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Predictive model of urinary tract infection after surgical treatment for women with endometrial cancer

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Abstract
Purpose The aim of the study was to identify risk factors associated with postoperative urinary tract infections (UTIs) following hysterectomy-based surgical staging in women with endometrial cancer.
Methods This is a retrospective study utilizing an institutional database (2008–2016) of stage I–IV endometrial cancer cases that underwent hysterectomy-based surgery. UTIs occurring within a 30-day time period after surgery were examined and correlated to patient clinico-pathological demographics.
Results UTIs were observed in 44 (6.4%, 95% confidence interval 4.6–8.2) out of 687 cases subsequent to the diagnosis of endometrial cancer. UTI cases were significantly associated with obesity, advanced stage, prolonged operative time, hysterectomy type, pelvic lymphadenectomy, non-β-lactam antibiotics, and intraoperative urinary tract injury (all, $p < 0.05$). On multivariate analysis, three independent risk factors were identified for UTIs: prolonged operative time [odds ratio (OR) 3.36, 95% CI 1.65–6.87, $p = 0.001$], modified-radical/radical hysterectomy (OR 5.35, 95% CI 1.56–18.4, $p = 0.008$), and an absence of perioperative β-lactam antibiotics use (OR 3.50, 95% CI 1.46–8.38, $p = 0.005$). In a predictive model of UTI, the presence of multiple risk factors was associated with significantly increased risk of UTI: 4.1% for the group with no risk factors, 7.3–12.5% (OR 1.85–3.37) for single risk factor group, and 30.0–30.8% (OR 10.1–10.5) for two risk factor group.
Conclusion Urinary tract infections are common in women following surgical treatment for women with endometrial cancer with risk factors being a prolonged surgical time, radical hysterectomy, and non-guideline perioperative antimicrobial agent use. Consideration of prophylactic antimicrobial agent use in a high-risk group of postoperative urinary tract infection merits further investigation.

Keywords Endometrial cancer · Urinary tract infection · Prediction model

Introduction

Urinary tract infections (UTIs) are a common reason for postoperative infectious complications in cancer patients [1, 2]. UTIs are associated with prolonged hospital stay, increased cost of care, and increased postoperative morbidity [3, 4]. The incidence of infectious complications in the perioperative period is known to be particularly elevated in cancer patients—a fourfold greater incidence than that seen in non-cancer populations [5].

Endometrial cancer is the most prevalent gynecologic malignancy in the United States, with an estimated 61,380 new cases and 10,920 deaths in 2017 [6]. The majority of patients are diagnosed with early-stage disease and

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undergo hysterectomy-based staging surgery with bilateral salpingo-oophorectomy and probable lymphadenectomy. Recently, there has been a paradigm shift of surgical procedures for endometrial cancer from standard laparotomy to minimally invasive surgery (MIS) [7, 8]. MIS, including robot-assisted procedures, has shown to lower complication rates and shorten hospitalizations compared to standard laparotomy, but with prolonged operative times [7]. The incidence of infectious complications after lengthy surgery is known to be elevated, and can be life-threatening in the perioperative period [9].

The factors associated with an increased risk of postoperative UTIs in women with endometrial cancer are not well described. Given that 7–13% of patients who undergo hysterectomy-based staging surgery are readmitted, and UTIs are one of the most common reasons for readmission, identification of UTI risk factors could improve postoperative management of endometrial cancer patients [10, 11]. The object of this study was to identify risk factors for postoperative UTIs in women with endometrial cancer.

Materials and methods

Study design and eligibility

After institutional review board (IRB) approval at the University of Southern California, endometrial cancer cases were identified using an institutional database. Eligibility criteria included consecutive cases of women with stage I–IV endometrial cancer who underwent hysterectomy-based surgical staging at Los Angeles County Medical Center and Keck Medical Center of the University of Southern California between January 2008 and February 2016. Exclusion criteria included women who did not undergo staging surgery, cases of uterine sarcomas, and endometrial hyperplasia. Eligible cases were divided into two groups: patients with a diagnosis of postoperative UTIs and patients without postoperative UTIs. For strengthening the reporting of observational studies in epidemiology (STROBE), guidelines were consulted for outlining the results of this retrospective cohort study [12]. Some of the patients included in prior studies [13, 14].

Clinical information

Archived medical records were reviewed to extract clinical information for eligible cases: (1) patient demographics at the time of surgery, including age, ethnicity, body mass index (BMI, kg/m^2), American Society of Anesthesiologists Physical Status (ASA-PS), presence of medical comorbidities (diabetes mellitus, hypertension, and hypercholesterolemia), and cigarette smoking; (2) tumor characteristics, including uterine weight (grams), tumor size (cm), cancer stage, histologic subtype, tumor grade, depth of myometrial invasion (%), and lymph-vascular space invasion (LVSI); (3) treatment pattern, including operating time (min), estimated blood loss (EBL, mL), surgical staging details (minimally invasive surgery, type of hysterectomy, and lymphadenectomy), intraoperative cystoscopy, and ureteral stent insertion; (4) complications in perioperative period, including blood transfusion ($\geq$5 units), urinary injury, vascular injury, bowel injury, hospital stay (day), wound infection including surgical site fascial deficiency or evisceration, readmission, sepsis, venous thromboembolism, and death; (5) characteristics relating to UTIs, including symptoms, type of prophylactic antibiotics before and during surgery, urine pathogens, and sensitivity for prophylactic antibiotics; and (6) survival outcomes, including disease-free survival (DFS) and overall survival (OS).

Study definitions

A UTI was defined as a patient with UTI symptoms and (1) a culture with $>10^3$ colonies/mL of uropathogens with urinary catheters, (2) a culture with $>10^5$ colonies/mL of uropathogens regardless of using urinary catheters, (3) a positive gram stain, or (4) a clinical diagnosis. These were based on prior manners [15, 16]. All cases of UTIs diagnosed within 30 days of the primary staging surgery were included in this study [17]. Prophylactic antibiotics were categorized based on American College of Obstetrics and Gynecology (ACOG) guidelines: β-lactam antibiotics (cephalosporin 1–2 generation), β-lactam alternatives (clindamycin and gentamicin), and non-standard antibiotics (clindamycin alone, ciprofloxacin alone, and other regimens) [18]. Stage for endometrial cancer was reclassified based on the 2009 International Federation of Gynecology and Obstetrics (FIGO) system. Histologic subtypes were divided into endometrioid and non-endometrioid. Minimally invasive surgery included robotic-assisted hysterectomy. Hysterectomy types were grouped into total simple hysterectomy and modified-radical hysterectomy/radical hysterectomy. Urinary stents were inserted before and during surgery. Postoperative complications were defined as occurring within 30 days from the hysterectomy-based surgical staging.

Statistical analysis

The primary interest of this analysis was to examine the prevalence of UTIs after hysterectomy-based surgical staging and the independent risk factors for UTIs in women with endometrial cancer. The secondary interest of analysis was to design a predictive model for UTIs in this population.

Continuous variables were examined for normality by Kolmogorov–Smirnov test and expressed with mean

[±standard deviation (SD)] or median (range) as appropriate. Student's *t* test or Mann–Whitney *U* test was used to assess statistical significance for continuous variables. Clinically relevant age cut-off (<60 vs. ≥60 years), the World Health Organization definition for BMI (<30, 30–39.9 ≥40 kg/m^2), surgical operating time (<300 vs. ≥300 min), estimated blood loss (<2000 vs. ≥2000 mL), and median time for hospital stay (0–3 vs. <3 days) were used for the cut-off values and selected in an priori manner [9, 19, 20]. Pearson's correlation coefficient value was determined among the continuous variables. Categorical variables were evaluated using Fisher's exact test or the Chi-squared test as appropriate.

A binary logistic regression model was used to identify independent contributing factors for postoperative UTIs. Significant covariates with $p < 0.10$ in univariate analysis were initially entered into the multivariate model; then, the least significant covariate was removed from the model until the final model retained significant covariates (conditional backward method). Magnitudes of statistical significance were expressed with adjusted odds ratio (OR) and 95% confidence interval (CI). Statistical significance of survival analysis was performed using the Log-rank test. The Kaplan–Meier method was used to construct survival curves. A *p* value of less than 0.05 was considered statistically significant (all, two-tailed hypothesis). The Statistical Package for Social Science software (version 24.0, Chicago, IL, USA) was used for all analyses.

Results

There were 687 cases of endometrial cancer that underwent hysterectomy-based surgical staging during the study period. Postoperative UTIs were observed in 44 (6.4%, 95% CI 4.6–8.2) cases. Patient demographics comparing

Table 1 Patient demographics of urinary tract infection-related endometrial cancer ($N = 687$)

Characteristics	Total	UTI (−)	UTI (+)	Odds ratio (95% CI)	*p* value
Number (%)	687 (100%)	643 (93.6%)	44 (6.4%)		
Age (year)	57.0 (23.8–86.9)	57.0 (23.8–86.8)	56.9 (31.1–86.9)		0.90
<60	428 (62.3%)	401 (93.7%)	27 (6.3%)	1	
≥60	259 (37.7%)	242 (93.4%)	17 (6.6%)	1.04 (0.56–1.95)	
Ethnicity					0.51
Hispanic	405 (59.0%)	377 (93.1%)	28 (6.9%)	1	
Non-Hispanic	282 (41.0%)	266 (94.3%)	16 (5.7%)	0.81 (0.43–1.53)	
BMI (kg/m^2)	32.9 (15.6–90.0)	33.1 (15.6–90.0)	30.6 (18.3–49.7)		
<30	253 (36.8%)	232 (91.7%)	21 (8.3%)	1	
30–39.9	250 (36.4%)	233 (93.2%)	17 (6.8%)	0.81 (0.42–1.57)	0.53
≥40	184 (26.8%)	178 (96.7%)	6 (3.3%)	0.37 (0.15–0.94)	**0.04**
ASA score					0.36
1–2	388 (56.5%)	366 (94.3%)	22 (5.7%)	1	
3–4	297 (43.2%)	275 (92.6%)	22 (7.4%)	1.33 (0.72–2.45)	
Diabetes mellitus					0.49
No	467 (68.0%)	435 (93.1%)	32 (6.9%)	1	
Yes	220 (32.0%)	208 (94.8%)	12 (5.5%)	0.78 (0.40–1.55)	
Hypertension					0.70
No	318 (46.3%)	294 (92.5%)	24 (7.5%)	1	
Yes	369 (53.7%)	349 (94.6%)	20 (5.4%)	0.70 (0.38–1.30)	
Hypercholesterolemia					0.64
No	478 (69.6%)	446 (93.3%)	32 (6.7%)	1	
Yes	209 (30.4%)	197 (94.3%)	12 (5.7%)	0.85 (0.43–1.68)	
Smoker					0.71
No	630 (91.7%)	589 (93.5%)	41 (6.5%)	1	
Yes	57 (8.3%)	54 (94.7%)	3 (5.3%)	0.80 (0.24–2.66)	

Number (%) or median (range) is shown. Percentages are shown per row except total column. Univariate analysis with binary logistic regression for *p* values comparing UTI cases and non-UTI cases. Significant *p* values are emboldened. Two missing for ASA score

UTI urinary tract infection, *BMI* body mass index, *ASA* American Society of Anesthesiologists Physical Status, *CI* confidence interval

Table 2 Tumor characteristics of urinary tract infection-related endometrial cancer ($N = 687$)

Characteristics	Total	UTI (−)	UTI (+)	Odds ratio (95% CI)	p value
Number (%)	687 (100%)	643 (93.6%)	44 (6.4%)		
Tumor size (cm)	3.0 (0.1–23)	3.0 (0.1–23)	3.6 (0.1–9)	1.05 (0.95–1.16)	0.34
Uterus size (g)	140 (18–4325)	138 (20–4325)	151 (18–1546)	1.00 (0.99–1.00)	0.70
Stage					
I	539 (78.5%)	511 (94.8%)	28 (5.2%)	1	
II–IV	148 (21.5%)	132 (89.2%)	16 (10.8%)	2.21 (1.16–4.21)	**0.02**
Histology					
Endometrioid	571 (83.2%)	537 (94.0%)	34 (6.0%)	1	
Non-endometrioid	116 (16.8%)	105 (91.3%)	10 (8.7%)	1.50 (0.72–3.14)	0.28
Tumor grade					
1–2	524 (76.3%)	494 (94.3%)	30 (5.7%)	1	
3	163 (23.7%)	149 (91.4%)	14 (8.6%)	1.55 (0.80–2.99)	0.20
Myometrial invasion (%)					
<50	526 (76.8%)	497 (94.5%)	29 (5.5%)	1	
≥50	158 (23.2%)	144 (91.1%)	14 (8.9%)	1.67 (0.86–3.24)	0.13
LVSI					
No	562 (82.3%)	531 (94.5%)	31 (5.5%)	1	
Yes	121 (17.7%)	109 (90.1%)	12 (9.9%)	1.89 (0.94–3.79)	0.08

Number (%) or median (range) is shown. Percentages are shown per row except total column. Univariate analysis with binary logistic regression for p values comparing UTI cases and non-UTI cases. Significant p values are emboldened. Three missing for Myometrial invasion and four missing for LVSI

UTI urinary tract infection, *LVSI* lymph-vascular space invasion, *CI* confidence interval

postoperative UTI cases ($n = 44$) and non-UTI cases ($n = 643$) are shown in Table 1. Across the two groups, the majority of women with endometrial cancer were less than 60 years old (62.3%), Hispanic ethnicity (59.0%), and obese (BMI $\geq$ 30 kg/m^2, 63.2%). Approximately, half of the patients had severe systemic diseases (ASA score 3–4, 43.2%) and hypertension (53.7%). One-third of the patients had comorbidities: diabetes mellitus (32.0%) and hypercholesterolemia (30.4%). Patient's age, ethnicity, BMI, ASA score, comorbidity rates, and cigarette smoking rates were similar between the groups with and without postoperative UTIs (all, $p > 0.05$).

Tumor characteristics were compared between the two groups (Table 2). The majority consisted of stage I (78.5%), endometrioid histology (83.2%), and low-grade tumor (76.3%). Tumor size, uterus size, histologic subtypes, tumor grade, deep myometrial invasion rates, and lymphovascular space invasion rates were similar between the two groups (all, $p > 0.05$). Advanced stage cases were significantly associated with postoperative UTIs compared to early-stage cases (10.8 vs. 5.2%, OR 2.21, 95% CI 1.16–4.21, $p = 0.02$).

Treatment patterns for endometrial cancer and perioperative complications were also compared between the two groups (Table 3). The majority underwent minimally invasive surgery (61.1%), simple hysterectomy (97.4%), intraoperative cystoscopy (64.9%), and received β-lactam antibiotics (88.9%). Readmissions were observed in 25 (3.6%) cases. Postoperative UTIs were associated with prolonged operative time (≥300 min, 10.7%), modified-radical/radical hysterectomy (22.2%), β-lactam alternatives (15.2%), and intraoperative urinary injury (38.5%) in univariate analysis ($p < 0.05$). Minimally invasive surgery and cystoscopy use during surgery were not associated with increased risk of postoperative UTIs ($p > 0.10$). Postoperative UTIs significantly correlated with longer hospital stay (OR 2.43, 95% CI 1.31–4.50, $p = 0.005$) and other postoperative complications, including readmission (OR 3.99, 95% CI 1.42–11.2, $p = 0.009$) and sepsis (OR 11.7, 95% CI 2.53–54.0, $p = 0.002$).

Prophylactic antibiotics given at the time of surgery and urine pathogens collected at the time of UTI diagnosis are shown in Table 4. The most common prophylactic antibiotics were cefoxitin (50.0%) followed by cefazolin (27.3%) and clindamycin and gentamycin (11.4%). Among the detected cases, more than a half of microorganisms showed a resistance to prophylactic antibiotics (60.6%). The median onset of UTIs was on postoperative day 7 (range 1–26). The most frequently isolated uropathogens were *Escherichia Coli* (36.4%) followed by *Enterococcus species* (16.3%), *Klebsiella pneumonia* (9.1%), and *Pseudomonas aeruginosa* (9.1%). The common symptoms of UTIs were

Table 3 Treatment patterns and complications of urinary tract infection-related endometrial cancer ($N = 687$)

Characteristics	Total	UTI (−)	UTI (+)	Odds ratio (95% CI)	p value
Number (%)	687 (100%)	643 (93.6%)	44 (6.4%)		
Operating time (min)	251 (65–735)	245 (65–735)	300 (132–589)		
<300	478 (69.9%)	456 (95.4%)	22 (4.6%)	1	
≥300	206 (30.1%)	184 (89.3%)	22 (10.7%)	2.48 (1.34–4.59)	**0.004**
Estimated blood loss (mL)	150 (10–3850)	150 (10–3850)	200 (25–1300)		
Minimal invasive surgery					
No	267 (38.9%)	246 (92.1%)	21 (7.9%)	1	
Yes	420 (61.1%)	397 (94.5%)	23 (5.5%)	0.68 (0.37–1.25)	0.22
Hysterectomy type					
Simple hysterectomy	665 (97.4%)	262 (94.1%)	39 (5.9%)	1	
mRH/RH	18 (2.6%)	14 (77.8%)	4 (22.2%)	4.59 (1.44–15.9)	**0.01**
Lymphadenectomy					
No	436 (63.5%)	415 (95.2%)	21 (4.8%)	1	
Yes	251 (36.5%)	228 (90.8%)	23 (9.2%)	1.99 (1.08–3.61)	**0.03**
Cystoscopy					
Not performed	241 (35.1%)	222 (92.1%)	19 (7.9%)	1	
Performed	446 (64.9%)	421 (94.4%)	25 (5.6%)	0.69 (0.37–1.29)	0.25
Stent insertion					
No	673 (98.0%)	631 (93.8%)	42 (6.2%)	1	
Yes	14 (2.0%)	12 (85.7%)	2 (14.3%)	2.50 (0.54–11.6)	0.24
Prophylaxis antibiotics					
β-lactam antibiotics	552 (88.9%)	526 (95.3%)	26 (4.7%)	1	
β-lactam alternatives	33 (5.3%)	28 (84.8%)	5 (15.2%)	3.61 (1.29–10.1)	**0.02**
Non-standard	36 (5.8%)	32 (88.9%)	4 (11.1%)	2.53 (0.83–7.69)	0.10
Intraoperative complication					
EBL >2000	10 (1.5%)	10 (100%)	0	na	0.99
Blood transfusion >5 units	8 (1.2%)	8 (100%)	0	na	0.99
Urinary injury	13 (1.9%)	8 (61.5%)	5 (38.5%)	10.2 (3.18–32.6)	**<0.001**
Vascular injury	4 (0.6%)	4 (100%)	0	na	0.99
Bowel injury	2 (0.3%)	2 (100%)	0	na	0.99
Postoperative complication					
Hospital stay (day)	3.0 (0–41)	3.0 (0–41)	4.5 (0.–21)		
0–3 days	449 (65.5%)	429 (95.5%)	20 (4.5%)	1	
<3 days	236 (34.5%)	212 (89.8%)	24 (10.2%)	2.43 (1.31–4.50)	**0.005**
Wound infection	77 (11.2%)	71 (92.2%)	6 (7.2%)	1.09 (0.44–2.70)	0.85
Readmission	25 (3.6%)	20 (80.0%)	5 (20.0%)	3.99 (1.42–11.2)	**0.009**
Sepsis	7 (1.0%)	4 (57.1%)	3 (42.9%)	11.7 (2.53–54.0)	**0.002**
Thromboembolism	10 (1.5%)	9 (90.0%)	1 (10.0%)	1.64 (0.20–13.2)	0.64
Mortality	1 (0.1%)	1 (100%)	0	na	0.99

Number (%) or median (range) is shown. Percentages are shown per row except total column. Univariate analysis with binary logistic regression for p values comparing UTI cases and non-UTI cases. Three missing for operating time, two missing for hospital days, and four missing for hysterectomy. 66 cases for antibiotics use were excluded for the administration after surgery continuing or unknown timing. Significant p values are emboldened

UTI urinary tract infection, *CI* confidence interval

Table 4 Urinary pathogen at urinary tract infection and prophylaxis antibiotics ($n = 44$)

Characteristics	No. (%)
Prophylaxis antibiotics	
Cefoxitin	22 (50.0)
Cefazolin	12 (27.3)
Clindamycin + gentamycin	5 (11.4)
Clindamycin	2 (4.5)
Cefazolin + metronidazole	1 (2.3)
Ciprofloxacin	1 (2.3)
Gentamicin + vancomycin	1 (2.3)
Sensitivity to prophylaxis antibiotics	
Sensitive	13 (39.4)
Resistance	20 (60.6)
Not tested	11 (–)
Postoperative date for UTI diagnosis (days)	7.0 (1–26)
Symptoms at UTI diagnosis	
Dysuria	16 (36.4)
High fever (≥38C°)	12 (27.3)
Abdominal or back pain	8 (18.2)
Urinary frequency	5 (11.4)
Hematuria	3 (6.8)
Septic	3 (6.8)
Nausea/vomiting	2 (4.5)
Fatigue	1 (2.3)
Urine turbid	1 (2.3)
Isolated microorganisms from urinary tract	
Escherichia coli	16 (36.4)
Enterococcus species[a]	7 (15.9)
Pseudomonas aeruginosa	4 (9.1)
Klebsiella pneumonia	4 (9.1)
Proteus mirabilis	3 (7.2)
Enterobacter cloacae	3 (7.2)
Citrobacter amalonaticus	2 (4.5)
Morganella morganii	1 (2.3)
Multiple species	7 (15.9)
Contaminated or undetected	9 (20.5)

Number (%) is shown. Percentages are based on available cases. UTI pathogens and symptoms at urinary tract infection diagnosis were duplicated

[a] Enterococcus species including three cases of enterococcus fecalis

UTI urinary tract infection

dysuria (36.4%), high fever (27.3%), abdominal or back pain (18.2%), and urinary frequency (11.4%).

Multivariate analysis was performed to determine independent risk factors associated with postoperative UTIs (Table 5). There were three independent risk factors identified in the analysis. These included non-β-lactam antibiotics (adjusted OR 3.50 95% CI 1.46–8.38, $p = 0.005$), prolonged operative time (≥300 min, adjusted OR 3.36 95% CI 1.65–6.87, $p = 0.001$), and modified-radical/radical hysterectomy (adjusted OR 5.35 95% CI 1.56–18.4, $p = 0.008$). The relative contribution of these three independent risk factors was examined to predict the risk of postoperative UTIs (Fig. 1). The risk of postoperative UTIs rose dramatically with an increasing number of risk factors (none 4.1%, one risk factor 8.1%, and two risk factors 30.4%, $p < 0.05$). The combination of risk factors associated with the highest prevalence of postoperative UTIs was operating time ≥300 min and non-β-lactam prophylactic antibiotics (50.0%).

Perioperative mortality rate (death occurring within 30 days of surgery) was observed in one case (0.2%, 95% CI 0–0.4) and was similar between the patients who developed postoperative UTIs and patients without postoperative UTIs ($p = 0.99$). Venous thromboembolism was the immediate cause of death. In survival analysis, postoperative UTIs were not associated with decreased disease-free survival (median time, 17.0 vs. 20.4 months; $p = 0.37$) or overall survival (median time, 18.8 vs. 22.1 months; $p = 0.55$) compared to without postoperative UTI group.

Discussion

The key findings of our study are that non-β-lactam antibiotic prophylaxis, prolonged operative time, and performance of modified-radical/radical hysterectomy are independent risk factors for postoperative UTIs in women with endometrial cancer. Multiple risk factors are associated with a markedly elevated risk of UTIs, suggesting a consideration of appropriate antibiotics prophylaxis in this cohort.

Perioperative complications and readmission costs are two important concerns for management of endometrial cancer. The rate of UTIs after conventional hysterectomies is reported to be approximately 0.5–4.2% in benign gynecological disease [9, 21, 22]. In our study, the rate of UTIs after hysterectomy-based staging surgery in women with endometrial cancer was 7.1%, which is relatively higher than the rates of prior studies in benign disease. Moreover, this risk correlated with other postoperative complications, including sepsis and readmission in the perioperative period. Readmission after surgery has been shown to increase the cost after surgery. Previous studies showed patients with complications in perioperative period had higher total charges than patients with no complications ($64,792 vs. $39,064), and the median cost for readmission was $9774 in women with endometrial cancer [11, 23]. Several studies have demonstrated that hospital readmissions affect not only the cost of care, but also the quality of care delivered to patients [24, 25]. Reducing the incidence of postoperative UTIs can improve the quality of care for women with

Table 5 Risk factors and prediction model for urinary tract infection

Characteristics	No.	UTI (%)	Multivariate		Multivariate (backward)	
			HR (95% CI)	*p* value	HR (95% CI)	*p* value
Stage						
I	539	5.2	1			
II–IV	148	10.8	1.33 (0.57–3.10)	0.51		
Operation time (min)						
<300	478	4.6	1		1	
≥300	206	10.7	2.87 (1.36–6.06)	**0.006**	3.36 (1.65–6.87)	**0.001**
Hysterectomy type						
Simple hysterectomy	665	5.9	1		1	
mRH/RH	18	22.2	3.35 (0.85–13.2)	0.09	5.35 (1.56–18.4)	**0.008**
Pelvic lymphadenectomy						
No	436	4.8	1			
Yes	251	9.2	1.25 (0.57–2.74)	0.58		
Prophylaxis antibiotics						
β-lactam antibiotics	552	4.7	1		1	
Non-β-lactam antibiotics	69	13.0	3.62 (1.50–8.74)	**0.004**	3.50 (1.46–8.38)	**0.005**
Urinary injury during surgery						
No	674	5.8	1			
Yes	13	38.5	1.22 (0.85–21.1)	0.08		

Number (%) is shown. When a logistic regression model was applied including all covariates with a *p* value less than 0.05 in univariate analysis, clinically important variables add to the model. Multivariate analysis with binary logistic regression for *p* values comparing UTI cases and non-UTI cases. Significant *p* values are emboldened. Three missing for operating time, 4 missing for hysterectomy, and 66 cases for antibiotics use were excluded for the administration after surgery continuing or unknown timing

UTI urinary tract infection, *CI* confidence interval, *mRH* modified-radical hysterectomy, *RH* radical hysterectomy

endometrial cancer and reduce the secondary complications and readmission costs.

Our study identified several independent prognostic factors for postoperative UTIs after hysterectomy-based surgical staging of endometrial cancer. First, non-β-lactam agents for anti-microbial prophylaxis were associated with increased risk of postoperative UTIs. A previous study shows that β-lactam antibiotics are associated with decreased rates of postoperative surgical site infections (SSIs) after conventional hysterectomy. In this study, patients receiving β-lactam alternatives and non-standard regimens had a significantly higher risk of SSIs [26]. Similarly, our study showed that non-β-lactam antibiotics are inferior in preventing postoperative UTIs compared to a standard β-lactam regimen. A possible explanation is that β-lactam antibiotics first generations, commonly used for surgical prophylaxis, are highly effective against *Escherichia coli*, *Klebsiella pneumonia*, and *Proteus mirabilis*, which are the predominant pathogens that cause UTIs [16, 27]. Given the risk of postoperative infections, steps should be taken to determine the veracity of any patient-reported penicillin allergies, and β-lactam antibiotics should be considered in appropriate cases. In cases of self-reported penicillin allergy, skin testing shows cross-reactivity with cephalosporins in only 10% of patients with a true penicillin allergy [28]. Additionally, cross-allergy is negligible with second- and third-generation cephalosporins [29]. Patients with negative results on penicillin skin testing and those without a history of anaphylactic reaction might be allowed to receive cephalosporins.

Second, prolonged operative time was associated with an increased incidence of postoperative UTIs. Prolonged operative time is known to increase postoperative infectious complications, especially surgical site infections. One study reported that postoperative UTIs correlate with operating time in gynecological surgery [9]. This association reflected to increased complexity of procedures that may result from increased uterine size, hysterectomy type, lymphadenectomy, lysis of adhesions, and conversion to laparotomy [24, 30, 31].

Third, modified-radical/radical hysterectomy had the greatest impact on the incidence for postoperative UTIs. These procedures seem to be associated with longer urinary catheterization and urinary stent placement. The protocols at our institution are to remove catheters on postoperative day 1 after a simple hysterectomy, postoperative days 5–7 after a modified-radical hysterectomy, and postoperative days 7–14 after a radical hysterectomy. The majority of

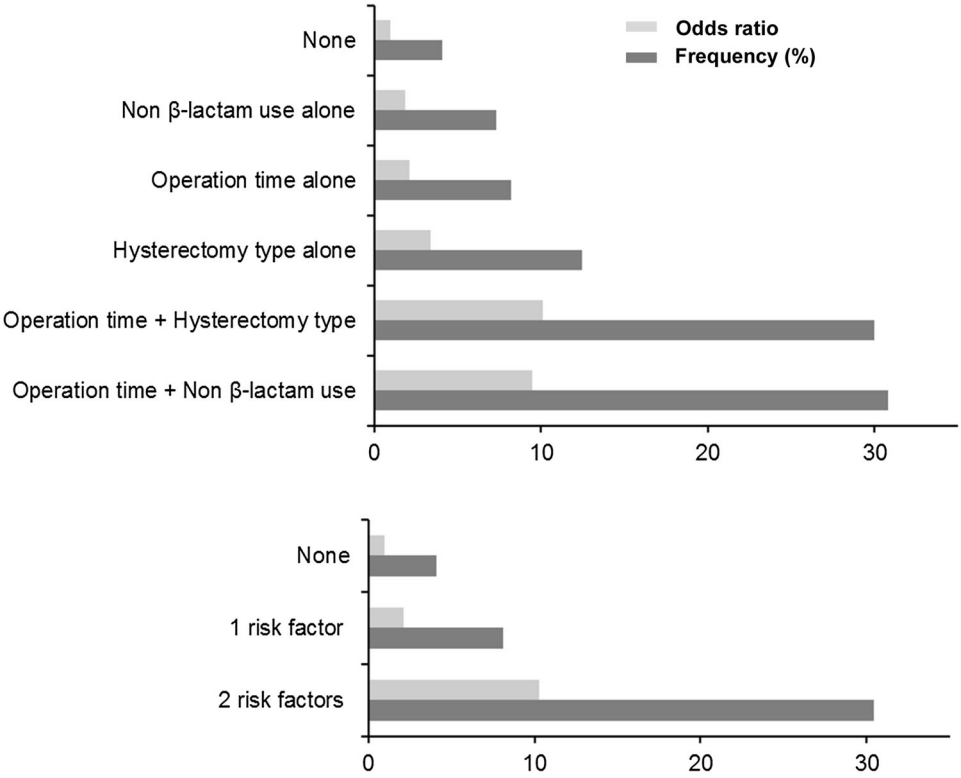

Fig. 1 Predictive model of UTI in endometrial cancer. Risk of postoperative urinary tract infection based on individual number of risk factors. Prevalence and odds ratio for UTI are shown based on the number of independent risk factors (operating time ≥300 min, non-β-lactam prophylaxis antibiotics use, modified-radical/radical hysterectomy type, $p < 0.01$)

patients without perioperative complications followed the protocol in this study. Several studies have shown that early removal of urinary catheters reduces UTI rates. For instance, enhanced recovery after surgery programs often included early catheter removal and reported a significantly reduced rate of postoperative UTIs [32]. In addition, the procedure of radical hysterectomy involves the potential for nerve injury and local inflammation, which may increase urinary retention after catheter removal.

Strengths of our study include the fact that we comprehensively evaluated the significance of postoperative urinary tract infections in a relatively large number of women with endometrial cancer. One of the limitations is the retrospective nature of this study that may miss potential confounding factors. For example, our patients may have visited or been readmitted at other local hospitals; thus, some data regarding symptoms or uropathogens would not be captured. Second, the antibiotic prophylaxis for hysterectomy procedures is commonly aimed at prevention of surgical site infections, not postoperative UTIs. In addition, a possible limitation in this study is that the majority of our cohort had stage I and low-grade endometrioid cancer, which is reflective of the relatively low incidence of disease mortality. Therefore, a type II error may occur when examining the relation between postoperative UTIs and survival outcomes.

Despite the limitations, our study identified several risk factors for UTIs after hysterectomy-based staging surgery in endometrial cancer. Accounting for these risk factors by adopting our predictive model of postoperative UTIs when determining whether to utilize longer-term antibiotic prophylaxis as well as proper selection of β-lactam candidates may improve patient outcomes and reduce the risk of readmission due to postoperative UTIs. Due to the costs associated with readmission resulting from postoperative UTIs, further studies regarding strategies to reduce postoperative UTIs with women in endometrial cancer may be warranted.

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Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All information in studies involving human participants was in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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