* Value
Extravesical technique ureteroneocystostomy, No (%)	16 (84)	12 (71)	.326
Male recipient, No. (%)	14 (67)	10 (50)	.279
Living donor, No. (%)	14 (67)	16 (80)	.335
Median 2nd WIT, min (range)	24 (14-80)	25.5 (13-56)	.886
Median CIT, min (range)	180 (96-1860)	156 (114-1260)	1.000
Median length of longest stricture, cm (range)	1.7 (0.5-5)	1.5 (0.5-5)	.439
Longest stricture > 3 cm, No. (%)	5 (24)	2 (10)	.240
Median months between kidney transplant and BD (range)	3 (0-139)	3 (0-135)	.484
> 3 months between kidney transplant and BD	8 (38)	8 (40)	.901
Location of stricture, No. (%)			
Total	2 (10)	1 (5)	.562
Proximal	2 (10)	1 (5)	
Distal	12 (57)	15 (75)	
Midureteral	2 (10)	0 (0)	
Multiple	3 (13)	3 (15)	
Type of balloon, No. (%)			
Cutting	4 (19)	3 (15)	.731
Regular	17 (81)	17 (85)	
Diameter of balloon, No. (%)			
3-4 mm	4 (19)	3 (15)	.942
5-6 mm	7 (33)	7 (35)	
7-8 mm	10 (48)	10 (50)	
Stented postdilatation, No. (%)	20 (95)	18 (90)	.520

Abbreviations: BD, balloon dilatation; CIT, cold ischemic time; SD, standard deviation; WIT, warm ischemic time

Outcome data were missing for 2 patients. Univariate analysis was used.

Discussion

Urologic complications, including urinary leakage and ureteral strictures, may occur as early and as late complications after kidney transplant. In this study, we analyzed the outcomes of balloon dilatation as a first treatment for ureter strictures after kidney transplant. The technical success rate was 86%, and the subsequent clinical success rate of balloon dilatation treatment was 47%. We could not identify any factors that may have contributed to a (non)successful outcome of a balloon dilatation.

Several other studies have reported on outcomes of balloon dilatation. Asadpour and associates reported on 24 patients with ureteral strictures of whom 11 (46%) had a successful outcome after balloon dilatation and PCN treatment.[8] Their results are comparable to the outcomes of our present study. Aytekin and associates[9] reported a balloon dilatation success rate of 90% in their cohort of 10 patients with late obstructions due to strictures, which is a higher success rate than shown in our cohort. Four patients had a recurrence of the stricture; therefore, a repeated balloon dilatation was necessary. In 2 of these patients, a metallic stent was placed. In only 1 patient, surgical revision of the ureterocystostomy after balloon dilatation was necessary. It should be noted that, in this study, a 7F double J catheter was inserted as standard care after balloon dilatation. This might have increased their success rate.[9] On the other hand, Juaneda and associates reported on 45 patients with ureteral strictures with a 45% success rate in placing a double J catheter after all balloon dilatations as well.[10] In a review by Haberal and associates, repeated balloon dilatation in resistant strictures, a cutting balloon for fibrotic strictures, and temporary postdilatation double J stenting were also advised.[11]

He and associates tried to define a treatment strategy for kidney transplant recipients who

develop ureteral obstruction. In their study, they defined 3 grades of ureteral strictures: grade 1 included hydronephrosis without an evidently strictured segment, grade 2 included hydronephrosis with ≤ 1-cm strictured segment, and grade 3 included hydronephrosis with > 1-cm strictured segment.[12] They proposed the following treatment options: grade 1 cases would receive prolonged stent insertion for 6 weeks, grade 2 cases would receive cystoscopy with incision or balloon dilatation followed by stent insertion for 6 weeks, and grade 3 would have surgery. When we applied this classification and treatment strategy to our cohort, 17 patients would fit the grade 2 classification; in 9 of these patients, balloon dilatation was successful. In our cohort, 33 patients had a stricture that could be classified as grade 3 and would therefore benefit from surgical treatment. However, 11 of these patients had successful balloon dilatation and would have been subjected to unnecessary surgical intervention when following this classification.[12] Based on the results of our cohort, we would advise performing a balloon dilatation before surgical revision, as it is less invasive, irrespective of the proposed grading system.

There are some limitations to this study. Despite our study including the highest number of balloon dilatations reported until now, the total of 50 patients is still low. Therefore, analyses of factors that could contribute to the success rate of balloon dilatation treatment cannot be performed reliably or perhaps none of the factors influenced the outcome. Furthermore, our treatment after balloon dilatation was different in our patients. In some, the PCN drain was left in situ; in others, the PCN was removed and a single pigtail in PCNU position or a double J catheter was placed instead. On the basis of the available literature, double J catheter placement has a favorable outcome; however, this would indicate that an additional cystoscopy would be necessary to remove the double J catheter.[9,12] A drain in the PCNU position would give the benefit of a stented stricture postdilatation treatment, lacking the risks of an additional cystoscopy.

We believe that balloon dilatation should be advocated as the first treatment for ureter strictures. It was clinically successful in 47% of patients, and it is less invasive than open surgical ureter reconstruction.

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