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ORIGINAL ARTICLE

Risk factors for symptomatic urinary tract infections in individuals with chronic neurogenic lower urinary tract dysfunction

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Study design: Retrospective investigation.
Objectives: To investigate the association of patient and injury characteristics, as well as bladder management, with the occurrence of patient-reported, symptomatic urinary tract infection(s) UTI(s) in patients with chronic neurogenic lower urinary tract dysfunction (NLUTD).
Setting: Tertiary urologic referral center.
Methods: The patient database was screened for patients with chronic (>12 months) NLUTD who had presented between 2008 and 2012. Patient characteristics, bladder evacuation management, the annual number of patient-reported, symptomatic UTIs and the type of prophylactic treatment to prevent UTIs were collected. Binary logistic regression analysis was used to investigate the effects of the investigated risk factors on the occurrence of symptomatic UTI(s) and recurrent symptomatic UTIs (⩾3 annual UTIs).
Results: The data of 1104 patients with a mean NLTUD duration of 20.3 ± 11.6 years were investigated. The evacuation method was a significant ($P \leqslant 0.004$) predictor for the occurrence of symptomatic UTI and recurrent symptomatic UTIs. The greatest annual number of symptomatic UTIs was observed in patients using transurethral indwelling catheters, and the odds of experiencing a UTI and recurrent UTIs were increased more than 10- and 4-fold, respectively. The odds of a UTI or recurrent UTIs were also increased significantly ($P \leqslant 0.014$) in patients using intermittent catheterization (IC). Botulinum toxin injections into the detrusor increased the odds of a UTI ~10-fold ($P = 0.03$).
Conclusions: The bladder evacuation method is the main predictor for symptomatic UTIs in individuals with NLUTD. Transurethral catheters showed the highest odds of symptomatic UTI and should be avoided whenever possible.
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INTRODUCTION

Urinary tract infections (UTIs) remain one of the most common morbidities in individuals with neurogenic lower urinary tract dysfunction (NLUTD).[1–4] Approximately one in five individuals with NLTUD suffers from recurrent UTIs, which affects the quality of life considerably.[5,6] The increased risk of UTIs in individuals with NLUTD is the result of the impaired storage and voiding functions. Thus, the key to controlling UTIs in individuals with NLUTD is to optimize their bladder management and to eliminate sources of infection, such as bladder stones or foreign bodies for example.[7,8] Furthermore, the administration of preventive or protective measures can be optimized by identifying individuals at risk and anticipating times of increased risk.

Many different risk factors for UTIs such as patient or injury characteristics, psychosocial or behavioral aspects, bladder evacuation method or residual urine have been considered.[9–12] However, there is insufficient evidence to assess the relevance of most of these factors.[9] Only injury severity and indwelling catheterization have been demonstrated to be associated with UTIs.[10,13,14]

We have therefore investigated the association of patient and injury characteristics, as well as bladder management, with the occurrence of patient-reported, symptomatic UTIs in patients with chronic NLUTD. The following hypotheses were tested: gender, age, injury severity, injury duration, injury etiology, bladder evacuation method and botulinum toxin (BTx) injections into the detrusor have a significant effect on the occurrence of (1) symptomatic UTI(s) and (2) recurrent symptomatic UTIs (⩾3 annual UTIs).

SUBJECTS AND METHODS

Subjects and collected data

The patient database of a tertiary urologic referral center was screened for patients with chronic (>12 months) NLUTD resulting from traumatic or non-traumatic spinal cord injury, myelomeningocele or multiple sclerosis, who had presented for a routine urodynamic investigation between April 2008 and March 2012. During the visit, data concerning bladder evacuation details, medication and symptomatic UTI were routinely collected using a standardized form. The patients were asked to report the number of symptomatic UTIs they had experienced during the past 12 months. Self-reported symptomatic UTIs were considered clinically relevant, because patients present for UTI treatment when they experience symptoms. A UTI was defined as a combination of clinical symptoms and laboratory findings (leukocyturia and bacteriuria).[6] The following signs and symptoms were considered signs and symptoms of a UTI: fever without another cause, new onset of incontinence or voiding problems,

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decreased bladder capacity, increased voiding or catheterization frequency, kidney or bladder discomfort, cloudy urine or hematuria without another cause.[15]

Patient characteristics, bladder evacuation methods, the annual number of symptomatic UTIs, the type of prophylactic treatment to prevent UTIs and the type of detrusor relaxation treatment were collected from paper and electronic patient charts. The annual number of symptomatic UTIs was collected for 3 consecutive years, to attenuate the effect of a single observation. Thus, patients with a follow-up shorter than 3 years were excluded.

The study had been approved by the local ethics committee, and all applicable institutional and governmental regulations concerning the ethical use of the data were followed.

Statistical analyses

The investigated patients were grouped for age and injury duration using 15- and 5-year increments, respectively.[16] According to international recommendations,[16] injury severity was categorized using the following groups: (1) American Spinal Injury Association Impairment Scale (AIS) D, (2) AIS A–C paraplegia, (3) AIS A–C low-level tetraplegia (C8–C5) and (4) AIS A–C high-level tetraplegia (C4–C1). The average annual number of symptomatic UTIs was determined by calculating the median of the values from 3 years, to attenuate the effect of a single observation. Binary logistic regression analysis was used to investigate the effects of gender, age, injury severity, duration and etiology, bladder evacuation method, detrusor relaxation by BTx injections and UTI prophylaxis on the occurrence of symptomatic UTI(s) (0 or >0 annual UTI) and recurrent symptomatic UTIs (<3 or $\geqslant 3$ annual UTIs). The occurrence rate of symptomatic UTI(s) and recurrent symptomatic UTIs and the 95% confidence intervals (CIs) were calculated for the significant predictors using the Clopper–Pearson exact binomial method. Normal distribution was assumed based on the central limit theorem, and data are thus presented as mean with standard deviation and 95% CI where appropriate. The statistical analyses were performed using the SPSS software (version 18.0.3; IBM, Somers, NY, USA). A *P*-value of $\leqslant 0.05$ was considered significant.

RESULTS

We identified 1324 patients with chronic NLUTD who had presented at least once at our center between April 2008 and March 2012 for a routine urodynamic investigation. A total of 219 patients were excluded because their follow-up was shorter than 3 years. One patient was excluded because no data was available concerning the annual number of UTIs. Thus, the data of 1104 patients with a mean age of 48 ± 14 years (range 12–87 years) were investigated. The mean duration of NLTUD was 20.3 ± 11.6 years (range 4.0–63.4 years). The characteristics of the evaluated patients are presented in Table 1.

The bladder evacuation method, BTx injections into the detrusor and prophylactic treatment to prevent UTI(s) were significant ($P \leqslant 0.049$) predictors for the occurrence of symptomatic UTI(s) and recurrent symptomatic UTIs (Table 2). The odds of experiencing a symptomatic UTI in patients voiding via transurethral indwelling catheters (TUC) (18/1104, 1.6%) were increased more than 10-fold compared with patients voiding spontaneously (71/1104, 6%) (Table 2). The occurrence rate of a symptomatic UTI was 83.3% and 29.6% for TUC and spontaneous voiding, respectively (Table 3). In patients using IC (427/1104, 39%), suprapubic catheterization (SPC) (120/1104, 11%) or triggered reflex voiding (299/1104, 27%), the odds of a symptomatic UTI were also increased significantly (Table 2). Approximately 70% of patients using IC suffered at least one symptomatic UTI per year (Table 3). Bladder voiding by TUC increased the odds of recurrent symptomatic UTIs more than fivefold compared with spontaneous voiding (Table 2). Half of the patients using TUC and ~30% of the patients using IC experienced more than two symptomatic UTIs per year (Table 3).

BTx injections increased the odds of a symptomatic UTI and recurrent symptomatic UTIs 1.7 and 1.55 times (Table 2). The occurrence rate of a symptomatic UTI in patients receiving BTx injections was 76.8% compared with 59.0% in those who did not (Table 3).

Table 1 The characteristics of the evaluated patients

Variables	*Groups*	N	*%*
Gender	Women	283	25.6
	Men	821	74.4
Age (years)	11–30[a]	129	11.7
	31–45	327	29.6
	46–60	413	37.4
	61–75	203	18.4
	>75	32	2.9
Injury severity	C1–C4 AIS A–C	73	6.6
	C5–C8 AIS A–C	249	22.6
	T1–S5 AIS A–C	622	56.3
	AIS D[a]	87	7.9
	Not determinable	73	6.6
Injury duration (years)	<6[a]	46	4.2
	6–10	194	17.6
	11–15	189	17.1
	16–20	182	16.5
	21–25	143	13.0
	26–30	126	11.4
	31–35	87	7.9
	36–40	59	5.3
	41–45	41	3.7
	> 45	37	3.4
Etiology	Traumatic SCI[a]	889	80.5
	Non-traumatic SCI	69	6.3
	MMC	86	7.8
	MS	60	5.4
Evacuation method	Spontaneous[a]	71	6.4
	SARS	93	8.4
	Straining	76	6.9
	Reflex	299	27.1
	IC[b]	427	38.7
	SPC	120	10.9
	TUC	18	1.6
Prophylaxis	No	709	64.2
	Yes	395	35.8
Botulinum toxin	No	959	86.9
	Yes	138	12.5
	Not determinable	7	0.6

Abbreviations: AIS, American Spinal Cord Injury Association Impairment Scale; botulinum toxin, botulinum toxin injections into detrusor; C1–C4, first to fourth cervical spinal cord segment; C5–C8, cervical spinal cord segments 5 to 8; IC, intermittent catheterization; MMC, myelomeningocele; MS, multiple sclerosis; prophylaxis, prophylactic treatment to prevent UTIs; reflex, triggered reflex voiding; SARS, sacral anterior root stimulation; SCI, spinal cord injury; SPC, suprapubic catheterization; straining, voiding by abdominal straining (Valsalva); T1–S5, first thoracic to fifth sacral spinal cord segment; TUC, transurethral indwelling catheter.
[a]Reference category for binary logistic regression.
[b]Single use, hydrophilic catheters in 423/427 patients (99%).

Table 2 Evaluating the effect of different predictors on the occurrence of urinary tract infections using binary logistic regression

Predictors	P-*value*	*UTI(s)*		P-*value*	*Recurrent UTIs*	
		Exp(B)	*95% CI Exp*(B)		*Exp*(B)	*95% CI Exp*(B)
Gender (men/women)	0.3	1.20	0.85–1.68	0.7	1.08	0.74–1.58
Age[a]	0.11		0.09			
Injury severity[a]	0.5		0.89			
Injury duration[a]	0.16		0.07			
Etiology[a]	0.1		0.21			
Evacuation method[a]	<**0.001**		**0.01**			
Spontaneous		*Reference category*			*Reference category*	
TUC	**0.002**	10.27	2.34–45.12	**0.018**	5.20	1.33–20.36
SPC	**0.018**	2.44	1.16–5.14	0.46	1.47	0.53–4.08
IC	<**0.001**	3.54	1.79–7.00	**0.04**	2.66	1.05–6.76
Reflex	**0.013**	2.56	1.21–4.79	0.13	2.10	0.81–5.40
Straining	0.22	1.66	0.74–3.68	0.66	1.28	0.42–3.91
SARS	0.15	1.77	0.82–3.82	0.88	1.09	0.37–3.19
BTx (no/yes)	**0.026**	1.70	1.07–2.71	**0.049**	1.55	1.00–2.40
Prophylaxis	<**0.001**	1.96	1.46–2.62	**0.001**	1.70	1.25–2.30

Abbreviations: AIS, American Spinal Cord Injury Association Impairment Scale; BTx, botulinum toxin detrusor injections; CI, confidence interval; C1–C4, cervical spinal cord segments 1 to 4; C5–C8, cervical spinal cord segments 5 to 8; Exp(*B*), odds ratio predicted by model; IC, intermittent catheterization; MMC, myelomeningocele; MS, multiple sclerosis; prophylaxis, prophylactic treatment to prevent urinary tract infections; recurrent UTIs, ⩾3 annual urinary tract infections; reflex, triggered reflex voiding; SARS, sacral anterior root stimulation; SCI, spinal cord injury; SPC, suprapubic catheterization; straining, voiding by abdominal straining (Valsalva); T1–S5, thoracic spinal cord segment 1 to sacral segment 5; TUC, transurethral indwelling catheter; UTI(s), >0 annual urinary tract infection(s).
P-values ⩽0.05 are indicated in bold.
[a]General odds are not calculated.

Table 3 Occurrence of urinary tract infections for the different categories of the significant predictors

Significant predictors	*UTI*		*Recurrent UTIs*		*Total*
	%/95% CI	*n*	*%/95% CI*	*n*	*%/n*
Evacuation method					
Spontaneous	29.6/19.3–41.6	21	9.9/4.1–19.3	7	100/71
Straining	47.4/22.0–39.0	36	14.5/4.7–15.8	11	100/120
SARS	53.8/43.1–64.2	50	15.1/8.5–24.0	14	100/93
SPC	58.3/49.0–67.3	70	17.5/11.2–25.5	21	100/120
Reflex	61.5/55.8–67.1	184	25.8/20.9–31.1	77	100/299
IC	70.5/65.9–74.8	301	31.2/26.8–35.8	133	100/427
TUC	83.3/58.6–96.4	15	50.0/26.0–74.0	9	100/18
Total	61.3/58.4–64.2	677	24.6/22.1–27.3	272	100/1104
Botulinum toxin					
No	59.0/55.8–62.1	566	23.0/20.4–25.8	221	100/959
Yes	76.8/68.9–83.6	106	36.2/28.2–44.8	50	100/138
Not determinable	71.4/29.0–96.3	5	14.3/0.4–57.9	1	100/7
Prophylaxis					
No	55.3/51.5–59.0	392	20.5/17.5–23.6	145	100/709
Yes	72.2/67.4–76.5	285	32.2/27.6–37.0	127	100/395

Abbreviations: Botulinum toxin, botulinum toxin injections into the detrusor; CI, confidence interval; IC, intermittent catheterization; prophylaxis, prophylactic treatment to prevent urinary tract infections; recurrent UTIs, ⩾3 annual UTIs; reflex, triggered reflex voiding; SARS, sacral anterior root stimulation; SPC, suprapubic catheterization; training, voiding by abdominal straining (Valsalva); TUC, transurethral indwelling catheter; UTI, >0 annual UTI.

A total of 395 patients (35.8%) were receiving prophylactic treatment for the prevention of UTIs (Table 1). The different types of prophylactic treatment are presented in Table 4. Phytotherapy and urine acidification were the two most common prophylactic regimens. The percentage of patients taking antibiotics for infection prophylaxis was 11% (Table 4). The odds of a symptomatic UTI and recurrent symptomatic UTIs were increased ~2-fold and 1.7 times, respectively, with prophylactic treatment (Table 2).

DISCUSSION

We have investigated the effects of patient and injury characteristics, as well as bladder management, on the occurrence of patient-reported,

Table 4 Prophylactic treatment for the prevention of urinary tract infections used by evaluated patients

Category	*Agent*	N	%[a]
Phytotherapy	Cranberries	215	54.3
	Horseradish and nasturtium	10	2.5
	Bearberry	2	0.5
	Undetermined	1	0.25
	Total	228	57.6
Urine acidification	Methionine	177	44.7
	Cider vinegar	2	0.5
	Total	179	45.2
Antibiotics	Nitrofurantoin	19	4.8
	Fuoroquinolone	9	2.3
	Trimethoprim, sulfamethoxazole	6	1.5
	Trimethoprim, sulfamethoxazole /fluoroquinolone	2	0.5
	Trimethoprim, sulfamethoxazole/fosfomycin	2	0.5
	Fosfomycin/cephalosporin	2	0.5
	Trimethoprim, sulfamethoxazole/nitrofurantoin	1	0.25
	Trimethoprim, sulfamethoxazole/rifampicin	1	0.25
	Cephalosporin	1	0.25
	Rifampicin	1	0.25
	Total	44	11.1
Vaccination	*Escherichia coli*	14	3.5
	E. coli, miscellaneous	1	0.25
	Total	15	3.8
Hhomeopathy	NA	4	1.0
Antibacterial	Methenamine hippurate	2	0.5
	D-mannose	2	0.5
	Total	4	1.0
Bladder irrigation	Sodium chloride solution	2	0.5
Undetermined	NA	1	0.25

Abbreviations: Miscellaneous, *Morganella morganii*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Enterococcus faecalis*; NA, not available.
[a]The sum of the percentages exceeds 100% because some patients are using several different prophylactic treatments.

symptomatic UTI in 1104 patients with chronic NLUTD (mean duration 20 years). The odds of experiencing a symptomatic UTI (>0 annual UTI) or recurrent symptomatic UTIs ($\geqslant 3$ annual UTIs) were significantly increased in patients using TUC or IC compared with those voiding spontaneously. Furthermore, BTx injections into the detrusor increased the odds of a symptomatic UTI or recurrent symptomatic UTIs significantly.

The bladder evacuation method was identified as the main predictor for the occurrence of symptomatic UTI(s). In patients using TUC, the odds of a symptomatic UTI and recurrent symptomatic UTIs were increased more than 10- and 5-fold, respectively. Accordingly, the highest percentage of patients affected with symptomatic UTI(s) (83%) was observed in the TUC group. This is in accordance with other studies.[9,10,14] Esclarin de Ruz *et al.*[10] have reported an odds ratio of ~8 for UTIs in patients with acute NLUTD using TUC. Thus, present and previous results confirm the increased risk of UTIs for TUC. Furthermore, high UTI rates have also been reported for voiding by SPC (i.e. 73%).[13,14] In the present study, the odds of a symptomatic UTI were increased 2.4 times in patients using SPC, and 58% were affected by at least one symptomatic UTI. However, there is also a report of reduced odds of UTI for SPC.[10] Several reports have documented lower UTI rates in patients using IC compared with those using TUC.[9,10,13,14] However, the UTI rates for IC (35%) were increased compared with spontaneous voiding.[10,13] In the present study, both the odds of a symptomatic UTI and recurrent symptomatic UTIs were increased in the IC group, and 71% were affected by UTIs. Furthermore, both the rates of symptomatic UTI and the odds for symptomatic UTI(s) were higher for IC compared with SPC, which is in accordance with a previous report.[17] We have also observed a considerable rate of symptomatic UTI in patients using triggered reflex voiding (i.e. 62%). Similarly, other investigators have reported increased UTI rates for triggered reflex voiding compared with spontaneous voiding; however, the observed rates were slightly lower (i.e. 44%).[10,13] The discrepancies between previously reported and present data are the result of differences in the duration of NLUTD, definition of a UTI, calculation of the UTI rate and study design.

The occurrence rate (77%) of symptomatic UTI(s) in patients receiving BTx injections into the detrusor was significantly greater compared with the rate (59%) in those who did not. Furthermore, the odds of a symptomatic UTI and recurrent symptomatic UTIs were increased ~1.5 times, respectively. In previous investigations, a decrease in the number of patients affected by UTIs and the incidence of UTIs was observed after BTx injections.[18,19] These results are not necessarily contradictory to the present ones, as patients may experience a decrease in the UTI rate after BTx injections but still suffer from UTIs more often than those who do not receive injections. Present data represent the situation under chronic BTx treatment, and thus no comparison can be made between the UTI rate before and the rate after starting BTx treatment. Furthermore, the causality between BTx injections and symptomatic UTIs should be considered cautiously because of the cross-sectional study design.

In the present study, patient and injury characteristics had no significant effect on the occurrence of symptomatic UTIs. This is largely in accordance with other reports.[10,11,13] Some investigators have observed increased UTI rates in patients with motor complete spinal cord injury,[13] cervical injury[10] or increased functional independence.[10] However, injury severity and level have a major impact on both functional independence and the chosen bladder evacuation method, and thus may represent confounding factors. We have included these factors in our statistical model.

Approximately every third patient was receiving prophylactic treatment for the prevention of UTIs. In these patients, the odds of a symptomatic UTI and recurrent symptomatic UTIs were significantly increased compared with those who did not receive prophylactic treatment. However, the occurrence of symptomatic UTIs was the reason for the prophylactic treatment and not *vice versa*. Yet, the prophylactic measures do not seem to be very successful in reducing the occurrence of symptomatic UTIs. Cranberry products and urine acidification using methionine were the two most common prophylactic regimens, which are reported to be the current clinical practice in the prevention of UTI in German-speaking spinal cord injury centers.[20] However, based on current evidence, cranberry products or urine acidification do not reduce the occurrence of symptomatic UTIs.[21,22] Long-term antibiotic treatment for UTI prevention is administered in most spinal cord injury centers.[20] In the present study, 11% of the patients were taking antibiotics for UTI prevention. However, antibiotic treatment for UTI prevention is not supported by current evidence.[23,24] Moreover, the risk of antibiotic resistance is increased under long-term treatment.[23,24]

The retrospective data collection and the mediocre accuracy (i.e. 66%) of the patient self-prediction of UTI[25] contribute to the uncertainty about the true number of annual symptomatic UTIs. However, the analyses of the present study are not based on the number of annual symptomatic UTIs but on the two categories 'UTI' (>0 annual UTI) and 'recurrent UTIs' ($\geqslant 3$ annual UTIs), which can be determined accurately and reliably. The causality between predictors and symptomatic UTIs should be considered cautiously because of the cross-sectional study design. Furthermore, some possible risk factors for symptomatic UTIs, such as the urodynamic situation, residual urine or bladder stones, were not included in our analysis. However, the urodynamic situation and the presence of bladder stones or relevant residual urine volumes are examined in our patients during routine follow-up visits, and appropriate measures are initiated, if required. Finally, the reported odds ratios should be interpreted with caution because of the wide CI.

Symptomatic UTIs have a considerable effect on the quality of life of individuals with NLUTD, and identifying individuals at risk and anticipating times of increased risk are key factors in the prevention and management of UTIs. On the basis of the present results, patient and injury characteristics do not represent risk factors for the occurrence of symptomatic UTIs in individuals with NLUTD. However, the bladder evacuation method is the main predictor for the occurrence of symptomatic UTIs. We have identified long-term TUC as the primary predictor of symptomatic UTIs in individuals with NLUTD. Thus, long-term TUC should be avoided whenever possible, inasmuch as further complications (e.g. bladder stones, cancer) are associated with this evacuation method.[26–28] Evacuation by SPC represents a valuable alternative, particularly with regard to symptomatic UTIs. In the present study, SPC has shown the lowest odds of symptomatic UTIs among catheter-based evacuation methods. The gold standard for bladder evacuation in individuals with NLUTD and sufficient manual dexterity is IC.[29] However, present results indicate that the odds of symptomatic UTIs are increased considerably for IC. Even though this does not represent a reason to abandon IC, protective and preventive measures should be initiated timely in these patients. The same conclusion can be drawn for triggered reflex voiding, which was associated with increased odds of a symptomatic UTI. Thus, further research regarding prophylactic measures to prevent symptomatic UTIs should be initiated, as currently used measures do not seem to be effective. Finally, increased odds of a symptomatic UTI and recurrent symptomatic UTIs should be anticipated in patients receiving BTx injections into the detrusor and appropriate prophylactic measures initiated.

CONCLUSIONS

The bladder evacuation method, rather than patient or injury characteristics, is the main predictor for the occurrence of symptomatic UTIs in individuals with NLUTD. Long-term TUC showed the highest odds of symptomatic UTI(s) and should thus be avoided whenever possible.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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