

## Postprint of Meta-Analysis of Risk Factors for Urinary Tract Infection in Patients with Neurogenic Bladder

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### Abstract

**Background** Urinary tract infection is the most common complication in patients with neurogenic bladder, severely affecting treatment efficacy and quality of life. Early identification of its related factors and targeted prevention and intervention are of great significance for improving patient prognosis. In recent years, research on influencing factors of urinary tract infection has been increasing, but conclusions remain controversial, and there is currently a lack of relevant systematic reviews and evidence-based medical support. **Objective** To systematically evaluate the risk factors for urinary tract infection in patients with neurogenic bladder. **Methods** Computerized searches were conducted in PubMed, Web of Science, Cochrane Library, Embase, CNKI, Wanfang, VIP, and Chinese Biomedical Literature Database for literature on risk factors for urinary tract infection in patients with neurogenic bladder, with the search period up to June 2022. The Newcastle-Ottawa Scale was used to assess the quality of included studies, and RevMan5.3 software was used for Meta-analysis. **Results**

A total of 13 studies were included, with 3219 cases. Meta-analysis results indicated that advanced age [OR=2.50, 95%CI (1.83, 3.41),  $P<0.00001$ ; OR=2.13, 95%CI (1.40, 3.25),  $P=0.0004$ ], female gender [OR=0.78, 95%CI (0.63, 0.96),  $P=0.02$ ], diabetes mellitus [OR=3.17, 95%CI (2.58, 3.89),  $P<0.00001$ ], hypoalbuminemia [OR=2.26, 95%CI (1.67, 3.06),  $P<0.00001$ ], stroke frequency \$ \$2 times [OR=3.30, 95%CI (1.70, 6.41),  $P=0.0004$ ], indwelling catheter [OR=2.88, 95%CI (2.09, 3.95),  $P<0.00001$ ], intermittent catheterization frequency \$ \$2 times/week [OR=2.44, 95%CI (1.62, 3.68),  $P<0.0001$ ], bladder irrigation frequency \$ \$3 times/week [OR=2.63, 95%CI (1.66, 4.17),  $P<0.0001$ ], bladder function training intervention time \$ \$2 weeks [OR=2.75, 95%CI (1.69, 4.46),  $P<0.0001$ ], and rehabilitation intervention time  $>7$  days [OR=3.03, 95%CI (1.42, 6.48),  $P=0.004$ ] were risk factors for urinary tract infection in patients with neurogenic bladder. **Conclusion** Advanced age, female gender, diabetes mellitus, hypoalbuminemia, stroke frequency \$ \$2 times, indwelling catheter,

intermittent catheterization frequency \$ \$2 times/week, bladder irrigation frequency \$ \$3 times/week, bladder function training intervention time \$ \$2 weeks, and rehabilitation intervention time >7 days are risk factors for urinary tract infection in patients with neurogenic bladder. Clinical medical staff can identify high-risk factors early and implement targeted control of modifiable factors to prevent or reduce the occurrence of urinary tract infection in patients. Due to limitations in the quality and quantity of literature included for certain factors, the conclusions drawn in this article still need to be validated by higher-quality studies.

## Full Text

### Meta-Analysis of Risk Factors for Urinary Tract Infection in Patients with Neurogenic Bladder

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## Abstract

**Background:** Urinary tract infection (UTI) is the most common complication in patients with neurogenic bladder, seriously affecting treatment efficacy and quality of life. Early identification of related factors and targeted prevention and intervention are crucial for improving patient prognosis. Although research on UTI influencing factors has increased in recent years, conclusions remain controversial, and no relevant systematic reviews or evidence-based medical support currently exist.

**Objective:** To systematically evaluate risk factors for urinary tract infection in patients with neurogenic bladder.

**Methods:** We searched PubMed, Web of Science, Cochrane Library, Embase, CNKI, Wanfang, VIP, and the China Biomedical Literature Database for litera-

ture on risk factors for UTI in neurogenic bladder patients, with a search cutoff of June 2022. The Newcastle-Ottawa Scale was used for quality assessment of included studies, and RevMan 5.3 software was used for meta-analysis.

**Results:** A total of 13 articles were included, comprising 3,219 cases. Meta-analysis results indicated that advanced age [OR=2.50, 95%CI (1.83, 3.41),  $P<0.00001$ ; OR=2.13, 95%CI (1.40, 3.25),  $P=0.0004$ ], female gender [OR=0.78, 95%CI (0.63, 0.96),  $P=0.02$ ], diabetes mellitus [OR=3.17, 95%CI (2.58, 3.89),  $P<0.00001$ ], hypoalbuminemia [OR=2.26, 95%CI (1.67, 3.06),  $P<0.00001$ ], stroke episodes \$ \$2 [OR=3.30, 95%CI (1.70, 6.41),  $P=0.0004$ ], indwelling catheter [OR=2.88, 95%CI (2.09, 3.95),  $P<0.00001$ ], intermittent catheterization \$ \$2 times/week [OR=2.44, 95%CI (1.62, 3.68),  $P<0.0001$ ], bladder irrigation frequency \$ \$3 times/week [OR=2.63, 95%CI (1.66, 4.17),  $P<0.0001$ ], bladder function training intervention time \$ \$2 weeks [OR=2.75, 95%CI (1.69, 4.46),  $P<0.0001$ ], and rehabilitation intervention time  $>7$  days [OR=3.03, 95%CI (1.42, 6.48),  $P=0.004$ ] were risk factors for UTI in neurogenic bladder patients.

**Conclusion:** Advanced age, female gender, diabetes mellitus, hypoalbuminemia, stroke episodes \$ \$2, indwelling catheter, intermittent catheterization \$ \$2 times/week, bladder irrigation frequency \$ \$3 times/week, bladder function training intervention time \$ \$2 weeks, and rehabilitation intervention time  $>7$  days are risk factors for UTI in neurogenic bladder patients. Clinical staff should identify high-risk factors early and implement targeted control of modifiable factors to prevent or reduce UTI occurrence. However, due to limitations in the quality and quantity of literature for certain factors, these conclusions require verification by higher-quality studies.

**Keywords:** neurogenic bladder; urinary tract infection; risk factors; meta-analysis

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Neurogenic bladder is a lower urinary tract dysfunction caused by neurological lesions, with common etiologies including cerebrovascular accidents, spinal cord injury, diabetes mellitus, and iatrogenic factors. It manifests as urinary retention, incontinence, pyelonephritis, urinary tract infection, and other storage or voiding problems [1-2]. Among these complications, urinary tract infection is the most common and significant, affecting approximately 20% of neurogenic bladder patients with recurrent UTIs. This not only severely impacts rehabilitation progress but is also associated with substantial morbidity and mortality, markedly reducing quality of life [3-4]. Therefore, preventing UTIs is a clinical priority for improving patient prognosis, making early identification of risk factors for UTI in neurogenic bladder patients essential. Recent studies have identified numerous risk factors, including advanced age, diabetes mellitus, long-term indwelling catheterization, and multiple intermittent catheterizations, though investigated factors and conclusions vary across studies. This meta-analysis aims to explore risk factors for UTI in neurogenic bladder patients to provide

an evidence-based reference for early identification and prevention of UTIs.

### 1.1 Literature Inclusion and Exclusion Criteria

**Inclusion criteria:** (1) Study population: patients with neurogenic bladder from various causes; (2) Study content: risk factors, influencing factors, or predictive factors for UTI in neurogenic bladder patients; (3) Study design: cohort or case-control studies; (4) Language: Chinese or English; (5) Outcome measure: UTI incidence.

**Exclusion criteria:** (1) Studies involving pediatric patients; (2) Duplicate publications; (3) Articles with data that could not be transformed or extracted for application.

### 1.2 Search Strategy

We searched PubMed, Web of Science, Cochrane Library, Embase, CNKI, Wanfang, VIP, and the China Biomedical Literature Database, with a timeframe from database inception to June 2022. We also traced references from included studies. Searches combined subject headings and free-text terms. Chinese search terms included “神经源性膀胱/神经源性膀胱功能障碍/神经源性下尿路功能障碍,” “尿路感染/泌尿系感染,” and “危险因素/影响因素/相关因素/预测因素.” English search terms included “urinary bladder, neurogenic bladder/neurogenic bladder dysfunction/neurogenic urinary bladder/neurogenic lower urinary tract dysfunction,” “urinary tract infections/urinary tract infection,” and “risk factor/influence factor/related factor/predictor.”

### 1.3 Literature Screening and Data Extraction

Two researchers independently conducted literature screening and data extraction according to inclusion and exclusion criteria, then cross-checked extracted information. Disagreements were resolved through discussion or consultation with a third party. Initial screening was performed by reviewing titles and abstracts to exclude irrelevant literature, followed by full-text review for final inclusion. Extracted data included first author, publication year, study type, sample size, UTI incidence, and included factors.

### 1.4 Literature Quality Assessment

The Newcastle-Ottawa Scale (NOS) [5] was used to evaluate cohort or case-control studies. The NOS total score is 9 points, with \$ \$4 points indicating low quality, 5-6 points moderate quality, and \$ \$7 points high quality. Disagreements between the two reviewers were resolved through discussion or by a third party.

### 1.5 Statistical Analysis

RevMan 5.3 software was used for statistical analysis. Dichotomous variables were expressed as odds ratios (OR) with 95% confidence intervals (CI). Hetero-

ogeneity was assessed using the  $X^2$  test. If  $P > 0.1$  and  $I^2 < 50\%$ , indicating no significant statistical heterogeneity, a fixed-effects model was used to combine effect sizes. If  $P \leq 0.1$  and  $I^2 \geq 50\%$ , indicating substantial heterogeneity, sensitivity analysis was performed to identify heterogeneity sources. If significant heterogeneity persisted, a random-effects model was used. Funnel plots were used to detect publication bias when  $\geq 10$  studies were included.

## 2.1 Literature Screening Process and Results

The initial search yielded 747 articles (601 English, 146 Chinese). After removing 223 duplicates and 506 articles through title and abstract screening, 18 articles remained. Full-text review resulted in final inclusion of 13 articles [6-18]. The literature screening process is shown in Figure 1 [Figure 1: see original paper].

## 2.2 Basic Characteristics and Quality Assessment of Included Literature

This study included 13 articles: 4 case-control studies and 9 cohort studies. NOS scores ranged from 6-8 points, with 7 high-quality articles ( $\geq 7$  points), indicating overall good methodological quality. Basic characteristics and quality assessments are shown in Table 1 and Table 2.

### 2.3.1 Age

Nine studies [6-7,11-13,15-18] addressed age as a factor for UTI in neurogenic bladder patients, with data from 5 studies available for pooled analysis. Three studies [11-12,15] reported the relationship between age  $\geq 60$  years and UTI, with no heterogeneity ( $I^2 = 0$ ). The fixed-effects model showed age  $\geq 60$  years was a risk factor [OR=2.50, 95%CI (1.83, 3.41),  $P < 0.00001$ ]. Two studies [7,13] reported age  $\geq 65$  years as a risk factor, also with no heterogeneity ( $I^2 = 0$ ) [OR=2.13, 95%CI (1.40, 3.25),  $P = 0.0004$ ], as shown in Figures 2 [Figure 2: see original paper] and 3 [Figure 3: see original paper].

### 2.3.2 Gender

Eleven studies [6-7,9-12,14-18] examined gender as a factor, with significant heterogeneity ( $P < 0.00001$ ,  $I^2 = 81\%$ ). After sensitivity analysis excluding two studies [9,12], heterogeneity decreased ( $I^2 = 21\%$ ). The fixed-effects model showed female gender was a risk factor [OR=0.78, 95%CI (0.63, 0.96),  $P = 0.02$ ], as shown in Figure 4 [Figure 4: see original paper].

### 2.3.3 Diabetes Mellitus

Ten studies [6-8,10,12-16,18] investigated diabetes as a factor, with substantial heterogeneity ( $P < 0.00001$ ,  $I^2 = 92\%$ ). After excluding three studies [6,10,13], heterogeneity decreased ( $I^2 = 46\%$ ). The fixed-effects model showed diabetes was

a risk factor [OR=3.17, 95%CI (2.58, 3.89),  $P<0.00001$ ], as shown in Figure 5 [Figure 5: see original paper].

### 2.3.4 Hypoalbuminemia

Seven studies [6-8,13,15-16,18] examined hypoalbuminemia, with heterogeneity ( $P=0.001$ ,  $I^2=73\%$ ). After excluding Shi et al. [13], heterogeneity resolved ( $I^2=0\%$ ). The fixed-effects model showed hypoalbuminemia was a risk factor [OR=2.26, 95%CI (1.67, 3.06),  $P<0.00001$ ], as shown in Figure 6 [Figure 6: see original paper].

### 2.3.5 Stroke Episodes

Two studies [12,16] addressed stroke episodes, with notable heterogeneity ( $P=0.06$ ,  $I^2=72\%$ ). Using a random-effects model, meta-analysis showed stroke episodes were a risk factor [OR=3.30, 95%CI (1.70, 6.41),  $P=0.0004$ ], as shown in Figure 7 [Figure 7: see original paper].

### 2.3.6 Urination Mode

Five studies [6-7,12,14,17] examined urination mode, with substantial heterogeneity ( $P<0.00001$ ,  $I^2=96\%$ ). After excluding Peng et al. [12], heterogeneity resolved ( $I^2=0\%$ ). The fixed-effects model showed indwelling catheterization was a risk factor [OR=2.88, 95%CI (2.09, 3.95),  $P<0.00001$ ], as shown in Figure 8 [Figure 8: see original paper].

### 2.3.7 Catheterization Duration

Seven studies [9-11,13,15-16,18] addressed catheterization duration, with data from 4 studies available for pooled analysis. Two studies [10,16] examined duration  $>7$  days, showing substantial heterogeneity ( $P<0.00001$ ,  $I^2=96\%$ ). Random-effects analysis indicated duration  $>7$  days was not a risk factor [OR=9.01, 95%CI (0.52, 157.63),  $P=0.13$ ]. Two studies [11,13] examined duration  $\geq 14$  days, also with heterogeneity ( $P=0.05$ ,  $I^2=73\%$ ). Random-effects meta-analysis showed duration  $\geq 14$  days was not a risk factor [OR=3.68, 95%CI (0.76, 17.87),  $P=0.11$ ].

### 2.3.8 Intermittent Catheterization Frequency

Four studies [11,13,15,18] examined intermittent catheterization frequency, with data from 3 studies [11,13,15] available for pooled analysis. No statistical heterogeneity was found ( $P=0.26$ ,  $I^2=25\%$ ). The fixed-effects model showed frequency  $\geq 2$  times/week was a risk factor [OR=2.44, 95%CI (1.62, 3.68),  $P<0.0001$ ], as shown in Figure 9 [Figure 9: see original paper].

### 2.3.9 Bladder Irrigation Frequency

Three studies [15-16,18] addressed bladder irrigation frequency, with data from 2 studies [15-16] available for pooled analysis. No statistical heterogeneity was observed ( $P=0.21$ ,  $I^2=36\%$ ). The fixed-effects model showed frequency  $\geq 3$  times/week was a risk factor [OR=2.63, 95%CI (1.66, 4.17),  $P<0.0001$ ], as shown in Figure 10 [Figure 10: see original paper].

### 2.3.10 Bladder Function Training Intervention Time

Three studies [7,11,15] examined bladder function training intervention time, with no heterogeneity ( $P=0.47$ ,  $I^2=0\%$ ). The fixed-effects model showed intervention time  $\geq 2$  weeks was a risk factor [OR=2.75, 95%CI (1.69, 4.46),  $P<0.0001$ ], as shown in Figure 11 [Figure 11: see original paper].

### 2.3.11 Rehabilitation Intervention Time

Three studies [10,16,18] addressed rehabilitation intervention time, with data from 2 studies [10,16] available for pooled analysis. Notable heterogeneity was observed ( $P=0.07$ ,  $I^2=69\%$ ). Random-effects meta-analysis showed rehabilitation intervention time  $>7$  days was a risk factor [OR=3.03, 95%CI (1.42, 6.48),  $P=0.004$ ], as shown in Figure 12 [Figure 12: see original paper].

### 2.3.12 Prophylactic Antimicrobial Use

Six studies [7,11-12,15-16,18] examined prophylactic antimicrobial use, with substantial heterogeneity ( $P=0.02$ ,  $I^2=69\%$ ). After sensitivity analysis excluding Cheng et al. [18], heterogeneity decreased ( $I^2=32\%$ ). Results showed prophylactic antimicrobial use was not a risk factor [OR=1.18, 95%CI (0.94, 1.48),  $P=0.15$ ].

## 3.1 Methodological Quality of Included Studies

Among the 13 included articles, 4 were case-control studies and 9 were cohort studies, with 9 published within the last 5 years. NOS quality scores ranged from 6-8 points, indicating moderate to high quality and overall reliable conclusions. Statistical heterogeneity primarily stemmed from differences in sample sizes, inclusion/exclusion criteria, and study regions.

## 3.2 General Factors Increasing UTI Risk in Neurogenic Bladder Patients

Advanced age, female gender, and hypoalbuminemia increased UTI risk. Older age correlated with higher UTI risk, likely because elderly patients have weakened organ function and immunity, often with comorbidities, consistent with Jiang et al. [19]. Female patients have shorter, wider urethras near the anus,

facilitating bacterial colonization and retrograde infection, especially in postmenopausal women with decreased estrogen levels, reduced urethral blood supply, and diminished muscular tone, consistent with Kakde et al. [20] and Jung et al. [21]. Serum albumin reflects nutritional status; decreased levels impair immune function, reduce lymphocyte counts, and diminish phagocytic capacity against pathogens, potentially increasing UTI risk [22]. Clinicians should strengthen management of elderly and hypoalbuminemic patients, regularly monitoring serum albumin levels and nutritional risk.

### 3.3 Disease-Related Factors Increasing UTI Risk

Diabetes mellitus and stroke episodes [2] increased UTI risk. Diabetic patients had 3.31 times higher UTI risk, possibly because hyperglycemia impairs neutrophil phagocytosis and self-defense, creating favorable conditions for bacterial growth while reducing tissue defense and repair functions [23]. For diabetic patients, dynamic blood glucose monitoring and control are essential for UTI prevention. Stroke patients, predominantly middle-aged and elderly with poor constitution requiring prolonged bed rest, have decreased pathogen resistance. Neurological damage correlates with extended bed rest and neural repair time, often requiring long-term catheterization and increasing UTI risk [24]. More stroke episodes correlate with more severe conditions and higher UTI risk [16]. Only 2 studies reported this relationship, requiring further verification.

### 3.4 Treatment-Related Factors Increasing UTI Risk

Indwelling catheterization, intermittent catheterization [2] times/week, bladder irrigation frequency [3] times/week, bladder function training intervention time [2] weeks, and rehabilitation intervention time >7 days increased UTI risk. However, whether catheterization duration >7 days, [14] days, or prophylactic antimicrobial use are risk factors remains uncertain. Indwelling catheterization, as an invasive procedure, disrupts normal anatomical structures, reduces local urethral resistance, and allows pathogens to enter via the catheter. Without urine flushing, bacteria accumulate locally, causing infection [18,25]. Strict aseptic technique during catheter replacement is essential to prevent retrograde infection. Higher intermittent catheterization frequency increases UTI risk, possibly because uropathogens like *E. coli* adhere tightly to urothelial cells via fimbriae, impairing normal urethral peristalsis. With the urethra's proximity to the anus harboring many pathogens, more catheterizations increase invasion opportunities [11]. Excessive bladder irrigation may cause mechanical bladder wall injury, mucosal damage, and increase urethral orifice infection risk [26]. Clinicians should optimize irrigation frequency. Appropriate bladder function training can reduce urinary retention severity, improve bladder function, and promote complete emptying to prevent UTIs [27,28]. Rehabilitation intervention reduces residual urine volume, and intervention timing affects UTI risk. Therefore, early rehabilitation training should be implemented to improve physical function and reduce UTIs.

### 3.5 Limitations

First, differences in sample sizes, case selection, and study regions across included studies may have contributed to heterogeneity and affected results. Second, we identified potential relationships between UTI risk and hospitalization duration [6,12], concurrent pulmonary infection [10], increased residual urine volume [13], low family support [13], bladder capacity <200mL [17], increased bladder pressure [17],  $WBC > 10 \times 10^9 / L$  [6], and urine  $pH > 7$  [6], but could not perform pooled analysis due to limited study numbers or non-extractable data. Future large-sample, prospective studies controlling for confounders should explore these factors.

### 4 Conclusion

This study demonstrates that advanced age, female gender, diabetes mellitus, hypoalbuminemia, stroke episodes  $\geq 2$ , indwelling catheterization, intermittent catheterization  $\geq 2$  times/week, bladder irrigation frequency  $\geq 3$  times/week, bladder function training intervention time  $\geq 2$  weeks, and rehabilitation intervention time  $> 7$  days are risk factors for UTI in neurogenic bladder patients. Only 2 studies contributed to pooled analyses for stroke episodes, bladder irrigation frequency, and rehabilitation intervention time, necessitating more high-quality research for validation and refinement to provide reliable evidence for early identification of high-risk patients and UTI prevention.

**Author Contributions:** HE Manlan was responsible for conceptualization, statistical analysis, and manuscript writing. YUAN Ping conducted feasibility analysis and manuscript revision. HE Manlan and HE Lei performed literature collection, organization, and evaluation. CHEN Lu was responsible for quality control and final approval of the manuscript.

**Conflict of Interest:** The authors declare no conflict of interest.

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