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MAJOR ARTICLE

Evaluation of a Ureteral Stent Removal Protocol in Adult Kidney Transplant Recipients

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Existing literature on best practices to reduce the risk of infectious complications associated with ureteral stent removal in kidney transplant recipients is limited. Prior to 2021, a formal process surrounding stent removal was not in place at our institution. In June 2021, a stent removal protocol was established. This protocol included the following: obtaining a preprocedure urine culture, prescribing universal culture-directed antimicrobial prophylaxis, earlier stent removal posttransplant, and patient education. We performed a retrospective quasi-experimental study of kidney transplant recipients who had their stents removed between July 2020 and June 2022. The primary outcome was the incidence of infectious complications within 30 days. Infectious complications were defined as urinary tract infection and bacteremia due to urinary source, as well as hospitalization, emergency department visit, or outpatient encounter for possible urinary tract infection. Secondary objectives included infectious and immunologic complications within 30 days to 1 year from transplant. During this study period, 239 adult kidney transplant recipients were included: 88 in the preprotocol group and 151 in the protocol group. The median time to stent removal was shorter in the protocol group (25 vs 36 days, $P < .001$). More patients in the protocol group received preprocedure antibiotics (99% vs 36%, $P < .001$). Infectious complications were higher in the preprotocol group (9% vs 3%, $P = .035$). Overall, the stent removal protocol was associated with fewer infectious complications (odds ratio, 0.18; 95% CI, 0.05–0.73). Further investigation is necessary to determine which individual interventions, if any, drive this benefit.

Keywords. antibiotic; antimicrobial; kidney; organ transplant; prophylaxis.

Ureteral stent insertion at the time of kidney transplantation decreases the risk of urologic complications such as anastomotic leak, stricture, or obstruction [1]. However, the benefits of minimizing mechanical complications should be weighed against the intrinsic risk of microbial colonization and associated urinary tract infections (UTIs) [1–3]. In a study by Alangaden et al, ureteral stenting was one of the strongest predictors of UTI after kidney transplantation, as 71% of patients with stents developed UTI as opposed to 33% of patients without stents ($P < .001$) [3]. While microbial colonization has not been shown to affect long-term graft function, infectious complications after stent removal can cause significant morbidity or mortality in the patient who is immunocompromised [1].

Several factors may increase the risk of infectious complications after stent removal, such as patient comorbidities, anomalies of the urinary tract, urinary obstruction, incomplete bladder emptying, and duration of stent induration [4]. Optimizing modifiable risk factors can potentially decrease complications posttransplant. Existing literature has found earlier stent removal, particularly within 3 weeks posttransplant, to be associated with a decreased incidence of UTIs, with no significant difference in the incidence of major urologic complications when compared with later removal (>3 weeks) [5, 6].

Additionally, the American Urological Association (AUA) best practice guidelines state that antimicrobial prophylaxis may be considered for clinical procedures, including removal of ureteral stents, especially when patient and procedural risk factors are present [7]. The 2022 European Association of Urology guidelines on urologic infections state that asymptomatic bacteriuria is considered a risk factor for infectious complications during ureteral stent placement or exchange; therefore, screening and treatment prior to the procedure are recommended [8].

Prior to 2021, a formal process surrounding stent removal was not in place at our institution and practices varied. In

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2021, a multidisciplinary group was established to develop a standard process surrounding ureteral stent removal after kidney transplantation. The protocol included: removing the stent at 3 weeks posttransplant, obtaining a urine culture within 1 week prior to stent removal, prescribing universal culture-directed antimicrobial prophylaxis, and providing patient education. This study sought to evaluate the impact of this protocol on infectious and immunologic complications following stent removal.

MATERIALS AND METHODS

Study Center

The University of Chicago Medicine (UCM) is an 811-bed academic medical center located on the South Side of Chicago, Illinois. UCM's kidney transplant program performs living and deceased donor kidney transplants. UCM performs around 150 kidney transplants per year. All kidney transplant recipients have a ureteral stent placed at the time of transplant surgery. These stents are later removed via clinic cystoscopy by the urologic surgical team unless the patient has a concurrent need requiring the operating room.

Intervention

Prior to 1 June 2021, there was no standard process for coordination between the urology and transplant nephrology divisions regarding antimicrobial prophylaxis and timing of ureteral stent removal. Ureteral stents were removed by the urology division approximately 4 to 6 weeks posttransplant. In 2021, a multidisciplinary working group was established to develop and implement a standardized stent removal process. This group consisted of physician, advanced practice nurse, and pharmacist representatives from transplant surgery, transplant nephrology, urology, and infectious diseases. The stent removal protocol implemented on 1 June 2021 included the following: (1) removing the stent at 3 weeks posttransplant, (2) obtaining a urine culture within 1 week prior to stent removal, (3) prescribing universal culture-directed antimicrobial prophylaxis, and (4) patient education (Supplementary Appendix 1). Patients with symptomatic UTIs at the time of stent removal were excluded and followed a separate treatment algorithm.

The patient's nephrologist ordered the preprocedure urine culture and antimicrobial prophylaxis. Antibiotic prophylaxis was guided by the preprocedure urine culture (Supplementary Tables 1 and 2). Patients with a positive preprocedure urine culture received a minimum 3 days of antimicrobial prophylaxis prior to the stent removal procedure. Those with a negative urine culture received 24 hours of cephalexin beginning the morning of stent removal (prior to the procedure). For ease of outpatient dosing, cephalexin was selected as an oral equivalent to the cefazolin recommended by the AUA best practice guidelines for transurethral cases, including stent removal [7]. Microbiologic and susceptibility data were not available for this specific patient population at the time. The Infectious Diseases and Antimicrobial Stewardship Program was available to answer questions for culture-directed therapy if the preprocedure urine culture grew an organism that was not covered by recommended therapies. Continuing antibiotics beyond the date of stent removal was not recommended.

Prior to proceeding with stent removal, urology staff screened to ensure that patients had taken the requisite antibiotics. Patients who were not adherent or were unsure of adherence to antibiotic prophylaxis were given intramuscular gentamicin within 30 to 60 minutes prior to the procedure. Removed ureteral stents were sent for microbial analysis. Patient education regarding when to reach out to the urology division for issues or concerns was also developed and reinforced (Supplementary Appendix 1).

Aside from the protocol interventions described so far, no other procedural or UTI management changes were made during the entire study period. Patients maintained routine posttransplant follow-up appointments, in which urinary symptoms were assessed and urine cultures were sent only when there was suspicion for a UTI.

Study Design

This retrospective, single-center, quasi-experimental study evaluated adult kidney transplant recipients at a large academic medical center between 1 July 2020 and 30 June 2022. Patients aged ≥18 years were included if they received an isolated kidney transplant and underwent ureteral stent removal during the study period. Patients were excluded if they died prior to stent removal. Patients who had the stent removed prior to 1 June 2021 (preprotocol group) were compared with those who had the stent removed on or after 1 June 2021 (protocol group).

Outcomes

The primary outcome was the incidence of infectious complications within 30 days after stent removal. Infectious complications were defined as UTI or bacteremia due to urinary source, as well as hospitalization, emergency department visit, or outpatient encounter (ie, clinic visit or telephone note) for possible UTI. UTIs were classified as cystitis or pyelonephritis. Cystitis was defined as bacteriuria and at least 1 of the following symptoms: dysuria, urinary frequency, urinary urgency, or suprapubic pain. Pyelonephritis was defined as bacteriuria and at least 1 of the following: fever, chills, malaise, hemodynamic instability, leukocytosis, flank/allograft pain, or bacteremia with the same organism as in the urine. Bacteremia due to urinary source was defined as a positive blood culture with UTI symptoms. Possible UTI included patients with bacteriuria who did not meet the definition for cystitis or pyelonephritis (ie, absence of a urine culture) but received antibiotics due to suspected

UTI after other causes were ruled out. Health care utilization was defined as a hospitalization, emergency department visit, or outpatient encounter due to possible UTI.

Secondary objectives were as follows: the incidence of the individual components of the primary composite outcome, acute kidney injury within 30 days after stent removal, biopsy-proven rejection within 1 year posttransplant, and mortality within 1 year posttransplant. Acute kidney injury was defined as an increase in serum creatinine >2 times the posttransplant baseline or a glomerular filtration rate decrease >50%.

Statistical Analysis

Descriptive statistics were calculated for the variables in the primary analysis and included mean (SD) and median (IQR). A *t* test was used to compare normally distributed variables, a Mann-Whitney test for nonnormally distributed variables, and a Fisher exact test for categorical variables between the groups. $P < .05$ was considered statistically significant. Stata version 16.1 was used for all analyses (StataCorp).

Multivariable logistic analyses were performed to identify variables associated with infectious complications, while adjusting for confounding variables. Variables in the bivariate analyses at $P < .2$ were included in the explanatory multivariable model at model entry (Supplementary Table 3). The protocol intervention was forced into the model, without the separate interventions. To limit collinearity, a sensitivity analysis was performed with the separate protocol interventions (ie, time to stent removal, receiving antibiotics within 1 week prior to and on the day of stent removal, and a positive preprocedure urine culture) but without the bundled protocol intervention (Supplementary Table 4).

Based on previously published literature, if a 9% rate of infectious complications is observed in the preprotocol group as compared with 2% in the protocol group, 330 patients would be needed to achieve a power of 0.8 and an alpha of 0.05.

Data were managed in a REDCap database [9]. This study received a formal Determination of Quality Improvement status according to UCM institutional policy. As such, this initiative was deemed not human subjects research and was therefore not reviewed by the institutional review board.

RESULTS

A total of 239 adult kidney transplant recipients with ureteral stent placement were eligible and included in the analysis during the study period. Eighty-eight patients (37%) were in the preprotocol group and 151 (63%) in the protocol group. Baseline characteristics such as age, gender, race, and comorbidities were similar between the groups (Table 1). More patients in the protocol group received antithymocyte globulin (rabbit) as induction immunosuppression. At the time of stent removal, the majority of patients were prescribed prednisone, tacrolimus, and mycophenolate mofetil as maintenance immunosuppression. Patients in the preprotocol group were on average receiving a lower daily dose of prednisone and tacrolimus but higher daily dose of mycophenolate mofetil. Despite the difference in tacrolimus dosing, there was no difference seen in the median trough levels of tacrolimus between the groups. Additional details regarding patients' immunosuppression regimen are summarized in Table 1.

The median time to stent removal from time of transplant was significantly longer in the preprotocol group vs the protocol group (36 vs 25 days, $P < .001$). Within 30 days prior to stent removal, more patients in the protocol group had posttransplant urine cultures performed as compared with the preprotocol group (94% vs 46%, $P < .001$; Table 2). The incidence of positive urine cultures obtained within 30 days prior to stent removal was similar between the groups (12.5% vs 14.2%, $P = .080$). In both groups, the most common organisms growing in the urine culture prior to stent removal were *Enterococcus* species and *Escherichia coli*.

Within 1 week prior to and on the day of stent removal, more patients received antibiotics in the protocol group vs the preprotocol group (99% vs 36%, $P < .001$). The most frequently given antibiotics in both groups were cephalexin and cefazolin. More patients in the protocol group received cephalexin than the preprotocol group (76% vs 25%, $P < .001$). Eight patients in the protocol group grew *Enterococci* on their preprocedure urine culture: 3 received cephalexin because the urine culture results did not return until after stent removal, and 5 received amoxicillin, ampicillin, or amoxicillin-clavulanic acid. There was no difference in the number of patients receiving trimethoprim-sulfamethoxazole (TMP-SMX) for prophylaxis (92% vs 89%, $P = .651$). Following stent removal, antibiotics were continued in 10 patients (11%) in the preprotocol group and 29 (19%) in the postprotocol arm for a median 4 days in both groups (Table 3). Reasons for continuing antibiotics after stent removal primarily included treatment of other infections (ie, fluid collection in abdomen, perinephric fluid collection, wound infection, sepsis, drain site infection, peritonitis, and cholangitis).

Infectious complications after stent removal were significantly greater in the preprotocol group than the protocol group (9% vs 3%, $P = .035$; Table 3). Three patients in the preprotocol group had bacteremia, as opposed to none in the protocol group. None of these patients had a preprocedure urine culture within 30 days prior to stent removal. Two patients had *Klebsiella* spp bacteremia and 1 had enterococcal bacteremia. The 2 patients with *Klebsiella* spp bacteremia did not receive any preprocedure antibiotics, and the patient with enterococcal bacteremia received preprocedure cephalexin. There was no difference in acute kidney injury, biopsy-proven rejection, or mortality between the groups. No antibiotic-related adverse effects were identified.

Table 1. Baseline Demographics and Transplant Characteristics

	Preprotocol (n = 88)	Protocol (n = 151)	*P* Value
Age, y	56.3 (45.9–64.9)	55.6 (44.2–63.6)	.573
Male	53 (60.2)	99 (65.6)	.408
Duration on dialysis prior to transplant, y	3 (0–6)	4 (1–6)	.271
Race			…
African American	47 (53.4)	90 (59.6)	
Caucasian	35 (39.8)	35 (23.2)	
Asian	3 (3.4)	10 (6.6)	
Other	2 (2.3)	11 (7.3)	
Unknown	1 (1.1)	5 (3.3)	
Ethnicity			…
Hispanic or Latino	11 (12.5)	24 (15.9)	
Not Hispanic or Latino	76 (86.4)	123 (81.5)	
Unknown	1 (1.1)	4 (2.2)	
Native kidney disease			
Diabetes	31 (35.2)	53 (35.1)	>.999
Hypertension	26 (29.5)	53 (35.1)	.379
Retransplant	12 (13.6)	14 (9.3)	.389
Polycystic kidney disease	6 (6.8)	10 (0.7)	.953
FSGS	6 (6.8)	9 (6.0)	.792
Glomerulonephritis	6 (6.8)	4 (2.6)	.178
Lupus	3 (3.4)	6 (4.0)	>.999
IgAN	2 (2.3)	6 (4.0)	.714
HIVAN	4 (4.5)	1 (0.7)	.063
Alport syndrome	0	2 (1.3)	.533
Congenital obstructive uropathy	1 (1.1)	1 (0.7)	>.999
aHUS	0	1 (0.7)	>.999
TMA	1 (1.1)	0	.368
Vasculitis	0	1 (0.7)	>.999
Other	8	5	.076
Comorbidities			
Hypertension	80 (90.9)	142 (94.0)	.364
Diabetes	36 (40.9)	63 (41.7)	.902
Active or previous smoker	43 (48.9)	58 (38.4)	.115
COPD	5 (5.7)	6 (4.0)	.539
Induction immunosuppression			
Antithymocyte globulin (rabbit)	57 (63.8)	123 (81.5)	.004
Antithymocyte globulin (rabbit) cumulative dose, mg/kg	5 (4.1–5.5); n = 57	4.8 (3.8–5.4); n = 123	.476
Basiliximab	37 (42.0)	35 (23.2)	.002
Basiliximab cumulative dose, mg	40 (40–40); n = 37	40 (40–40); n = 35	.637
Maintenance immunosuppression at time of stent removal			
Prednisone	87 (98.9)	150 (99.3)	>.999
Prednisone mg/d, mean (SD)	7.7 (4.1); n = 87	10.3 (4.7); n = 150	<.001
Tacrolimus	87 (98.9)	148 (98.0)	>.999
Tacrolimus, mg/d	6 (4–10); n = 87	10 (6–13); n = 148	<.001
Tacrolimus trough, mcg/mL	8.6 (6.8–10.1)	8.5 (6.9–10.65)	.295
Mycophenolate mofetil	76 (86.4)	131 (86.8)	.932
Mycophenolate mofetil mg/d, mean (SD)	1725 (442); n = 76	1492.37 (508); n = 131	.001
Mycophenolic acid	9 (10.2)	18 (11.9)	.690
Mycophenolic acid mg/d	1080 (720–1440); n = 9	720 (720–1440); n = 18	.278
Azathioprine	0	1 (0.7)	>.999
Cyclosporine	1 (1.1)	0	.368
Deceased donor	65 (73.9)	119 (78.8)	.225

Data are presented as median (IQR) or No. (%) unless noted otherwise.

Abbreviations: aHUS, atypical hemolytic uremic syndrome; COPD, chronic obstructive pulmonary disease; FSGS, focal segmental glomerulosclerosis; HIVAN, HIV-associated nephropathy; IgAN, immunoglobulin A nephropathy; TMA, thrombotic microangiopathy.

Table 2. Stent Removal Characteristics

	Preprotocol (n = 88)	Protocol (n = 151)	*P* Value
Time to stent removal, d	36 (32–40)	25 (23–31)	<.001
Stent removed while patient was hospitalized	21 (23.9)	32 (21.2)	.632
Urinalysis within 30 d prior to stent removal	65 (73.9)	111 (73.5)	.302
>20 WBCs	10 (15.4)	8 (7.2)	.087
10–20 WBCs	24 (36.9)	52 (46.8)	.251
0–5 WBCs	31 (47.7)	51 (45.9)	.820
Urine culture within 30 d prior to stent removal	40 (45.5)	141 (94.4)	<.001
Positive urine culture	5 (12.5)	20 (14.2)	.080
Organisms growing in most recent urine culture prior to stent removal[a]			
Enterococcus spp	3 (7.5)	8 (5.7)	.751
Escherichia coli	1 (2.5)	5 (3.5)	.418
Gardnerella vaginalis	0	3 (2.0)	.299
Citrobacter spp	1 (2.5)	1 (0.7)	>.999
Klebsiella spp (excluding *K aerogenes*)	1 (2.5)	0	.368
Pseudomonas spp	0	1 (0.7)	>.999
Morganella morganii	0	1 (0.7)	>.999
Candida glabrata	0	1 (0.7)	>.999
Other	0	1 (0.7)	>.999
No growth or mixed flora without specific organism identified	35 (87.5)	120 (85.1)	<.001
Received antibiotics preprocedure[a,b]	32 (36.4)	150 (99.3)	<.001
Cephalexin	8 (25.0)	114 (76.0)	<.001
Cefazolin	10 (31.3)	14 (9.3)	.604
Ciprofloxacin	6 (18.9)	7 (4.7)	.473
Levofloxacin	0	7 (4.7)	.049
Cefdinir	0	4 (2.7)	<.001
Cefepime	3 (9.4)	4 (2.7)	.710
Amoxicillin	0	4 (2.7)	.161
Vancomycin	1 (3.1)	4 (2.7)	.654
Tobramycin	0	4 (2.7)	.300
Gentamicin	3 (9.4)	2 (1.3)	.360
Other[c]	5 (15.6)	7 (4.7)	.764
TMP-SMX for prophylaxis at time of stent removal[d]	81 (92.0)	135 (89.4)	.651
Received antibiotics postprocedure	10 (11)	29 (19)	.148
Duration of antibiotics postprocedure, d	4 (2–15)	4 (2–7)	…

Data are presented as median (IQR) or No. (%).

Abbreviations: TMP-SMX: trimethoprim-sulfamethoxazole; WBC, white blood cell.

[a]Not mutually exclusive.

[b]Does not include TMP-SMX for prophylaxis.

[c]Amoxicillin-clavulanate, ampicillin, ceftazidime-avibactam, ceftriaxone, clindamycin, daptomycin, ertapenem, linezolid, meropenem, metronidazole, piperacillin-tazobactam.

[d]TMP-SMX dosed at 80–400 mg daily (renally adjusted as needed).

Multivariate logistic regression analysis demonstrated age, history of retransplant, chronic obstructive pulmonary disease (COPD), prednisone dose, and protocol implementation as significantly associated to infectious complications (Table 4). Age, retransplant, COPD, and prednisone dose were associated with an increased risk of infectious complications following stent removal, while protocol intervention was significantly associated with a lower risk of infectious complications (odds ratio, 0.18; 95% CI, 0.05–0.73; $P = .016$) following stent removal. A sensitivity analysis did not find an association between any individual protocol interventions and infectious complications (Supplementary Table 5).

Table 3. Primary and Secondary Outcomes

	Preprotocol (n = 88)	Protocol (n = 151)	*P* Value
Infectious complications[a]	8 (9.1)	4 (2.6)	.035
UTI	6 (6.8)	4 (2.6)	.178
Cystitis	1 (17)	2 (50)	.500
Pyelonephritis	5 (83)	2 (50)	.500
Bacteremia	3 (3.4)	0	.049
Hospitalization	6 (6.8)	1 (0.7)	.011
ED visit without hospitalization	0	1 (0.7)	>.999
Outpatient encounter	5 (5.7)	2 (1.3)	.104
Acute kidney injury	16 (18.2)	29 (19.2)	.845
Within 1 y from transplant			
Biopsy-proven rejection	4 (4.5)	7 (4.6)	>.999
Mortality	6 (6.8)	5 (3.3)	.220
Antibiotic-related adverse effects	0	0	…

Data are presented as No. (%).

Abbreviations: ED, emergency department; UTI, urinary tract infection.

[a]Not mutually exclusive.

Table 4. Multivariate Logistic Regression Assessing Variables Related to Infectious Complications

	Odds Ratio (95% CI)	*P* Value
Age	1.04 (.98–1.11)	.202
Retransplant	5.86 (1.14–30.26)	.035
Chronic obstructive pulmonary disease	10.06 (1.82–55.71)	.008
Prednisone dose	1.18 (1.03–1.35)	.014
Protocol intervention	0.18 (.05–.73)	.016

DISCUSSION

After implementing a standardized stent removal protocol, we observed a lower rate of infectious complications within 30 days and no change in immunologic complications within 1 year from transplant. This finding was demonstrated in our primary analysis and supported by multivariate logistic regression analysis. To our knowledge, this study is the first to demonstrate the utility of implementing a standardized stent removal protocol in reducing the incidence of infectious complications and health care utilization.

The AUA guidelines state that antimicrobial prophylaxis may be considered in patients undergoing stent removal, especially when patient and procedural risk factors are present [7]. These recommendations are based on historical studies suggesting

that antimicrobial prophylaxis at the time of catheter removal may lower the risk of symptomatic UTIs, including 1 small study in renal transplant recipients [10, 11]. The 2019 Infectious Diseases Society of America asymptomatic bacteriuria guideline recommends screening and treating asymptomatic bacteriuria for patients undergoing endoscopic urologic procedures associated with mucosal trauma. However, this does not include cystoscopy with removal of internal ureteric stents [12]. These recommendations are largely based on a meta-analysis evaluating antimicrobial prophylaxis for transurethral prostatic resection, in which bacteriuria and septicemia incidence decreased with the use of antimicrobial prophylaxis [13]. Furthermore, literature comparing the use of antimicrobial prophylaxis vs no prophylaxis in ureteral stent removal in adult kidney transplant recipients has reported no significant differences in the incidence of UTI after stent removal [4, 14, 15]. These results have led many to believe that additional antimicrobial prophylaxis at time of stent removal does not reduce the risk for UTIs. Yet, conflicting data exist, leading to practice variations. A meta-analysis by Antonelli et al found that the median proportion of positive blood cultures was 2% in studies using antimicrobial prophylaxis before stent removal, as compared with 9% in studies without antimicrobial prophylaxis [16]. Among the 20 studies reviewed in the meta-analysis, the average time of stent removal ranged from postoperative days 4 to 25, and the use and choice of antibiotic prophylaxis before stent removal were heterogeneous.

Another key part of the stent removal protocol was the implementation of a more stringent timeline for ureteral stent removal. The 2018 European Association of Urology guidelines on renal transplantation advise centers to remove stents earlier than 6 weeks after transplant; however, there is no consensus regarding the appropriate time of stent removal within those 6 weeks posttransplant [8]. Existing literature has found earlier stent removal, particularly within 3 weeks of placement, to be associated with a decreased incidence of UTIs and no significant difference in incidence of major urologic complications as compared with later removal [4, 5].

In our study, the entire stent removal protocol was associated with a reduced risk of infectious complications. However, neither routine antimicrobial prophylaxis nor early stent removal alone was associated with a reduced risk of infectious complication, and we are unable to ascribe the benefit to any specific aspect of the protocol. Still, it is reasonable to believe that the protocol in its entirety contributed to the improved outcomes associated with the bundled protocol. Unique to our study, the majority of patients were receiving opportunistic infection prophylaxis with TMP-SMX. Additionally, patients received universal culture-directed therapy for antimicrobial prophylaxis for stent removal, and most patients received cephalexin. In contrast, the majority of recipients in the antimicrobial prophylaxis group in the study by Lee et al used fluoroquinolone (75%) and not TMP-SMX prophylaxis (55%) [14]. Notably, our epidemiologic pattern was consistent with that of Lee et al, who had *Enterococcus faecalis* and *E coli* as the 2 most prominent organisms growing in urine cultures following stent removal in kidney transplant patients.

Consistent with previous literature, the multivariate logistic regression analysis found that age, retransplant, COPD, and prednisone were associated with an increased risk of infectious complications. Older kidney transplant recipients have been shown to be at higher risk than younger recipients for infectious complications [17]. Additionally, patients who are exposed to immunosuppression before transplant can have an increased risk of infection—this describes our patients who underwent retransplantion and maintained some degree of immunosuppression following the first transplant. Although the link between COPD and an increased risk of infectious complications is not entirely clear, this association has been described. Inhaled anticholinergic agents, such as ipratropium and tiotropium, have been associated with an increased incidence of acute urinary retention as well as UTIs [18, 19]. Last, higher prednisone dose is an indicator of a higher degree of immunosuppression as compared with lower doses; therefore, the link between prednisone dose and infectious complications can be clearly understood, as patients with a higher degree of immunosuppression are more likely to be at an increased risk for infection [20].

Our study has several limitations. First, our stent removal protocol had multiple components. As a result, we cannot definitively distinguish if any one of these components contributed more to the decreased risk of infectious complications than the others. We performed regression and sensitivity analyses in attempts to mitigate the risk of confounding, although unmeasured confounders could still affect the results. Second, this was a retrospective study, which means that we relied on documentation in the electronic medical record and had to make assumptions when data were missing. For example, we assumed that patients were adherent with antibiotics and that any issues with adherence would be documented. Yet, this limitation of inaccurate documentation would have affected both groups, and the urology division asked patients about antibiotic compliance prior to stent removal. We also did not have preprocedure urine cultures for everyone in the preprotocol group, and we assumed that patients who did not have a urine culture did not have preprocedure bacteriuria. Third, this was a single-center study, and differences in patient and transplant characteristics may limit the external validity of our study. Microbiologic epidemiology and antimicrobial resistance patterns may differ as well, and other centers may not achieve the same results. Furthermore, most of our patients received TMP-SMX for opportunistic infection prophylaxis, and other transplant centers may have different stent removal timelines posttransplant. In centers that already remove stents within 3 weeks posttransplant, this type of intervention may not be as effective.

Fourth, given the quasi-experimental study design, there were several differences between the groups in our study. More patients in the protocol arm received antithymocyte globulin (rabbit) than the preprotocol group. Our institution has shifted to prefer antithymocyte globulin (rabbit) over time, which explains why more patients in the protocol group received it than the preprotocol group. Additionally, our institution was using more basiliximab during the height of the COVID-19 pandemic, due to fear of complete T-cell depletion with antithymocyte globulin (rabbit). The exposure to increased immunosuppression in the protocol group should have theoretically resulted in an increase in infectious complications; however, despite more antithymocyte globulin (rabbit) use, protocol implementation decreased infectious outcomes after urinary stent removal.

Fifth, our reliance on a culture to define a UTI may undercall UTIs if patients were unable to obtain a culture, particularly in the outpatient setting. However, this definition is consistent with the 2019 guideline on UTI in solid organ transplant recipients from the American Society of Transplantation Infectious Diseases community of practice, which describes a UTI as the growth of a uropathogen in the urine and the necessity of symptoms [21]. To account for this potential limitation, we included patients with a "possible UTI" as part of our composite end point if they had a hospitalization, emergency department visit, or outpatient encounter. Reliance on nephrologists to diagnose UTIs may influence the results, although this reflects real-world practice, as routinely screening for asymptomatic bacteriuria posttransplant is not recommended [12].

Sixth, protocol deviation was observed in 39 patients (16%) who continued antibiotics after stent removal. However, since the median duration of antibiotics postprocedure was the same between the groups, we believe that this is unlikely to have biased the efficacy of the results. Finally, we were unable to capture data to evaluate the potential long-term implications on antimicrobial resistance, if antimicrobial prophylaxis is routinely used. Our study was not designed to evaluate the impact of prescribing antimicrobial prophylaxis only to patients with preprocedure bacteriuria.

CONCLUSION

Ureteral stenting and direct manipulation of the ureter during stent removal increase the risk of infectious complications in renal transplant recipients [2, 3, 8, 14, 15]. Existing literature is limited on best practices to reduce infectious complications associated with ureteral stent removal, leading to practice variations [21, 22]. Our study demonstrated that the implementation of a standardized stent removal protocol—including obtaining a preprocedure urine culture, prescribing universal culture-directed antimicrobial prophylaxis, and targeting stent removal at 3 weeks posttransplant—was associated with a reduction in infectious complications.

While routine screening for bacteriuria and antibiotic prophylaxis in this setting are controversial, antimicrobial stewardship principals promote the appropriate use of antimicrobials to improve patient outcomes. Our results demonstrate the benefits of a standardized stent removal protocol on reducing the rate of infectious complications and subsequent health care utilization and costs. Future directions include evaluating the impact of each protocol component on the rate of infectious complications, including prescribing antimicrobial prophylaxis only to patients with preprocedure bacteriuria.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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