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Original Article: Clinical Investigation

Development and validation of a nomogram predicting recurrence risk in women with symptomatic urinary tract infection

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Abbreviations & Acronyms
HPV = human papillomavirus
HSV = herpesvirus
LUTIRE = lower urinary tract infection recurrence risk
QoL = quality of life
ROC = receiver operating characteristic
UTI = urinary tract infection

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Objectives: To develop and externally validate a novel nomogram predicting recurrence risk probability at 12 months in women after an episode of urinary tract infection.
Methods: The study included 768 women from Santa Maria Annunziata Hospital, Florence, Italy, affected by urinary tract infections from January 2005 to December 2009. Another 373 women with the same criteria enrolled at Santa Chiara Hospital, Trento, Italy, from January 2010 to June 2012 were used to externally validate and calibrate the nomogram. Univariate and multivariate Cox regression models tested the relationship between urinary tract infection recurrence risk, and patient clinical and laboratory characteristics. The nomogram was evaluated by calculating concordance probabilities, as well as testing calibration of predicted urinary tract infection recurrence with observed urinary tract infections. Nomogram variables included: number of partners, bowel function, type of pathogens isolated (Gram-positive/negative), hormonal status, number of previous urinary tract infection recurrences and previous treatment of asymptomatic bacteriuria.
Results: Of the original development data, 261 out of 768 women presented at least one episode of recurrence of urinary tract infection (33.9%). The nomogram had a concordance index of 0.85. The nomogram predictions were well calibrated. This model showed high discrimination accuracy and favorable calibration characteristics. In the validation group (373 women), the overall c-index was 0.83 ($P = 0.003$, 95% confidence interval 0.51–0.99), whereas the area under the receiver operating characteristic curve was 0.85 (95% confidence interval 0.79–0.91).
Conclusions: The present nomogram accurately predicts the recurrence risk of urinary tract infection at 12 months, and can assist in identifying women at high risk of symptomatic recurrence that can be suitable candidates for a prophylactic strategy.

Key words: nomogram, quality of life, recurrence, urinary tract infection, validation.

Introduction

UTI is one of the most common infectious diseases.[1,2] In particular, after an initial UTI, approximately 20–30% of women with a UTI will have a second UTI within 6 months, and 3% will experience a third UTI during that time period.[3] Recently, Ciani *et al*. showed that the mean annual direct cost per patient as a result of UTI was €229 (range €53–241).[4] Furthermore, women with recurrent UTI reported a high indirect cost as a result of the number of working days lost. Although the important impact of UTI on the clinical practice, in terms of high indirect costs and working days lost, the recurrence risk prediction of UTI episode currently lacks dedicated and validated tools. Risk factors for recurrent urinary infection are generally both related to bacteria and the patient's behavior, such as *Escherichia coli* adherent to vaginal and bladder epithelial cells,[5] asymptomatic bacteriuria treatment,[6] the use of a spermicide or a diaphragm,[7] delayed postcoital micturition[8] or the ABO-blood-group non-secretor phenotype.[1] Hooton *et al*., by using a longitudinal cohort study on 796 young women, found that among sexually active young women the risk of symptomatic UTI was strongly and independently associated with recent sexual intercourse, recent use of a diaphragm with spermicide and a history of recurrent urinary tract infections.[1] Furthermore, Czaja *et al*. showed that sexual intercourse in the setting of periurethral colonization appears to be the most important trigger event for recurrent UTI among young women.[9] However, the existence of a bladder reservoir and its interplay with the intestinal reservoir as potential sources of periurethral colonization and bacteriuria must be defined further.[9] As a result of these issues, we can identify those women that might have a higher risk of recurrence; but up to the moment, no specific and validated tool has been developed. Furthermore, a predicting tool should be useful to reduce the use of prophylactic antibiotics. In fact, we should use prophylactic antibiotic prevention only in those women, identified to be at high risk of symptomatic recurrence. The aim of the present study was to develop and externally validate a novel tool for predicting recurrence risk probability at 12 months after an UTI episode.

Methods

Study design

In order to identify all demographic, clinical or laboratory parameters that are more frequently associated with UTI recurrence risk in women and develop a prognostic model, named LUTIRE, capable of predicting the probability of recurrence at 12 months, all data of patients collected in our dedicated database were reviewed.

Patients and data collection

All consecutive women attending the Department of Urology, Santa Maria Annunziata Hospital, Florence, Italy, for recurrent UTI between January 2005 and January 2010, and who had all nomogram variables documented were identified for analysis. Furthermore, all consecutive women attending the Department of Urology, Santa Chiara Regional Hospital, Trento, Italy, with the same criteria between January 2010 and June 2012 were identified. The present study included 871 women enrolled from January 2005 to December 2009 (Florence). Of these, 103 patients were excluded because of missing data. Finally, analysis targeted 768 evaluable patients. A total of 373 women enrolled from January 2010 to June 2012 (Trento), were used to externally validate the nomogram.

Inclusion and exclusion criteria

Women were eligible for inclusion if they were older than 18 years and had ≥2 recurrences of UTI in the 6 months prior the present study analysis, in line with Wagenlehner *et al.*[10] In addition, an episode of UTI was defined as acute uncomplicated cystitis. The diagnosis of acute uncomplicated cystitis has been based on a focused history of urinary irritative symptomatology (dysuria, frequency and urgency) and the absence of vaginal discharge or irritation in those women who have no other risk factors for complicated UTI.[11] Furthermore, in accordance with Hooton, we defined recurrent UTI as a symptomatic UTI that follows clinical resolution of an earlier UTI generally, but not necessarily, after treatment.[11] We excluded all women affected by major concomitant diseases, such as diabetes, liver and/or renal failure, known anatomical abnormalities or malignancy of the urinary tract, vesical stones, and neurogenic bladder; furthermore, all women with bladder diverticula, foreign bodies, chronic retention or had polycystic kidney disease and upper tract stones were also excluded because of the higher risk of UTI development. Similarly, women who tested positive for *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Neisseria gonorrhoeae* or HSV 1 or 2 and HPV were excluded, as the nomogram is not applicable to these women. Only women positive for uropathogens in two or more consecutive cultures (colony-forming unit $\geq 10^5$/mL) were included. All samples have been collected at room temperature and immediately taken to the laboratory under refrigerated conditions by each patient. All urine samples were analyzed for cultures and aliquot for DNA extraction, and polymerase chain reaction for *C. trachomatis*, *N. gonorrhoeae*, HSV 1/2 and HPV detection.[6] In brief, the DNA extraction and purification from all biological materials was carried out by DNeasy Tissue Kit (Qiagen, Spa, Italy). *C. trachomatis* DNA polymerase chain reaction was carried out by using the Roche COBAS AMPLICOR CT/NG reagents kits and instruments (Roche Molecular Systems, Branchburg, NJ, USA), while the presence of both genital herpes viruses was investigated in all the biological materials by Alpha Watch HSV1/2 (Alphagenics-Diaco-Biotechnology, Trieste, Italy) and HSV1/2 Genotype TechPlate (Diatech, Trieste, Italy). Finally, the presence of genital HPV was investigated by Alpha Watch HPV (Alphagenics-Diaco-Biotechnology). Microbiological culture was carried out in accordance with the methods described by Hooton *et al.*[1] We considered the following bacteria as uropathogens: enteric Gram-negative rods, enterococci, *Staphylococcus saprophyticus* and group B streptococci.[12]

Clinical and laboratory predictor identification

The following predictors, age, marital status, sexual intercourse per week, number of sexual partners in the last year, hormonal status, contraceptive use, smoking, alcohol use, parity, number of previous UTI per year, bowel function, type of pathogens isolated (Gram-positive/negative), water intake, previous treatment of asymptomatic bacteriuria, response to oral antibiotic therapy, use of food supplements (cranberry), were used in univariate and multivariate logistic regression models addressing the risk of recurrence. Asymptomatic bacteriuria was defined by the presence of at least 10^5 colony-forming units of uropathogen bacteria per mL in a culture of a midstream urine specimen obtained from an asymptomatic woman on a routine scheduled visit.[6] Demographic characteristics were collected and recorded during the medical interview; furthermore, the following specific questions were made in order to obtain homogenous data to analyze. Each woman was asked to report on hormonal status (fertility status/postmenopausal status), bowel function (normal, chronic constipation, chronic diarrhea), daily water intake (<2000 or ≥2000 mL/day)[13] and the relief of symptoms after oral antibiotic therapy.

Questionnaires and urological visits

Patient QoL was measured by using an Italian version of the Quality of Well-Being, a validated, multi-attribute health scale.[14] This scale was selected because it has been successfully applied to acute illnesses, whereas other QoL scales, such as the SF-36 Health Survey, are more suitable in chronic cases.[15] Higher scores on the Quality of Well-Being reflect better QoL.

Statistical and ethical considerations

Differences between groups were evaluated with independent *t*-tests for continuous variables and χ^2-tests for categorical variables. Univariate analysis of variance (ANOVA) was carried out; furthermore, multivariate relative risk was calculated by using Cox proportional hazards regression. Coefficients of multivariate logistic regression models were then used to develop a nomogram predicting the probability of UTI recurrence at 12 months. The variables were selected for the final multivariate model by forward stepwise selection. Furthermore, the bootstrapping method was used to correct for over-fit, and the bias-corrected coefficients obtained from multivariate analysis were used to construct the final score. Accuracy of the score was quantified using the ROC curve. To determine the nomogram-predicted probability of UTI recurrence, we applied the score to all 373 women enrolled in the other period (validation set). Accuracy of the score was then quantified using the area under the curve for external validation. $P < 0.05$ was considered statistically significant. Furthermore, for our nomogram discrimination, we used the overall c-index as a natural extension of the ROC curve area. All reported P-values were two-sided. Statistical analyses were carried out using SPSS 11.0 for Apple-Macintosh (SPSS, Chicago, IL, USA). The study was carried out in line with Good Clinical Practice guidelines and with the ethical principles laid down in the latest version of the Declaration of Helsinki.

Results

Data from 1141 consecutive women affected by recurrent UTI were extracted from the database. All clinical and laboratory characteristics of women included in the present study are described in Table 1. Data were stratified for study phases (development and external validation). In our dataset (768 patients), 261 women presented at least two recurrence episodes of UTI (34.0%). The mean number of recurrence per year was 2.8 (ranging from 1 to 4). The mean time between two episodes was 4.6 months (SD 5.12).

Microbiological findings

The most common isolated bacterial strains in the nomogram development phase are *E. coli* (486 out of 768, 63.2%) and *Enterococcus faecalis* (153, 19.9%). The extended-spectrum beta-lactamase *E. coli* were found in 35 women (7.2%). Furthermore, 699 women (91%) showed at least one episode of asymptomatic bacteriuria; 361 underwent antibiotic treatment, whereas 338 did not. In contrast, in the nomogram external validation phase, the most common isolated bacterial strains were *E. coli* (239 out of 373, 64.0%) and *E. faecalis* (77 out of 373, 20.6%), too. The extended-spectrum beta-lactamase *E. coli* were found in 11 women (4.6%). Furthermore, quinolone-resistant *E. coli* were found in 81 women (16.6%). However, we did not find any significant impact of quinolone-resistant *E. coli* on recurrence, probably because of the low number of quinolone-resistant strains. Finally, 324 women (86.8%) showed at least one episode of asymptomatic bacteriuria; 201 underwent antibiotic treatment, whereas 123 did not.

Univariate and multivariate analysis results

We identified the following independent predictors of UTI recurrence: number of sexual partners, bowel function, type of pathogens isolated (Gram-positive/negative), hormonal status, number of UTI recurrences and previous treatment of asymptomatic bacteriuria. The use of oral contraceptives, water intake and parity were associated with UTI recurrence risk in the univariate model ($P = 0.02$; $P = 0.03$; $P = 0.01$), but were not confirmed with multivariate analysis. The use of food supplements has been excluded from the analysis because of the high

Table 1 Patient clinical and laboratory characteristics at time of enrolment time, stratified by study phase

			P
Total enrolled patients	1141		
Group	Training set	Validation set	
No. patients	768	373	
Mean age (years)	49.2 ± 5.8	48.9 ± 6.1	0.42
Marital status			
Married	410 (53.3)	178 (47.7)	0.07
Single	358 (46.7)	195 (52.3)	
Sexual intercourse per week	1.87 ± 0.1	1.88 ± 0.1	0.11
No. partners in the past year			
1	321 (41.7)	157 (42.1)	0.47
2	303 (39.5)	138 (36.9)	
≥3	144 (18.8)	78 (21.0)	
Hormonal status			
Premenopausal	583 (75.9)	280 (75.0)	0.76
Postmenopausal	185 (24.1)	93 (25.0)	0.56
Contraceptive use	321 (41.7)	149 (39.9)	
Oral hormonal	151/321 (47.1)	72/149 (48.3)	
Condom	89/321 (27.7)	46/149 (30.8)	
Coitus interruptus	81/321 (25.2)	31/149 (20.9)	
Smoking			
Yes	280 (36.5)	119 (31.9)	0.23
Alcohol			
Yes	131 (17.0)	70 (18.7)	0.50
Parity			
Nulliparity	145 (18.8)	66 (17.6)	0.68
Multiparity	623 (81.2)	307 (82.4)	
Daily water intake			
<2000 mL/day	461 (60.0)	214 (57.3)	0.40
≥2000 mL/day	307 (40.0)	159 (42.7)	
Clinical and microbiological data			
Bowel function			
Normal	469 (61.1)	234 (62.7)	0.60
Abnormal	299 (38.9)	139 (37.3)	
Chronic constipation	266 (88.9)	112 (80.5)	
Chronic diarrhea	33 (11.1)	27 (19.4)	
No. UTI per year			
Mean (range)	2.7 (1–4)	2.8 (1–4)	0.11
<3	153 (19.9)	75 (20.1)	0.93
≥3	615 (80.1)	298 (79.9)	0.52
Mean time between two episodes (months)	4.5 ± 5.1	4.7 ± 4.9	
Start of recurrent UTI history (months)	21 ± 4.4	20 ± 4.6	0.09
QoL score at baseline (mean)	0.63 ± 0.01	0.63 ± 0.03	
Bacterial strains			
E. coli	486 (63.3)	239 (64.1)	0.76
E. faecalis	153 (19.9)	77 (20.6)	
E. faecium	29 (3.8)	21 (5.6)	
Klebsiella spp.	64 (8.3)	22 (5.8)	
Streptococcus agalactiae	17 (2.3)	8 (2.2)	
Serratia spp.	19 (2.4)	6 (1.7)	

Data in parentheses are percentage unless otherwise specified.

Table 2 Univariate and multivariate analysis results of factors affecting recurrence-free in 768 patients enrolled in the training set

Categories (variables)	Univariate analysis (*P*) HR (95% CI)	Multivariate analysis (*P*) HR (95% CI)
Age	0.76 (HR 0.81; 95% 0.17–1.23)	0.76 (HR 0.81; 95% 0.17–1.23)
Marital status	0.26 (HR 0.72; 95% 0.15–1.43)	0.65 (HR 1.01; 95% 0.54–1.41)
Sexual encounters per week	0.09 (HR 1.22; 95% 0.67–1.98)	0.07 (HR 1.10; 95% 0.64–1.77)
No. partners	0.01 (HR 3.06; 95% 2.00–3.99)	0.003 (HR 2.97; 95% 1.50–3.67)
Contraceptive use	0.02 (HR 1.80; 95% 1.16–2.21)	0.12 (HR 1.61; 95% 0.87–1.79)
Hormonal status	0.03 (HR 4.52; 95% 3.10–5.65)	0.001 (HR 5.97; 95% 4.11–6.51)
Smoking	0.08 (HR 0.81; 95% 0.14–1.33)	0.76 (HR 0.90; 95% 0.34–1.45)
Alcohol use	0.56 (HR 1.04; 95% 0.50–1.75)	0.07 (HR 1.32; 95% 0.80–1.83)
Parity	0.01 (HR 0.91; 95% 0.17–1.94)	0.09 (HR 0.71; 95% 0.07–1.01)
No. UTI per year	0.03 (HR 2.16; 95% 1.98–2.77)	0.003 (HR 3.17; 95% 2.54–3.88)
Bowel function	0.02 (HR 2.96; 95% 2.11–4.07)	0.001 (HR 3.44; 95% 2.81–5.89)
Type of pathogens isolated (Gram-positive/negative)	0.01 (HR 3.11; 95% 2.32–4.78)	0.001 (HR 3.91; 95% 2.66–4.35)
Water intake	0.03 (HR 2.12; 95% 1.87–3.02)	0.11 (HR 2.22; 95% 1.57–3.09)
Previous treatment of asymptomatic bacteriuria	0.03 (HR 4.96; 95% 3.54–6.69)	0.001 (HR 5.44; 95% 3.51–7.81)
Response to oral antibiotic therapy	0.55 (HR 0.61; 95% 0.25–1.08)	0.87 (HR 0.99; 95% 0.21–1.44)

P-values were calculated using two-sided log–rank test.

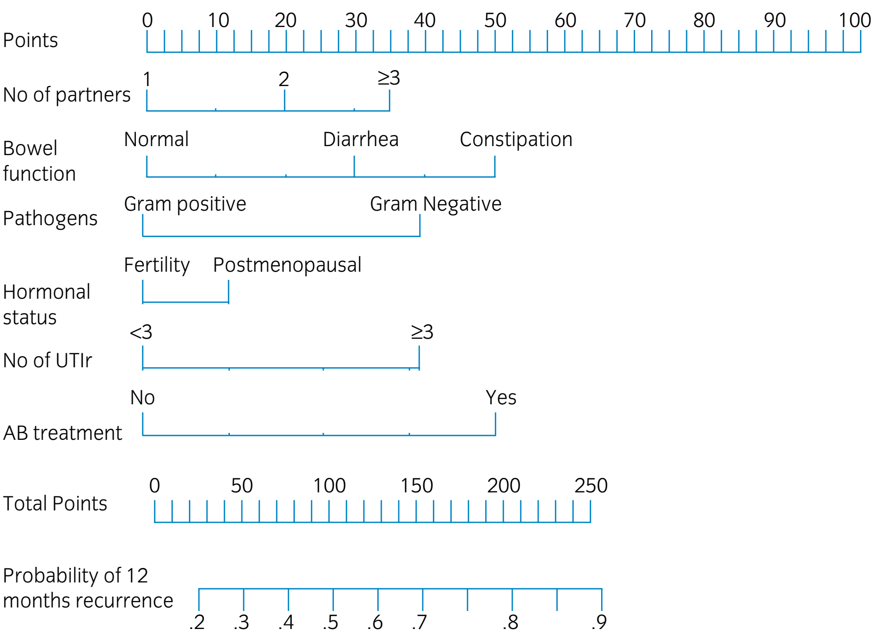

Fig. 1 Proposed nomogram to predict 12-month recurrence risk. To calculate the recurrence probability, identify patient values on each axis, then for each draw a vertical line upwards to the "points" axis. This determines how many points each variable generates. Add the points for all variables and locate this sum on the "total points" line. Then draw a vertical line downwards from this point and identify the recurrence risk probability at 12 months. No of partners = number of partners in the last year; Bowel function = normal, chronic constipation, chronic diarrhea; Pathogens = type of pathogens isolated at the last UTI (Gram-positive or Gram-negative); Hormonal status = fertility status or postmenopausal status; No of UTIr = number of UTI recurrences; AB treatment = previous treatment of asymptomatic bacteriuria.

variability of product used. However, the most common food supplements used were: oral administration of cranberry or other herbal remedies and the use of probiotics to restoring the normal vaginal flora. The univariate and multivariate analysis results are described in Table 2.

Nomogram development and validation

A nomogram was, then, constructed incorporating all predictors identified by the multivariate analysis (Fig. 1). The concordance index between data obtained from the score and the real data was 0.78 after using bootstrapping to correct for overfitting. Calibration plots of the nomogram-predicted probabilities and the actual number of recurrences in the external cohort are shown in Figure 2. In the validation group (373 women) the overall c-index was 0.83 ($P = 0.003$, 95% CI 0.51–0.99), while the area under the ROC curve was 0.85 (95% CI 0.79–0.91).

Discussion

Hooton *et al*. developed a simple risk prediction model by using the information about the number of days with intercourse and contraceptive use (diaphragm and spermicide) for predicting the risk of UTI recurrence.[1] They found that an unmarried, 24-year-old female university student who had sexual intercourse without a diaphragm and spermicide on three of the past seven days had a risk of UTI that was 2.6-fold greater than that of a similar student who had not had intercourse in the previous week.[1] This study highlights the role of recurrence

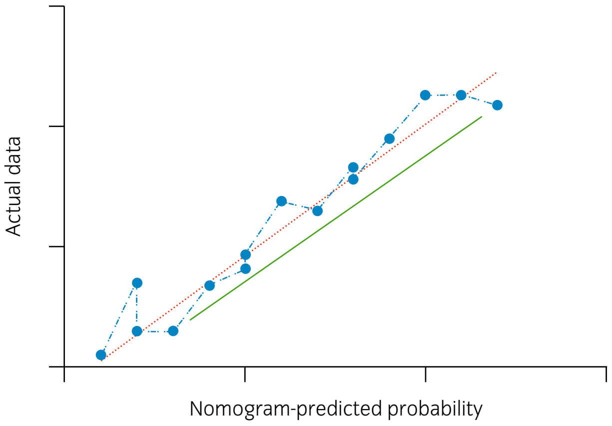

Fig. 2 Calibration curves for the nomogram-predicted the probability of 12-month recurrence. Curves for a hypothetical ideal nomogram are represented by the dashed lines and those for the current nomogram are represented by solid lines.

risk-predicting tools in the management of women with UTI. In the present study, for the first time, we developed and validated an easy nomogram based on several parameters both from the patients and the bacteria for predicting the recurrence of UTI risk. Our LUTIRE nomogram, in fact, is able to predict with a good accuracy the probability of a new UTI episode in women. The LUTIRE nomogram is based on the following parameters that need to be discussed.

Women's sexual behavior

Scholes *et al*. found that the frequency of intercourse in the previous month, 12-month spermicide use and a new sexual partner in the previous year were independent risk factors for recurrent UTI.[16] In the present study, we found a strong correlation between the number of sexual partners (≥3 partners per years) and a higher recurrence risk. We did not find any correlation between the use of diaphragm–spermicide use and recurrence risk, because of the low number of patients that used these contraceptive methods.

Hormonal status

It is well known that the incidence of UTI in women increases with advancing age.[17] Raz, a few years ago, showed by a placebo-controlled, double-blind study, a correlation between reduced estrogenic hormone levels after menopause and the development of recurrent UTI, highlighting the fact that estrogens stimulate proliferation of *Lactobacillus* in the vaginal epithelium, causing reduction of vaginal pH, thereby preventing vaginal colonization by Enterobacteriaceae.[18] Recently, Lüthje *et al*. highlighted that estrogen induced the expression of antimicrobial peptides, thereby enhancing the antimicrobial capacity of the urothelium and restricting bacterial multiplication. Furthermore, they suggested the application of estrogen in postmenopausal women suffering from recurrent UTI.[19]

Bowel function and water intake

It is also well known that fecal–perineal–urethral contamination is the most probable explanation for infections caused by enteric bacteria in women, as shown by several authors evaluating the genotype of *E. coli* strains causing UTI in women.[20] Furthermore, Loening-Baucke *et al*., evaluating a cohort of 234 chronically constipated and encopretic children with a mean follow up of 15 months, showed that constipation treatment resulted in the disappearance of daytime urinary incontinence in 89% and night-time urinary incontinence in 63% of patients, and disappearance of recurrent urinary tract infections in all patients who had no anatomical abnormality of the urinary tract.[21] With regard to water intake, literature data are discordant. Eckford *et al*. documented a reduction of recurrent UTI in premenopausal women with adequate hydration with urine osmolality <1105, using an osmolality probe at home,[13] whereas other studies did not find the same correlation.[16] However, we did not include the water intake in the nomogram because of the fact that the results obtained by using the univariate analysis have not been confirmed by multivariate analysis.

Type of isolated bacterial strains (Gram-negative/positive)

We found that the presence of Gram-negative bacteria was associated with a higher likelihood of recurrence, in particular if *E. coli* was found. The higher frequency of Gram-negative bacteria in women with recurrent UTI seems to be as a result of a greater propensity for uropathogenic coliforms to adhere to the uroepithelial cells of recurrently infected women as compared with cells from women without recurrent infection.[5,22]

Role of asymptomatic bacteriuria treatment

Recently, Cai *et al*. found that antibiotic treatment of asymptomatic bacteriuria in young women with recurrent UTI is not only unnecessary, but harmful.[6] In fact, they found that in women who had undergone antibiotic treatment, the rate of *E. coli* decreased over time, whereas the prevalence of *E. faecalis* increased gradually, suggesting that *E. faecalis* should be an important defense mechanism that effectively interferes with the establishment of many important enteric pathogens, such as *E. coli*.[6] In our population, approximately 55% of all women in both cohorts received treatment for asymptomatic bacteriuria, despite clear evidence of no benefit and some harms. However, the high percentage of treated women is probably as a result of the lack of adherence to international guidelines on UTI.[23] Finally, the present study showed a few limitations to take into account. First, the possible selection bias because of the fact that those women are higher recurrent patients and have undergone several antibiotic treatments. However, the number of women with frequent recurrences in their life is increasing, probably because of the indiscriminate use of antibiotic drugs and the consequent increase of multiple-resistance bacteria. Another limitation was the exclusion of sexually transmitted diseases. We excluded them in order to obtain a homogenous group of patients to enrol and because of the fact that sexually transmitted diseases need to be cured in a specific way. Finally, the LUTIRE nomogram patients at increased risk for recurrent UTI might receive non-antibiotic prevention strategies starting immediately after successful treatment of an acute UTI episode.[24]

In conclusion, our new nomogram has proved easy to use and sufficiently accurate to predict the recurrence risk in women affected by recurrent UTI. Furthermore, it was able to select patients at high risk of symptomatic recurrence to plan appropriate prevention strategies.

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Conflict of interest

None declared.

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Editorial Comment

Editorial Comment from Dr Takahashi to Development and validation of a nomogram predicting recurrence risk in women with symptomatic urinary tract infection

First of all, I sincerely welcome this novel nomogram, lower urinary tract infection recurrence risk (LUTIRE), which predicts the risk of recurrence of symptomatic urinary tract infection (UTI) in women.[1] The authors made a comprehensive list of candidate predictors and analyzed them statistically. By using this nomogram, the high-risk female population can be selected and optimum target subjects can be focused on efficiently. In future clinical studies, we will determine efficient criteria for patient selection, because this and the background have a strong impact on the results and conclusions. For instance, there was a well-written article concluding that cranberry juice could not prevent recurrent UTI in healthy college women at all.[2] However, the comment in "To the Editor"[3] indicated that the actual UTI recurrence rate was unexpectedly lower than the rate originally anticipated in a placebo group, and that more participants were necessary to obtain adequate power in that study. If the LUTIRE nomogram can be applied properly to this kind of research, the difficulty in selecting optimal subjects could be reduced or vanish.

Regrettably, the authors excluded "the use of food supplements" from the analysis because of the high variability of products used. The use of food supplements, especially cranberry products, is expected to be an ideal preventive strategy for patients with recurrent UTI,[4] because it inhibits the development of resistant bacteria. If possible, cranberry juice or products as candidate risk predictors should be evaluated together with verification of the LUTIRE nomogram itself in the future.

The authors showed that the type of pathogen isolated (Gram-positive/negative) is one of the important predictors. A recent interesting study revealed that *Escherichia coli* could be isolated from both voided midstream urine and catheterized urine specimens in women with symptoms of cystitis; however,