Is It Really the Foley? A Systematic Review of Bladder Management and Infection Risk

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Background: The belief that intermittent catheterization results in fewer infections than indwelling catheters is commonly expressed in the spinal cord injury literature. Some practice guidelines strongly recommend intermittent over indwelling catheterization due to concerns about infections and other complications. However, studies on this topic are of low quality. Guidelines from the Consortium for Spinal Cord Medicine suggest the data regarding infection risk are mixed, and they do not recommend one bladder management method over the other. **Objectives**: To compare risk of bias in studies reporting higher rates of urinary tract infection (UTI) with indwelling catheters to studies that found equal rates of UTI between indwelling and intermittent catheterization, and to describe implications in clinical decision-making. **Methods**: A systematic search of PubMed, CINAHL, Embase, and SCOPUS databases from January 1, 1980, to September 15, 2020, was conducted. Eligible studies compared symptomatic UTI rates between indwelling and intermittent catheterization. We used a risk of bias assessment tool to evaluate each study. **Results**: Twenty-four studies were identified. Only three of these reported significantly higher UTI risk with indwelling catheters, and all three demonstrated a critical risk of bias. More than half of the studies reported differences in UTI risk of less than 20% between the two methods. Studies with larger (nonsignificant) differences favoring intermittent catheterization were more susceptible to bias from confounding. **Conclusion**: The hypothesis that indwelling catheters cause more UTIs than intermittent catheterization is not supported by the scientific literature. Most studies failed to demonstrate a significant difference in UTI risk, and studies with nonsignificant trends favoring intermittent catheterization were more susceptible to bias from confounding. Perceived risk of infection should not influence a patient's choice of catheter type. **Key words**: *bladder management, infection prevention, urinary tract infection*

Introduction

Several different clinical practice guidelines address spinal cord injury (SCI) neurogenic bladder and the considerations that affect clinical decision-making when choosing between bladder management methods (BMM). Relative risk of infection may be an important factor in BMM selection. However, studies addressing this topic have produced mixed results. Guidelines from the Consortium for Spinal Cord Medicine acknowledge this discrepancy, reporting, "Conflicting data exist related to the risk of symptomatic infection in individuals using indwelling catheters versus other methods of bladder management."[1]

Other guidelines present a less ambiguous perspective on infection risk among the various BMM. Some include strong recommendations for intermittent catheterization (IC) over indwelling (IND), citing reduced infection risk as one of the benefits.[2-5] Guidelines from the European Association of Urology and the Infectious Diseases Society of America (IDSA) describe IC as the "gold standard" or "standard of care," a sentiment repeated by other authors.[6-8] Guidelines from the Centers for Disease Control and Prevention, IDSA, and the Association for Professionals in Infection Control and Epidemiology (APIC) [5,9,10] suggest IC as an alternative to IND as a means of urinary tract infection (UTI) prevention in the SCI population.[9,11,12] However, the studies cited to support these recommendations are very low quality, and other studies with conflicting results are not mentioned.

Potential sources for the conflicting results include heterogeneity between studies in patient populations, definitions of UTI, and methods of controlling for potential confounders. In addition to BMM, other proposed risk factors for UTI in

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SCI have included disruption of the intravesical glycosaminoglycan layer, bladder ischemia, impaired secretory immunoglobulin A response, and other immunological deficiencies.[13]

The issue of confounding related to immune status may be particularly important. Research into dysfunction of the immune system in SCI demonstrates a continuously evolving state of immune dysfunction that begins almost immediately after onset of SCI and continues into the chronic phase—the Spinal Cord Injury Immune Deficiency Syndrome (SCI-IDS). This syndrome appears to result from denervation of lymphoid organs and dysregulation of the sympathetic nervous system.[14] It produces profound changes in both innate and adaptive immune responses that appear to be clinically significant in animal models and in retrospective human studies.[15-17] Most important to this topic, SCI-IDS appears to be most pronounced in the first 30 to 90 days postinjury, more pronounced in patients with cervical and upper thoracic lesions, and more pronounced in those with more complete SCI.[16,18-21] Guidelines from the Consortium for Spinal Cord Medicine report this demographic is also more likely to utilize IND.

If sufficient overlap exists between those who are most likely to be severely immunosuppressed and those who are most likely to utilize IND, then SCI-IDS may represent an important confounder that could bias study results in favor of IC. None of the studies included in this review directly measured the immunological status of their subjects. However, neurological level of injury, injury severity, and acuity of SCI are all factors related to severity of SCI-IDS, and controlling for all three of these covariates might serve as a reasonable alternative. Many of the studies collected data on patients' level and severity of injury, and some of them accounted for time since initial SCI. Others enrolled only patients with chronic SCI, who were outside the timeframe of most profound immunosuppression. Studies that control for these factors should be less susceptible to confounding from SCI-IDS.

Another possible source of heterogeneity of results could relate to differences in definitions of UTI and in methods of outcome assessment. In 1992, the National Institute on Disability and Rehabilitation Research produced a consensus statement in which UTI in the SCI population was defined as bacteriuria with pyuria and new-onset signs or symptoms.[22] However, bacteriuria and pyuria are very common in asymptomatic patients, and some of the nonspecific symptoms included in various definitions have demonstrated poor predictive value in diagnosing UTI.[22-25] In this context, an unblinded clinician, who may be more inclined to attribute nonspecific symptoms to UTI in patients with one BMM over another, could introduce further bias. Studies with better designs required fever—which is more objective and relatively specific to infection— for the diagnosis of UTI.

We hypothesized that studies demonstrating higher UTI rates for those using IND would be more susceptible to bias related to inadequate controlling for level, completeness, and time since injury—factors that are also correlated with depressed immune function. We also hypothesized that this group of studies would be more susceptible to bias related to nonspecific definitions of UTI. The ROBBINS-I tool was developed by Cochrane as an organized framework to explore these potential sources of bias and to grade their severity.[26] The purpose of this review was to compare risk of bias among studies that reported higher rates of UTI with IND to those that reported similar rates between IND and IC and to make inferences that might assist in clinical decision-making.

Methods

Eligibility criteria

We chose to focus on studies involving adults with SCI published between January 1, 1980, and September 15, 2020. Only studies published in English were included. Studies needed to provide a comparison between incidence of UTI in patients using IND versus IC (groupings such as "catheterized vs. non-catheterized" were not acceptable). Diagnosis of UTI could not be based solely on urine culture results; the studies had to draw a clear distinction between bacteriuria and symptomatic UTI.

Search strategy

We conducted a search of the PubMed, CINAHL, Embase, and SCOPUS databases. The search was limited to the dates listed above. In the PubMed database, we used the following terms: Urinary tract OR urinary tract infections OR bacteriuria OR neurogenic bladder OR neuropathic bladder (USING BOTH keywords / MeSH terms) AND Paraplegia OR quadriplegia OR spinal cord injur*. This search strategy was adapted to the other databases as appropriate. Articles cited in references of candidate articles were also evaluated. We did not register the protocol for this systematic review.

Study selection

Two reviewers (M.D. and E.R.) evaluated the titles and abstracts of the articles retrieved. Full-text articles were retrieved for studies with abstracts compatible with the selection criteria. Final inclusion in the review required consensus among the authors.

Risk of bias assessment

The ROBINS-I tool presents a systematic method of evaluating nonrandomized studies, with specific criteria for grading risk of bias in seven different domains: bias due to confounding, bias in measurement of outcomes, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended intervention, bias due to missing data, and bias in selection of the reported result. All of the studies had limitations in several of the seven domains, but most of these limitations would not predictably favor one BMM over another. Therefore, the choice was made to focus efforts on the two domains mentioned previously: bias due to confounding and bias in measurement of outcomes. The Cochrane Collaboration provides a ROBINS-I Tool Template, a series of questions as a guide to using the tool. The authors divided the studies among themselves and completed the ROBINS-I Tool Template for each study. For studies that differentiated between self-IC and IC-by-attendant (IC-A), the authors reasoned that the most appropriate comparison would be between IND and IC-A, because both methods tend to be used more often in the early acute phase of SCI and in those with more severe neurological impairment. Results of each analysis were compared among the authors for consensus, and the severity of bias for each of the two domains was assigned according to guidance provided by the ROBINS-I tool guide.

The rationale for assigning various categories of risk is summarized in **Table 1**. Given the low positive predictive value of urine culture, pyuria, and many of the subjective, nonspecific symptoms often attributed to UTI, we required the presence of fever in order to assign the most favorable grade in bias in measurement of outcomes. Studies relying on patient self-report of UTIs that did not require confirmatory urinalysis or urine culture received the least favorable grade. For the bias due to confounding domain, studies had to either exclude acutely injured patients, who would presumably be inside the expected window of most profound immunosuppression, or control for neurological level, completeness, and acuity of injury in order to qualify for the most favorable grade.

Results

The search yielded 24,378 articles. Of these, 24 articles met our eligibility criteria[6,7,11,27-47] (**Figure 1**). Among these, the term "indwelling" referred exclusively to suprapubic catheters (SPC) in two studies.[32,39] Four studies divided the IND group into separate categories of urethral and suprapubic catheters for comparison between the groups.[11,28,29,34] For the remaining 18 studies, the "indwelling" group was composed almost entirely of urethral catheters. No important differences were found between infection rates with urethral versus suprapubic indwelling catheters. Among IC groups, five studies differentiated between self-IC and IC-A.[6,28,29,31,43] For these studies, we compared results between IND and IC-A.

Only four studies reported statistically significant differences in UTI risk in direct comparisons between IC and IND. Three studies reported significantly higher UTI rates associated with IND,[11,38,44] and one study reported a significantly higher UTI rate associated with IC-A.[28] Given the paucity of statistically significant results, we chose to divide the studies into two groups: those that contained at least one finding that reported a greater

Table 1. Rationale for grading

	Grade	Rationale for grading
Bias due to confounding	Moderate	Did not directly measure or control for SCI-IDS but did control for acuity and severity of SCI (both level and AIS grade); or studied only patients with chronic SCI, who were expected to be less likely to be affected by immune system dysfunction
	Serious	At least one known important, potentially confounding domain (acuity, severity of SCI) was not appropriately measured, or not controlled for. **Studies with this designation are inherently unable to differentiate between relationships of *association* and *causation.***
	CRITICAL	Confounding inherently not controllable.
Bias in measurement of outcomes	Low	Rigorous definition of UTI requiring pyuria, bacteriuria, and fever. Blinded assessor of outcomes.
	Serious	Definition of UTI requires confirmed pyuria and bacteriuria but also relied on vague or nonspecific symptoms. Unblinded assessor.
	Serious +	Relied on patient self-reporting of UTI, without confirmation of pyuria or bacteriuria.

Note: AIS = American Spinal Injury Association Impairment Scale; SCI = spinal cord injury; SCI-IDS = Spinal Cord Injury Immune Deficiency Syndrome; UTI = urinary tract infection.

than 20% increased rate of UTI in those utilizing IND and those that did not (**Table 2**).

Fewer than half of the studies (11 out of 24) reported a greater than 20% increased rate of UTI in those utilizing IND.[6,7,11,34,38,40,42-45,47] Among the remaining 13 studies, seven reported higher UTI rates in those using IC or IC-A,[28,29,31,32,36,37,39] and six reported little or no difference in UTI rates between the two methods.[27,30,33,35,41,46]

Bias due to confounding

The findings from the risk of bias due to confounding analyses are summarized in **Table 2**. All three studies with significant findings in favor of IC demonstrated critical risk of bias due to confounding (confounding that was inherently not controllable):

1. The study by Esclarin et al.[11] has been cited by several clinical practice guidelines to support the use of IC over IND.[5,9,10] In this study, the incidence of UTI was measured in UTIs per 100 person days. Acutely injured patients were admitted with urethral catheters, which remained in place until close monitoring of urinary output was no longer indicated. Then, all patients were transitioned to IC, with a median length of stay of 207 days. This practice pattern ensured that nearly all "Foley days" occurred during the early acute phase of SCI that corresponds to the period of most profound immune suppression from SCI-IDS, and a substantial portion of IC days occurred after this time.
2. In the study by Singh et al.,[44] practice patterns in the initial hospitalization were similar to those in Esclarin et al.: acutely injured patients were admitted with IND, which they kept for an average of 25 days, and were then strongly encouraged to adopt IC. Many

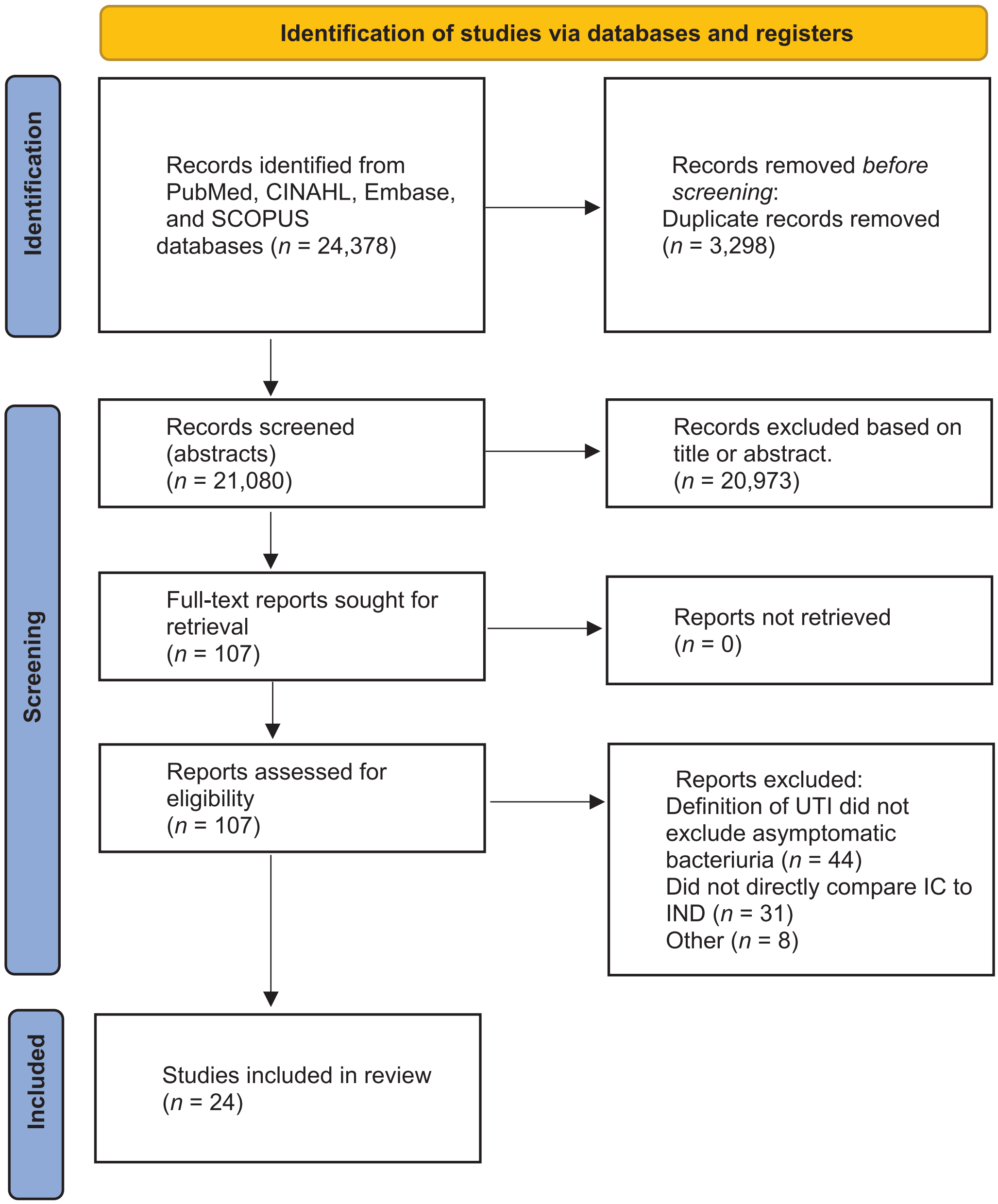

Figure 1. PRISMA flow diagram showing the results of the searches.

patients changed BMM. The patients were followed for 1 year and were assigned to the BMM group according to the method that they had used for the majority of time since injury, with no apparent effort to match UTIs with the BMM used at the time of infection.

3. In the study by McGuire and Savastano,[38] the proportion of persons with tetraplegia in the IND group was more than twice that in the IC group. Completeness of injury was not recorded, and those with IND underwent cystoscopy every 3 months, a procedure that carries a risk of UTI as a complication.

Among the eight studies demonstrating a nonsignificant, >20% difference in unadjusted UTI rates, risk of bias was found to be critical in three,[40,43,44] serious in three,[6,42,45] and moderate in two.[7,34] Krebs et al.[34] deserves attention, as it has been cited by clinical practice guidelines[2,4] to support

Table 2. Risk of bias due to confounding

Author, year	Patient groups	ROBINS-I grade, and rationale	Findings
Studies reporting similar UTI rates between BMM, or with results favoring IND			
Anderson et al., 2019[27]	Total *N* = 369 IND = 192 IC-A = 41	**Moderate**: NLOI, injury severity, and acuity were subjected to multivariate analysis.	Incidence rate ratio for UTI: IND: 5.97 IC-A: 6.05
Cardenas & Mayo, 1987,[28] acute arm of study	Total *N* = 705 IUC = 114 SPC = 36 IC-A = 103	**Serious:** Did not control for AIS or acuity.	% patients who experienced UTI while admitted: IUC: 42% SPC: 47% IC-A: 58%
Cardenas & Mayo, 1987,[28*] chronic arm of study	Total *N* = 371 IUC = 57 SPC = 16 IC-A = 24	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	% outpatients who experienced UTI in outpatient setting: IND: 44% SPC: 56% IC-A: 83%
Chen et al., 2014[29]	Total *N* = 894 IUC = 102 SPC = 103 IC = 163	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	% of patients who experienced UTI: IUC: 33% SPC: 37% IC: 41%
Drake et al., 2005[30]	Total *N* = 196 IUC = 40 SPC = 7 IC = 20	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS grade less important.	"no significant difference in risk of UTI for [IND] (P=0.17), IC (P=0.45)"
Goodes et al., 2020[31]	Total *N* = 70 [a]	**Serious**: Did not account for acuity of SCI.	Incidence of UTI per 100 person-days: IUC: 1.3 IC-A: 2.0
Grundy et al., 1983[32b]	Total *N* = 28 SPC = 14 IC = 14	**Serious**: Did not control for NLOI or AIS.	Febrile UTI per 100 catheter-days: SPC: 0.6 IC: 0.7
Hennessey et al., 2019[33]	Total *N* = 143 [b]	**Serious**: Did not control for AIS or acuity.	Incidence of UTI per 1000 person-days: IND: 8.33 IC: 6.84

(continues)

Table 2. Risk of bias due to confounding *(cont.)*

Author, year	Patient groups	ROBINS-I grade, and rationale	Findings
Ku et al., 2005[35]	Total *N* = 175 IUC = 29 SPC = 42 IC = 48	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	% patients with febrile UTI: IUC: 41% SPC: 31% IC: 42%
Liguori et al., 1997[36]	Total *N* = 81 IND = 11 IC = 32	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	No. of UTIs within the past 1 and 3 years: IND: 1 and 4 IC: 2 and 6
Lloyd et al., 1986[37]	Total *N* = 204 IUC = 129 SPC = 21 IC = 21	**Serious**: did not control for NLOI and AIS.	% of patients who experienced febrile UTI: IUC: 8.6% SPC: 19% IC: 19%
Mitsui et al., 2000[39]	Total *N* = 61 SPC = 37 IC = 27	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	% of patients who experienced UTI: SPC: 12% IC-A: 26%
Ploypetch et al., 2013[41]	Total *N* = 100 IUC = 54 IC = 26	**Serious**: Did not control for acuity of SCI.	% of patients who experienced UTI: IUC: 52% IC:42%
Timoney & Shaw, 1990[46]	Total *N* = 52 IUC = 14 SPC = 4 IC = 28	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	% of patients who experienced recurrent febrile UTI: IUC: 38% SPC: not reported IC: 36%
Studies with at least one finding showing a 20% or greater increased incidence of UTI with IND compared to IC			
Afsar et al., 2013[6]	Total *N* = 164 IND = 16 IC = 104	**Serious**: Did not control for NLOI, AIS, or acuity.	Number of UTIs per year: IND: 3 IC: 2
Esclarin et al., 2000[11]*	Total *N* = 128 IUC = 128 SPC = 10 IC = 124	**CRITICAL**: All IND catheter-days occurred during early acute period. Substantial portion of IC-days occurred later.	Incidence of UTI per 100 catheter days: IUC: 2.72 SPC: 0.34 IC: 0.41

(continues)

Table 2. Risk of bias due to confounding *(cont.)*

Author, year	Patient groups	ROBINS-I grade, and rationale	Findings
Krebs et al., 2016[34]	Total *N* = 1104 IUC = 18 SPC = 120 IC = 427	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	% of patients with at least 1 and 3 or more UTI per year: IUC: 83% and 50% SPC: 58% and 18% IC: 71% and 31%
McGuire & Savastano, 1986*	Total *N* = 35 IND = 13 IC = 22	**CRITICAL**: Proportion of persons with tetraplegia in IND group was more than twice that in the IC group. IND group underwent cystoscopy every 3 months.	% of patients who experienced febrile UTI: IND: 92% IC: 32%
Nunn et al., 2015[40]	Total *N* = 143[a]	**CRITICAL:** Most IND catheter-days occurred during early acute period. Substantial portion of IC-days occurred later.	No. of UTIs per patient: IND: 1.36 IC: 0.79
Roth et al., 2019[42]	Total *N* = 1282 IUC = 190 SPC = 81 IC = 753	**Serious**: Did not control AIS or acuity.	Adjusted odds ratio for UTI rate and UTI hospitalization: IND: 4.16 and 2.90 IC: 3.42 and 2.06
Sekulić et al., 2015[43]	Total *N* = 540 IND = 31 IC-A = 69 Self-IC = 278	**CRITICAL**: Patients with IND had longer lengths of stay. Incidence of UTI-per-catheter-day was not calculated. Did not control for acuity.	Odds of experiencing UTI during inpatient admission: IND: 1.18 IC-A: 0.87
Singh et al., 2011[44]	Total *N* = 545 IUC = 224 SPC = 24 IC = 180	**CRITICAL**: Disproportionate use of IND in the early acute phase. Did not match UTIs with BMM at time of UTI. Did not control for NLOI, AIS, or acuity.	Incidence of UTI per 100 person-days: IUC: 2.68 IC: 0.34
Stillman et al., 2018[45]	Total *N* = 169 IND = 74 IC = 35	**Serious/Moderate:** Before multivariate analysis, those with IND suffered more UTIs than those on IC. After multivariate analysis, no difference between IND and IC was found.	Multiple data points regarding unadjusted incidence of UTI. After adjustment for level and severity of SCI, "UTI did not differ between [IND] and IC."
Togan et al., 2014[47]	Total *N* = 93 IND = 57 IC = 24	**Serious**. Did not control for AIS or acuity.	% of patients experiencing UTI: IND: 33% IC: 17%

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Table 2. Risk of bias due to confounding *(cont.)*

Author, year	Patient groups	ROBINS-I grade, and rationale	Findings
Yildiz et al., 2014[7]	Total *N* = 337 IUC = 12 IC = 243	**Moderate**: Excluded acute SCI, adjustment for NLOI and AIS less important.	% of patients experiencing UTI: IUC: 41% IC: 17%

Note: Total *N* reflects all bladder management methods, not exclusively IC or IND. AIS = American Spinal Injury Association Impairment Scale; BMM = bladder management method; IC = intermittent catheterization, without differentiating between self-IC and IC-A; IC-A = intermittent catheterization by attendant; IND = indwelling, undifferentiated; IUC = indwelling urethral catheter; NLOI = neurological level of injury; SPC = suprapubic catheter.
[a]Randomized controlled trial.
[b]Number of patients in each group varied over time, calculated UTIs per catheter-day.
*Statistically significant.

the clinical use of IC over IND. The authors of this study performed binary logistic regression analysis to control for neurologic level and completeness of injury. The study relied on self-reported UTIs in 1104 patients, including 427 using IC, 120 using SPC, and only 18 using IUC. Results for the IUC group showed dramatically wide confidence intervals. They found significantly higher odds of experiencing UTI in those using either IUC or IC over the reference group (spontaneous voiding). There was no significant difference between IC and IUC. Interestingly, the odds of experiencing UTI were not significantly higher in the SPC group than in the spontaneously voiding group.

In contrast, more than half of the studies included in the review reported little or no difference (<20%) in UTI risk between IC and IND. Studies in this group tended to demonstrate less susceptibility to bias from confounding and from outcome measurement. Among these studies, risk of bias was found to be serious in six[28,31,32,33,37,41] and moderate in the remaining eight.[27-30,35,36,39,46] Five of them used multivariate analysis to account for acuity, level, and/or completeness of injury,[27,30,31,35,36] and one was a randomized controlled trial.[30]

Bias in measurement of outcomes

Findings from the risk of bias due to measurement of outcomes analyses are summarized in **Table 3**. Similar to the findings for bias due to confounding, studies seeming to favor IC tended to be more susceptible to bias related to outcome measurement. Among the studies that seemed to favor IC, only one study[11] (which showed critical risk of bias due to confounding) utilized a definition of UTI that required fever, rather than nonspecific, subjective symptoms such as increased spasticity, cloudy urine, autonomic dysreflexia (AD), etc. Four of them relied on patient self-report.[7,34,42,45] In contrast, two of the catheter-neutral studies required a more objective definition of UTI,[28,46] and only one relied on patient-reported UTIs.[36]

Discussion

Our findings are in stark contrast with sentiments commonly expressed in clinical practice guidelines and in many of the articles reviewed for this article. For example, Ku et al. claimed, "It is well known that clean intermittent catheterization involves a lower incidence of urinary tract infections than indwelling catheterization." Some articles described patients who chose IND over IC as noncompliant.[6,33,48.49] Others suggested that healthcare providers who did not quickly transition patients to IC are failing to implement best practices.[50.51] Some suggested that infection risk should be a primary driving factor in choosing of IC over IND.[2,42,52]

We found that the available body of literature over the past four decades does not support these assertions. The majority of studies that met our

Table 3. Risk of bias in measurement of outcomes

Author, year	Non-specific definition?	Self-reported UTIs?	ROBINS-I grade
Studies with no significant findings or nonsignificant trends in favor of IC			
Anderson et al., 2019[27]	X		Serious
Cardenas & Mayo, 1987,[28] acute phase			Low
Cardenas & Mayo, 1987,[28] chronic phase		X	Serious
Chen et al., 2014[29]	X		Serious
Drake et al., 2005[30]	X		Serious
Goodes et al., 2020[31]	X		Serious
Grundy et al., 1983[32]			Low
Hennessey et al., 2019[33]	X		Serious
Ku et al., 2005[35]	X		Serious
Liguori et al., 1997[36]	X	X	Serious+
Lloyd et al., 1986[37]	X		Serious
Mitsui et al., 2000[39]	X		Serious
Ploypetch et al., 2013[41]	X		Serious
Timoney & Shaw,1990[46]			Low
Studies with at least one finding showing a 20% or greater increased incidence of UTI with IND compared to IC			
Afsar et al., 2013[6]	X		Serious
Esclarin et al., 2000[11]			Low
Krebs et al., 2016[34]	X	X	Serious+
McGuire, & Savastano 1986			Low
Nunn et al., 2015[40]	X		Serious
Roth et al., 2019[42]	X	X	Serious+
Sekulić et al., 2015[43]	X		Serious
Singh et al., 2011[44]	X		Serious
Stillman et al., 2018[45]	X	X	Serious+
Togan et al., 2014[47]	X		Serious
Yildiz et al., 2014[7]	X	X	Serious+

Note: + = diagnosis of UTI was based on patient self-report, with no objective confirmation involving urinalysis or culture.

inclusion criteria (87%) failed to demonstrate a significant difference in UTI rates between the two methods. Furthermore, more than half of the studies reported IND infection rates that were lower[28,29,31,32,36,37,39] or no worse than[27,30,33,35,41,46] those reported for IC or IC-A. All but one of the studies that reported marginally higher rates of UTI with IND failed to control for key covariates, and the three studies with statistically significant results demonstrated a critical risk of bias. The quality of the studies reporting equal rates of UTI between the BMM was also low, but the majority of them were judged to be less susceptible to confounding.

Despite this lack of support from the literature, several articles referred to IC as the "standard procedure,"[6,29] "method of choice,"[37] or "gold standard."[7,39] Some hospitals transitioned all patients from IND to IC.[11,6,31,33] This pronounced preference for IC was not limited to studies reporting higher rates of UTI in the IND group. For example, Goodes et al.[31] noted that "our findings suggest that early removal of IDCs may be beneficial," despite finding that the number of UTIs per 100 person days was more than 50% higher in the IC-A group than the IND group. Ku et al., quoted earlier, reported UTI rates that were identical between IC and IUC and lower for SPC. These types of discrepancies underscore challenges with the peer-review process.

Authors cited a variety of sources in their support of IC over IND. These references had important limitations:

- Several of the articles cited were not included in this review because they failed to directly compare infection risk between IC and IND[2,53-55] or because they failed to differentiate between symptomatic infection and asymptomatic bacteriuria.[56]
- Two studies were found to have critical risk of bias due to confounding in this review.[11,38]
- One study reported a significant difference in UTI risk between IUC and spontaneous voiding but not between IUC and IC.[34]
- Several references were not clinical trials but rather were review articles and practice guidelines, which based their recommendations on the studies noted above.

Although most articles that met our inclusion criteria failed to find significant associations between BMM and UTI, several of them identified other covariates that *were* significantly associated. Three studies reported greater UTI rates in persons with more rostral injuries,[11,30,45] two reported fewer UTIs in patients with AIS D injuries,[27,30] four studies reported more UTIs in those with motor complete SCI,[31,35,45] and two studies reported higher rates of UTI in the early acute phase.[27,41] These findings support our concern that the SCI-IDS may be a relevant confounder that deserves consideration in future infection-related studies.

The most dramatic associations occurred between UTI and bladder behavior during urodynamic testing. Esclarin et al.[11] reported the presence of vesicoureteral reflux increased the odds of UTI 23-fold, and Ploypetch et al.[41] reported a 21-fold increase. Sekulić et al.[43] reported that a "hyper-reflexive bladder" increased the odds of UTI 59-fold.

Factors like bladder behavior, severity, and acuity of injury often influence choice of BMM. Commonly cited reasons patients give for reverting from IC to IND include incontinence between catheterizations, dependence on caregivers, and lack of hand function.[1] IND use has been correlated with more rostral level of injury and with acuity of SCI[6,11,31]; these factors also correlate with enhanced susceptibility to infection.[16,18-21] This combination of risk factors support the findings in a recent meta-analysis that reported an increased *association* between UTI and IND.[52] Our review suggests that any assumptions about a *causal* link between the various BMM and UTI are erroneous.

Limitations

This review was limited to a relatively small number of studies. The only randomized trial in this review involved 28 patients.[32] Heterogeneity of study design and patient populations precluded pooling of results to allow for meta-analysis. When possible, we chose to compare UTI rates related to IND with IC-A (rather than self-IC), because we felt the neurological status of patients of the IC-A group would more closely resemble that of the IND group. This may not be an accurate or relevant assumption.

Conclusion

The scientific literature does not support the common belief that IND confers a greater risk of UTI than IC. The majority of studies failed to demonstrate a significant difference between the two BMM. Studies with nonsignificant trends appearing to favor IC were fewer in number than those without such trends, and they were more susceptible to bias from confounding. Perceptions about risk of infection should not drive clinical decision-making when choosing between IND and IC.

Conflicts of Interest

The authors declare no conflicts of interest.

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