

Risk factors predicting fever following trans-urethral prostatectomy

Kamil Malshy *, Omri Nativ , Omer Sadeh , Tareq Aro , Alexander Kastin , Alexander Kravtsov , Gilad E. Amiel , Michael Mullerad and Azik Hoffman

Rambam Health Care Campus, HaAliya HaShniya St 8, PO box 9602 Haifa 31096, Israel

*Correspondence: Kamilmalshy@gmail.com (Kamil Malshy)

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Purpose: Fever occurring post transurethral resection of prostate (TURP) due to urinary tract infection (UTI) is a well-known complication. A better knowledge of pre-operative risk factors will aid the prevention and treatment of this complication. Herein we aimed to describe the risk factors for postoperative fever in a cohort of patients undergoing TURP in a single institute. **Methods:** A total of 177 patients underwent transurethral resection of prostate (TURP) between January 2016 and August 2017 in our Institute. Postoperative fever was defined as $\geq 38^{\circ}\text{C}$ up to a week after surgery. Other reasons for post-operative fever were excluded. We collected data for indwelling catheter, antibiotic prophylactic treatment, positive preoperative urine culture, diabetes mellitus (DM), combined cystolithotripsy and prostate size. **Results:** All patients received antibiotic prophylaxis prior to the TURP procedure. Patients with negative urine culture were treated with IV Amikacin + Ampicillin ($n = 83$), whereas patients with positive bacterial cultures were treated as per antibiotic sensitivity profile ($n = 93$). One patient developed fever in the negative culture group, compared to 8 in the positive urine culture group ($P = 0.0375$). No patient developed septic shock. Smaller prostate size ($\text{RR} = 1.06$, CI-95\% , $1.01-1.12$, $P = 0.016$), positive urine culture ($\text{RR} = 3.85$, CI-95\% , $1.33-100$, $P = 0.033$) and older age ($\text{RR} = 1.1$, CI-95\% , $1.01-1.21$, $P = 0.031$) were all predictors of postoperative fever. In contrast, TURP combined with cystolithotripsy ($P = 0.99$), indwelling urethral catheter ($P = 0.155$), and patients with DM ($P = 0.256$) were not predictors of post-operative fever. **Conclusions:** Positive urinary bacterial culture prior to TURP is a frequent event. Although positive urinary culture increased the risk of post TURP fever, none of these events caused significant morbidity. Surprisingly, a smaller prostate size increased the risk of postoperative fever. This fact suggests that the degree of infection is attributed to the level of obstruction and not to the volume of the prostate.

Keywords

Benign prostatic hyperplasia; transurethral resection of prostate; risk factors; post-operative fever; bacterial urine culture; prostate size

1. Introduction

Benign prostatic hyperplasia (BPH) is one of the most common medical conditions in older men. Prostate enlargement is observed in approximately 40% of men in their 50s, and about 70% in their 60s [1]. Up to 15%-25% of men aged 50-65 years suffer from Lower Urinary Tract Symptoms (LUTS), influencing their quality of life [2]. Treatment options include lifestyle modifications, medical therapies [3], and surgical intervention.

Transurethral Resection of Prostate (TURP) continues to be considered the gold standard surgical procedure for BPH [4]. In selected patients, TURP is the surgical treatment of choice when medical treatment modalities fail. This procedure, which consists of removal of prostate tissue via transurethral electrocautery, is considered highly effective, but involves absorption of irrigation fluid into the bloodstream during the procedure. Risk of complications such as bleeding, urinary tract infection, TURP syndrome and sepsis are present. Urinary tract infection (UTI) is the most common complication following TURP [5]. The rate of UTI after monopolar or bipolar TURP, ranges from 4.1-6.2% and 2.6-8.4%, respectively [6]. Osman et al., [7] reported some risk factors for persistent bacteriuria following TURP, including older age, previous history of diabetes mellitus (DM), large prostate size, positive preoperative bacterial urine culture, preoperative catheter use, previous urological interventions, large size of sheath, long duration of operation, postoperative catheter events, and postoperative manual wash. Furthermore, not all bacteriuria events following TURP present with fever, and therefore are under-reported. Herein we aimed to evaluate the risk factors predicting fever due to UTI after TURP surgery at our institution.

2. Patients & methods

2.1 Study design

Retrospective data from 177 consecutive TURP patients from January 2016 to August 2017 in the tertiary urology department were collected (Table 1). Following an institutional IRB approval (RMB-0254-16), computerized patient medical files were reviewed for the presence of post-operative fever, defined as body temperature $\geq 38^{\circ}\text{C}$ during the first 7 days following the procedure. Alternative post-operative fever origin was excluded by physical examination, chest X-ray and culture collection. Presence of indwelling catheter, DM, previous antibiotic treatment, pre-operative urine culture status, and combined cystolithotripsy with

Table 1. Patient demographic data

Number of Patients	177
Age (Mean \pm SD, Range)	71 \pm 8.7 (59-91)
Prostate Size (Median \pm SD, Range), cm ³	44.5 \pm 23.9 (9-150)

SD = Standard deviation.

TURP were recorded. Prostate size estimation was determined by transabdominal ultrasound prior to surgery.

2.2 Statistical analysis

Fisher's Exact test for discrete variables and Mann-Whitney test for ordinal and continuous variables were used to compare between clinical characteristics and post TURP fever. Next, multivariate logistic regression for statistically significant variables was performed. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS software (SPSS 25.0; SPSS Inc. Chicago, IL, USA).

3. Results

177 patients with a mean age of 71 \pm 8.7 years underwent TURP during the study period. All patients received antibiotic prophylaxis prior to the procedure. 83 patients with negative urine culture were treated empirically with intravenous Amikacin + Ampicillin as per institutional policy. 94 patients with positive urine culture were treated based on their individual antibiotic sensitivity profiles. All procedures were completed without complications. 9/177 (5.1%) patients developed post-operative fever. 1/83 (1.2%) of the negative culture group developed fever, compared to 8/94 (8.5%) in the positive urine culture group ($P = 0.0375$). 58 patients had DM, of which 4 (6.9%) developed post-operative fever, compared to 5/119 (4.2%) in non-diabetic patients ($P = 0.48$). 59 patients had permanent urethral catheter prior to the procedure, of which 5 (8.5%) developed post-operative fever, compared to 2 (3.4%) in the remaining patients that were not on a permanent urethral catheter. 12 patients underwent additional cystolithotripsy, of which none developed post-operative fever (Table 2 and Fig. 1). Median prostate size was 44.5 \pm 23.9 cm³ (range: 9-150 cm³).

Surprisingly, small prostate size increased the risk of fever; median prostate size was 25 cm³ in patients who developed fever ($n = 9$) compared to 46 cm³ in all other patients ($P = 0.016$) (Fig. 2). On multivariate logistic regression, smaller prostate size (RR = 1.06, CI-95%, 1.01-1.12), positive urine culture (RR = 3.85, CI-95%, 1.33-100) and older age (RR = 1.1, CI-95%, 1.01-1.21) were all predictive factors of postoperative fever ($P < 0.05$).

4. Discussion

TURP is the most common surgical intervention for benign prostate enlargement. The procedure includes transurethral resection and removal of prostate tissue while irrigating with 5% glycine solution or saline. UTI is the most common post-operative complication [5]. Most, but not all UTI's, will present with post-operative fever. Patient-related and surgical procedure-related risk factors are well defined. Post-operative fever following TURP is associated with prolonged hospitalization, additional antibiotic treatment, and subsequently increases cost and morbidity [8]. Better characterization of patients at risk of post-operative fever may im-

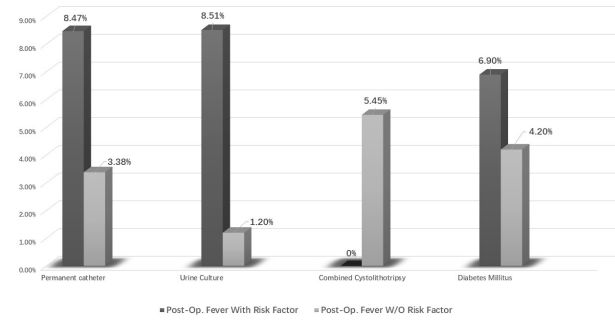


Figure 1. Percentage of post-operative fever cases when combining all risk factors groups.

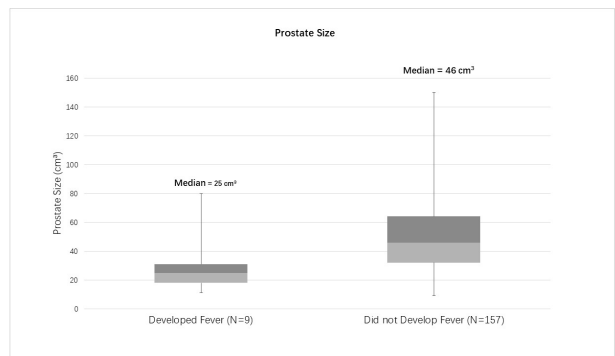


Figure 2. Preoperative Prostate size in cm³ measured by transabdominal ultrasound.

prove practice and management of these patients. In our current study, 5.1% of patients of the entire cohort developed fever during the first week after the TURP procedure. Remarkably, a similar outcome (6.1%) was reported by Wagenlehner et al., [9] who conducted a multicenter study in Germany with 376 patients; consistently, Schneidewind et al., who also undertook a large multicenter study with 400 patients in Germany, also reported a similar outcome of 4.9% of patients developing fever [10]. No patient developed sepsis. Pre-operative positive bacterial urine culture was identified as a risk factor for developing post-operative fever (8.5% vs. 1.2%, RR = 3.85 range 1.33-100, $P < 0.05$). DM, indwelling urethral catheter and TURP combined with cystolithotripsy were reported by Osman et al., [7] as independent risk factors for bacteriuria, but did not increase the risk for post-operative fever in our cohort. This was ostensibly due to the strict following of pre-operative antibiotic coverage in our practice, preventing bacteriuria from becoming bacteremia. Higher complication rates were also previously described for longer TURP procedures. Due to our concern regarding record bias in accessing length of procedure, based on operation room registration in our cohort, we used prostate size as an indirect way of accessing operative time. Osman et al., reported prostate size larger > 60 cm³ as a risk factor for UTI post-operatively [7]. In contrast, we found that smaller prostate size slightly increased the risk for post-operative fever with an RR of 1.06. We assumed that operation time was not associated with risk of UTI in our cohort, however, patients with a smaller prostate size had increased incidence of pre-operative uri-

Table 2. Univariate analysis of predictive factors for post-operative fever (> 38 °C)

Parameter	Risk Factor	N (%)	Post-operative fever		P-Value
			+	-	
All		177	9 (5.08%)	168 (94.92%)	
Permanent Catheter	Yes	59 (33.3%)	5 (8.47%)	54 (91.52%)	NE
	No	118 (67.6%)	4 (3.38%)	114 (96.6%)	
Preoperative Urine Culture	Positive	94 (53.1%)	8 (8.51%)	86 (91.4%)	P < 0.05
	Negative	83 (46.9%)	1 (1.20%)	82 (98.8%)	
Combined Cystolithotripsy	Yes	12 (6.7%)	0 (0%)	12 (100%)	NE
	No	165 (93.3%)	9 (5.45%)	156 (94.5%)	
Diabetes Mellitus	Yes	58 (32.7%)	4 (6.9%)	54 (93.1%)	NE
	No	119 (67.2%)	5 (4.2%)	114 (95.8%)	
Prostate Size (Median = 44.5 cm ³)		166	9 (5.4%) (Median 25 cm ³)	157 (94.6%) (Median 46 cm ³)	P < 0.05

°C-Degree Celsius, NE-Not Estimable.

nary retention and were more likely to carry indwelling catheter prior to TURP, subsequently having more bacteriuria and fever. Nevertheless, no statistically significant correlation was observed between prostate size and indwelling catheter ($P = 0.21$) or positive urine culture ($P = 0.25$), probably due to the relatively small size of the cohort.

In our patient cohort, we faced a high rate of positive urine culture prior to TURP (53.1%) and positive urine culture among patients with indwelling catheter (92%). Our practice is to treat with prophylactic intravenous antibiotic on the same day of the surgery and not postpone the procedure when facing a pre-operative positive culture, since it is difficult to achieve sterile urine in patients with indwelling catheter. While this practice might not eliminate the risk of UTI, we found an acceptable rate of post-operative UTI (8.5%), without additional risk of uro-sepsis.

Previous studies suggested that DM is a risk factor for post-operative UTI [7, 11]. Our current data showed that 6.9% of the diabetic patients developed fever, compared to 4.2% of the non-diabetic patients ($P = 0.48$). Most patients in our cohort were treated properly, as recorded by preoperative hemoglobin A1C blood level (data not shown), therefore eliminating this risk factor. None of the 12 patients who had cystolithotripsy with TURP developed post-operative fever, suggesting that our practice of preoperative antibiotic prophylaxis was sufficient and effective for this group of patients as well.

Our current study has several limitations; the present cohort included TURP conducted by several surgeons. Additionally, no post-operative urine culture samples were collected routinely regardless of fever workup, reducing our ability to diagnose bacteriuria. A relatively low number of fever events influences the ability to identify additional risk factors as well. However, our findings represent a real-life practice of preventing post TURP fever in a tertiary hospital. Despite several known risk factors, our data show that adhering to perioperative urine culture collection practice, proper antibiotic treatment, and noticing urinary obstruction prior to surgery, markedly reduces the risk of fever due to UTI and sepsis. Additional trials to establish the optimal pre- and perioperative antibiotic therapy and preoperative indwelling catheter management to prevent post-operative bacteriuria are warranted.

Author contribution

Kamil Malshy - Protocol and project development, data collection and manuscript writing; Omri Nativ - Data analysis and manuscript editing; Omer Sade - Data collection; Tareq Aro - Data collection; Alexander Kastin - Procedure surgeon; Alexander Kravtsov - Procedure Surgeon; Gilad E. Amiel - Manuscript editing; Michael Mullerad - Manuscript editing, protocol Development; Azik Hoffman - Data analysis and manuscript editing.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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