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The Duration of Antibiotics Prophylaxis at The Time of Catheter Removal After Radical Prostatectomy: Clinically-Integrated, Cluster, Randomized Trial

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Conflicts of interest
Andrew Vickers is named on a patent for a statistical method to detect prostate cancer that has been commercialized by OPKO Health. Andrew Vickers receives royalties from sales of the test and has stock options in OPKO Health. Behfar Ehdaie is a consultant for Consultant Myriad Genetics, and has received an honorarium from Koelis for an educational webinar.

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Background and Objective:

Prophylactic antibiotics are routinely given at the time of catheter removal post radical prostatectomy (RP). The low rate of infectious complications entails that large sample sizes are required for randomized controlled trials (RCTs), a challenge given the cost of standard RCTs. We evaluated infectious complications associated with 1 vs 3 days of prophylactic antibiotics at the time of catheter removal post RP using a novel, clinically-integrated trial with randomization at the surgeon level.

Methods:

Surgeons were cluster randomized for periods of 3 months to prescribe 1-day versus 3-day regimen of prophylactic antibiotics at the time of catheter removal. The primary endpoint was an infectious complication as routinely captured by nursing phone call within 10 days of catheter removal and defined as: positive urine cultures ($\geq 10^5$ CFU) and at least 1 of the following symptoms: fever (>38C), urgency, frequency, dysuria or suprapubic tenderness.

Results:

A total of 824 patients were consented and underwent RP, with respectively, 389 and 435 allocated to 1-and 3-day antibiotics, predominately ciprofloxacin. Accrual was achieved within 3 years: 95% and 88% of patients received the allocated 3-day or 1-day antibiotic regimen, respectively. There was 0 UTI (0%) in the 1-day regimen and 3 UTIs (0.7%) in the 3-day regimen, meeting our prespecified criterion for declaring the 1-day regimen to be non-inferior.

Conclusion:

A clinically integrated trial using cluster randomization accrued rapidly with no important logistical problems and negligible burden on surgeons. If surgeons choose to prescribe empiric prophylactic antibiotics after catheter removal following RP, then the duration should not exceed 1 day.

Introduction

A Foley catheter is placed after radical prostatectomy to enable primary healing of the anastomosis of the bladder to the urethra. Typically, an indwelling catheter is used for 7 days. There is an increasing risk of bacterial infection with each additional day of catheterization and despite observations that catheter-associated bacteriuria is usually asymptomatic, uncomplicated and resolves spontaneously, up to 30% of patients develop urinary symptoms.[1, 2] In addition, 40% of patients have bacteriuria (>1,000 cfu/mL) prior to catheter removal after radical prostatectomy.[3] Despite the potential risk of infection related to bacteriuria after catheter removal associated with incomplete bladder emptying or anastomotic leak leading to pelvic abscess, the routine practice of prophylactic antibiotic administration prior to catheter removal is controversial, with a dearth of evidence from well-controlled trials. Consequently, practice patterns vary widely nationally and current guidelines provide broad recommendations to treat empirically in high risk patients or obtaining a urinalysis prior to catheter removal.[4]

Observational studies are limited by variability in practice patterns regarding the type of antibiotic or duration of treatment. A recent cross-sectional study reported that 60% of 237 surveyed urologists routinely gave antibiotics prior to catheter removal.[5] Extrapolation of data from 2 RCTs suggested a benefit for antibiotic treatment prior to procedures in men with prior catheterization and is used to justify antibiotic administration prior to catheter removal after RP.[6, 7] A RCT of antibiotic prophylaxis prior to catheter removal reported a rate of approximately 6% within 6 weeks of catheter removal.[8] However, a review of the literature by the Infectious Disease Society of America concluded that prophylactic antibiotic therapy is not routinely recommended for catheter placement, removal, or replacement in the routine clinical setting.[9]

In the current era of increasing bacterial resistance, the appropriate utilization of antibiotics is critical. Some current guidelines suggest obtaining a urinalysis prior to catheter removal and initiating treatment based on the presence of bacteriuria or using empiric therapy for patients at increased risk of infectious complications.[4] However, routine urinalysis prior to catheter removal presents logistic challenges for clinical staff, including difficulties obtaining non-contaminated samples, timely follow-up of urinalysis in clinic and changing antibiotics if resistance is identified from urine cultures. Consensus is lacking regarding the optimal prophylaxis for catheter removal after RP. Subsequently, the standard practice at our hospital varies from infectious disease guidelines and is to empirically treat all patients with Ciprofloxacin beginning 24 hours prior to catheter removal and continuing for 3 days without obtaining a urinalysis.

We conducted an ongoing, rolling Phase III study examining the effects of modifications to surgical technique after RP using several methodologic innovations designed to streamline the study and provide robust data at minimum cost, including integration of the clinical and research databases, simplified eligibility criteria, factorial designs, and cluster randomization with crossover.[10] Our aim was to compare the incidence of infectious complications using the standard approach of routine prophylaxis compared to more restricted treatment consisting of only 1 day of antibiotic prophylaxis at the time of catheter removal.

Methods

Patients were consented to a protocol in which surgeons were cluster randomized on a crossover basis for periods of 3 months to prescribe a 1-day or a 3-day regimen of prophylactic antibiotics at the time of catheter removal. The primary endpoint was an infectious complication as routinely captured by nursing phone call within 10 days of catheter removal and defined as: positive urine cultures (≥105 CFU) and at least 1 of the following symptoms: fever (>38C), urgency, frequency, dysuria or suprapubic tenderness. Routine urine cultures were not obtained on every patient. A urine culture was obtained as part of a workup for symptoms reported by patients including fever (>38C), urgency, frequency, dysuria or suprapubic tenderness. An infectious complication would be reported if the urine culture was positive (≥105 CFU). As part of routine practice, antibiotics were given after a urine culture was obtained. The ascertainment of data was standardized with establishment of nursing training to assess for UTI symptoms and these methods were used in our prior study.[11] All patients received a phone call from nurses within 10 days of surgery and patients who presented to outside hospitals had their records sent to MSK. Every patient undergoing RP for initial treatment management for prostate cancer was eligible. Eligible patients are approached initially by the attending surgeon and the general outline of the rolling Phase III study is discussed. Surgeons were expected to do what they felt was best for the patient irrespective of assignment of antibiotic protocol; however, if they had equipoise for the option of antibiotic duration, then they would be directed by the randomization assignment. The duration of antibiotics was recorded in the medical chart and if a duration was chosen inconsistent with the randomization assignment, then a justification was recorded. Patients were consented to collection of data for the dual purposes of routine clinical care and research.

The study was nested within a rolling Phase III study examining the effects of modifications to surgical technique on outcome after RP. Ten surgeons enrolled to the study and each surgeon was cluster randomized for periods of 3 months using randomly permuted blocks of 4. Each comparison was randomized separately. Randomization was conducted by the Biostatistics service at MSKCC. Surgeons and nursing staff were contacted by a research data coordinator at the start of each three-month period to be informed as to allocation. They were asked to confirm their understanding of this in writing. The research data coordinator checked case notes in the weeks following the change of allocation to ensure that surgeons complied. The data management system for the trial was the CAISIS database, the database used for routine clinical management of patients undergoing RP.

The current rate of urinary tract infection following RP is less than 1%. We used a non-inferiority approach such that rejecting the null hypothesis allowed us to conclude that a short course of antibiotics does not raise infection rates. Due to low event rates, and the possibility of zero events in one or both arms, traditional non- inferiority power calculations based on asymptotic approximations are unreliable. We therefore specified a decision rule and then used exact methods to give the properties of that decision rule under various true infection rates in the experimental arm. The decision rule was that the observed infection rate in the short course antibiotics group should not be >0.35% greater than in the standard longer course arm, equivalent to >1 more patient with infection in a trial with 300 patients per arm. Assuming a true infection rate of 0.5% in the control arm, such a trial had an 82% chance of rejecting the

null hypothesis of inferiority if there was truly no difference in infection rates and a 94% probability of failing to reject if 1 day antibiotics led to an absolute 2% increase.

The study was approved by the Institutional Review Board (IRB # 11-096) and study progress was overseen by the MSKCC Data and Safety Monitoring Board (DSMB) for Phase III clinical trials.

Results

The trial accrued rapidly and we decided to continue accrual to 800 patients, as this would give us >80% power to reject non-inferiority if the shorter antibiotic course led to a 1% increase in the risk for infection. A total of 824 patients were randomized to the 1-day (n=389) or 3-day (n=435) antibiotic regimen. Ciprofloxacin was the most commonly prescribed prophylactic antibiotic. Accrual was achieved within 3 years and 44% of all patients who underwent RP at our institution were enrolled in the study period. The randomization design resulted in a balanced distribution of the clinicopathological features between the two groups (Table 1). Although compliance with randomization was very high in both arms, there was slightly better compliance with the 3-day regimen (p<0.001) as 8.7% of patients in the 1-day arm in fact receiving three days of antibiotics. This effect was driven by a group of surgeons who accrued only small numbers of patients on the trial. It seems that is these clinics, patients were sometimes prescribed the standard 3-day regimen in place of the randomized allocation.

There were no UTIs in the 1-day regimen compared to 3 UTIs (0.7%) in the 3-day regimen (Table 2). With fewer UTIs observed in the shorter antibiotics duration arm, the pre-specified threshold was met to reject the null hypothesis and conclude 1 day of antibiotics is not inferior to a 3-day regimen.

There were two patients who reported potential symptoms of a UTI who did not have a culture to confirm UTI; both patients were in the 1-day randomization group. Repeating the analyses with this less stringent definition of UTI led to the same conclusion as the primary analysis with a lower rate of UTI in the 3-day randomization group compared to the 1-day randomization group (Table 2).

We also conducted a per protocol analysis comparing rates of UTI by the prescribed duration of antibiotics rather than the randomized duration. Again, the patients prescribed 1-day duration had lower rates of UTI with 1 / 351 (0.3%) of patients prescribed 1-day duration experiencing UTI, compared to 2 / 439 (0.5%) prescribed 3 days of antibiotics.

We sought to understand if there were any patient characteristics associated with enrollment into the trial. While there was largely a balance in patient characteristics, some characteristics such as, lower ASA (p = 0.023) and lower biopsy grade group (p = 0.025) that were associated with a higher probability of enrollment. Table 3

The trial was an integrated design, where patients are randomized to duration of antibiotics based on the date of treatment. This design does not blind the surgeon or consenting professional to the randomization arm the patient will be assigned. We assessed whether the current randomization assignment was associated with enrollment into the trial. We found that during the 3-day duration, patients were more likely to be enrolled compared to 1-day, although this difference was small (47% vs 42%; p = 0.021).

Discussion

We did not see an increase in infections associated with reducing antibiotic duration from 3 days to 1 day at the time of Foley catheter removal after radical prostatectomy. The overall rate of infectious complications was very low, and all 3 patients with an adverse event occurred in the 3-day antibiotic group. Based on the results of this Phase III clinical trial, we urge guideline committees to recommend restricting the duration of prophylactic antibiotics to 1-day in the absence of routine urinalysis evaluation prior to Foley catheter removal.

Our study is timely given the emergence of antibiotic-resistant bacteria attributed to antibiotic prescribing misuse and overuse.[12] Antibiotic use in surgical specialties and specifically urology is a potential target for antibiotic stewardship efforts due to the large quantities of antibiotics prescribed.[13] Importantly, antibiotic stewardship programs have been demonstrated to reduce unnecessary antibiotic prescriptions.[14] A recent study of patients who underwent common urologic procedures, the rate of guideline-discordant antibiotic use was high mostly because of overprescribing in the postprocedural period. [15] After elective abdominal non-urologic surgery, patients who received prophylactic antibiotics 24 hours prior to urinary catheter removal had a lower incidence of febrile UTI compared to those not prescribed an antibiotic (4.9% v 21.6%, p<0.001).[16] In contrast, a smaller prospective randomized trial did not demonstrate a difference in bacteriuria between the antibiotic and placebo cohorts (16% v 13%) prior to removal of catheters in place for 2 to 7 days.[17] Finally, an observational study of excluding antibiotic prophylaxis reported 7% of patients experienced an infectious complication within 6 weeks of catheter removal.[18] The increased incidence of infections in the study could be explained by the longer indwelling catheter duration (10 days) and more inclusive definition of infectious complications. A primary barrier contributing to the limited evidence to guide management after RP is attributable to the known logistical challenges conducting randomized controlled trials. The overall low incidence of infectious complications after catheter removal post RP would make traditional randomized controlled trial expensive, resource intensive, and most likely not feasible in short time without a rapid accrual uncharacteristic of surgical clinical trials.

Allocation concealment is incomplete in a cluster randomized trial, leading to the possibility of selection bias. There were some differences between groups, in particular, patients were more likely to be accrued and more likely to receive their randomization allocation on the three-day arm. That said, any resulting bias was modest: 5 – 7% absolute risk difference between groups and no impact on our results. The differences in compliance are clearly a bias towards the inferior 3-day arm. With respect to accrual differences, we might hypothesize that patients deemed to be at high-risk of infection would not be accrued if they were on the 1-day arm. This would affected approximately 50 patients. In order for this to have led to an additional infection in the 1-day arm, the infection rate would have needed to be 2%, more than 5 times higher than the average event rate. An additional infection in the 1-day arm would not have changed our results: there would have had to be 4 more infections. This would support our contention that an imperfect trial that is completed is better than a perfect trial that is never done. While these observations will inform future clinical-integrated cluster randomized studies, particularly with respect to closer monitoring of enrollment rates by arm, they also demonstrate that such studies can provide data to inform practice. We note that a

trial on a rare event such as an infectious complication needs to be very large and so hence is only practicable using the clinically-integrated trial approach.

The rapid accrual of this study and the high consent rate are of note. In a typical surgical RCT, fewer than 1% of eligible patients are accrued.[19] Although our qualitatively higher accrual rate might be explained in part by the relatively low-stakes nature of our study question, we also attribute our success to a design that minimizing patient burden. In a clinically-integrated trial, the experience of patients on vs. off the trial is identical other than with respect to the randomized intervention. There are no extra procedures, questionnaires, visits or tests. Moreover, we found that randomization of the surgeon was easier for patients to understand compared to randomization of the patient. Patients were told that their health care team would always evaluate them and decide based on their best clinical judgment, only using the computer allocation if they were 50:50 as to the best approach. Our impression is that patients find this formulation easier to understand and accept that being told that they personally would be randomized.

The generalizability of our results is limited by conducting the study in a single tertiary care hospital. Ciprofloxacin was the most commonly prescribed antibiotic in our study. In July 2016, the US Food and Drug Administration (FDA) strengthened the "black box" warning following an initial safety announcement in May 2016, recommending avoidance of fluoroquinolones for uncomplicated infections such as acute exacerbation of chronic bronchitis, uncomplicated urinary tract infections, and acute bacterial sinusitis.[20] Further, the length of the study was 10 days to detect catheter-associated infectious complications in the perioperative period. We acknowledge that post-surgical infections associated with the catheter could occur beyond 10 days and not measured in our study. In a similar study, Berrondo et al measured infectious complications for 6 weeks after catheter removal and reported 5 out 8 patients experienced an infectious complication within 10 days.[8] Despite these limitations, we believe that other antibiotic options recommended for urinary tract infections will be effective with a restricted duration. Further, the generalizability limitations are mitigated by the simplified eligibility criteria as there was no requirement besides that a patient is scheduled for radical prostatectomy for initial treatment of prostate cancer. The strengths of our study include randomization of both antibiotic duration protocols and the strict definition of an infectious complication.

We were able to conduct a RCT using cluster randomization demonstrating that a restricted duration of prophylactic antibiotics for 1-day was not inferior to a 3-day duration in regard to infectious complications after catheter removal post RP. We demonstrated that the novel methodology of clinically-integrated trials is feasible, enables rapid accrual of patients and minimizes burden to patients and clinicians.

References

1.   Sedor, J. and S.G. Mulholland, *Hospital-acquired urinary tract infections associated with the indwelling catheter.* Urol Clin North Am, 1999. **26**(4): p. 821-8.

2.   Warren, J.W., *Catheter-associated urinary tract infections.* Int J Antimicrob Agents, 2001. **17**(4): p. 299-303.

3.   Banks, J.A., et al., *Bacteriuria and antibiotic resistance in catheter urine specimens following radical prostatectomy.* Urol Oncol, 2013. **31**(7): p. 1049-53.

4.   Wolf, J.S., Jr., et al., *Best practice policy statement on urologic surgery antimicrobial prophylaxis.* J Urol, 2008. **179**(4): p. 1379-90.

5.   Wazait, H.D., et al., *Antibiotics on urethral catheter withdrawal: a hit and miss affair.* J Hosp Infect, 2004. **58**(4): p. 297-302.

6.   Grabe, M., A. Forsgren, and S. Hellsten, *A short antibiotic course given in conjunction with and after catheter removal consecutive to transurethral prostatic resection.* Scand J Urol Nephrol, 1984. **18**(3): p. 193-9.

7.   Duclos, J.M., P. Larrouturou, and P. Sarkis, *Timing of antibiotic prophylaxis with cefotaxime for prostatic resection: better in the operative period or at urethral catheter removal?* Am J Surg, 1992. **164**(4A Suppl): p. 21S-23S.

8.   Berrondo, C., et al., *Antibiotic prophylaxis at the time of catheter removal after radical prostatectomy: A prospective randomized clinical trial.* Urol Oncol, 2019. **37**(3): p. 181.e7-181.e14.

9.   Hooton, T.M., et al., *Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America.* Clin Infect Dis, 2010. **50**(5): p. 625-63.

10. Vickers, A.J. and P.T. Scardino, *The clinically-integrated randomized trial: proposed novel method for conducting large trials at low cost.* Trials, 2009. **10**: p. 14.

11. Recabal, P., et al., *Quality improvement initiative to reduce variability and improve stewardship of antimicrobial prophylaxis for transrectal prostate needle biopsy.* World J Urol, 2020. **38**(4): p. 965-970.

12. Llor, C. and L. Bjerrum, *Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem.* Ther Adv Drug Saf, 2014. **5**(6): p. 229-41.

13. Hicks, L.A., et al., *Outpatient antibiotic prescribing and nonsusceptible Streptococcus pneumoniae in the United States, 1996-2003.* Clin Infect Dis, 2011. **53**(7): p. 631-9.

14. Recabal, P., et al., *Quality improvement initiative to reduce variability and improve stewardship of antimicrobial prophylaxis for transrectal prostate needle biopsy.* World J Urol, 2019.

15. Khaw, C., et al., *Assessment of Guideline Discordance With Antimicrobial Prophylaxis Best Practices for Common Urologic Procedures.* JAMA Netw Open, 2018. **1**(8): p. e186248.

16. Pfefferkorn, U., et al., *Antibiotic prophylaxis at urinary catheter removal prevents urinary tract infections: a prospective randomized trial.* Ann Surg, 2009. **249**(4): p. 573-5.

17. Wazait, H.D., et al., *A pilot randomized double-blind placebo-controlled trial on the use of antibiotics on urinary catheter removal to reduce the rate of urinary tract infection: the pitfalls of ciprofloxacin.* BJU Int, 2004. **94**(7): p. 1048-50.

18. Pinochet, R., et al., *Role of short-term antibiotic therapy at the moment of catheter removal after laparoscopic radical prostatectomy.* Urol Int, 2010. **85**(4): p. 415-20.

19. Stewart, J.H., et al., *Participation in surgical oncology clinical trials: gender-, race/ethnicity-, and age-based disparities.* Ann Surg Oncol, 2007. **14**(12): p. 3328-34.

20.   *FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. Food and Drug Administration website.*

Table 1. Patient Characteristics. Statistics give are median (IQR) or frequency (%).

Characteristic	Antibiotics Duration Randomization Assignment	
	3 Days, N = 435	1 Day, N = 389
Age at RP, median (IQR)	63 (58, 68)	62 (58, 67)
Race, n (%)		
White	366 (89%)	325 (88%)
Black	25 (6.1%)	29 (7.9%)
Asian	14 (3.4%)	8 (2.2%)
Other	8 (1.9%)	6 (1.6%)
Unknown	22	21
Minimally Invasive RP, n (%)	418 (96%)	372 (96%)
ASA, n (%)		
I/II	275 (64%)	255 (66%)
III/IV	158 (36%)	132 (34%)
Unknown	2	2
BMI, median (IQR)	28.4 (26.1, 31.0)	27.7 (25.8, 30.4)
Unknown	87	89
Preoperative PSA (ng/ml), median (IQR)	6.2 (4.3, 9.0)	6.1 (4.4, 8.2)
Unknown	2	1
Biopsy Gleason Grade Group, n (%)		
1	32 (7.4%)	41 (11%)
2	223 (52%)	200 (51%)
3	82 (19%)	66 (17%)
4-5	96 (22%)	82 (21%)
Unknown	2	0
RP Gleason Grade Group, n (%)		
1	19 (4.4%)	19 (4.9%)
2	263 (61%)	235 (61%)
3	86 (20%)	81 (21%)
4-5	61 (14%)	51 (13%)
Unknown	6	3
ECE, n (%)	225 (52%)	182 (47%)
SVI, n (%)	54 (12%)	44 (11%)
Unknown	1	0
N Stage, n (%)		
Nx	18 (4.1%)	4 (1.0%)
N0	357 (82%)	353 (91%)
N1	60 (14%)	32 (8.2%)
Duration of prescribed antibiotics, n (%)		
1 Day	15 (3.5%)	336 (88%)
3 Days	406 (95%)	33 (8.7%)
Other	5 (1.2%)	11 (2.9%)
Unknown	9	9
Prescribed antibiotics, n (%)		
Ciprofloxacin	407 (96%)	362 (95%)
Bactrim	12 (2.8%)	13 (3.4%)
Sulfamethoxazole-Trimethoprim	4 (0.9%)	1 (0.3%)
Cefuroxime	1 (0.2%)	1 (0.3%)
Cephalexin	1 (0.2%)	1 (0.3%)
Amoxicilin	1 (0.2%)	0 (0%)
Levaquin	0 (0%)	1 (0.3%)
Macrobid	0 (0%)	1 (0.3%)
Unknown	9	9

Table 2. Comparison of urinary tract infection

	Antibiotics Duration Randomization Assignment	
Characteristic	3 Days, N = 435	1 Day, N = 389
Urinary Tract Infection	3 (0.7%)	0 (0%)
Unconfirmed/Suspected Urinary Tract Infection	3 (0.7%)	2 (0.5%)

Table 3. Enrollment among eligible patients. Statistics are median (IQR); n (%) with p-values calculated by Wilcoxon rank-sum test; chi-square test of independence respectively

Characteristic	N	Enrolled in Antibiotics Axis		p-value
		No, N = 1,036	Yes, N = 824	
Age at RP	1,860	63 (58, 68)	63 (58, 68)	0.5
Race	1,754			0.050
Asian		37 (3.8%)	22 (2.8%)	
Black		75 (7.7%)	54 (6.9%)	
Other		36 (3.7%)	14 (1.8%)	
White		825 (85%)	691 (88%)	
ASA	1,853			0.023
I/II		613 (59%)	530 (65%)	
III/IV		420 (41%)	290 (35%)	
Bx Gleason Grade Group	1,851			0.025
1		101 (9.8%)	73 (8.9%)	
2		457 (44%)	423 (51%)	
3		221 (21%)	148 (18%)	
4-5		250 (24%)	178 (22%)	
Preoperative PSA (ng/ml)	1,852	6.3 (4.4, 9.0)	6.1 (4.4, 8.6)	0.4
Salvage RP	1,860	15 (1.4%)	8 (1.0%)	0.5
Rx Randomization Duration	1,860			0.021
1 Day		546 (53%)	389 (47%)	
3 Days		490 (47%)	435 (53%)	