

Risk Factors for Urosepsis After Ureteroscopy for Stone Disease: A Systematic Review with Meta-Analysis

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Abstract

Introduction: Urosepsis is a serious potential complication of ureteroscopic procedures for stone disease, yet the risk factors for this complication are not well characterized. The purpose of this systematic review with meta-analysis was to identify potential risk factors for urosepsis after ureteroscopy (URS) for stone disease.

Materials and Methods: We performed systematic searches of Medline, Embase, and the Cochrane Central Register of Controlled Trials for studies reporting at least one prospectively defined risk factor for urosepsis after URS. Studies that only reported rates of isolated fever, urinary tract infection (UTI), or pooled infectious complications were excluded. The risk factors evaluated in this review were age, sex, body mass index, diabetes mellitus, ischemic heart disease, recent UTI, pyuria, hydronephrosis, stone history, stone size, preoperative stent placement, preoperative positive urine culture, and procedure time. A random effects meta-analysis model with inverse variance weighting was used where the statistic of interest was the odds ratio for dichotomous variables and the mean difference for continuous outcomes.

Results: In 13 studies (5 prospective) with 5597 patients, the pooled incidence of postoperative urosepsis was 5.0% (95% confidence interval: 2.4–8.2). Six risk factors were statistically associated with increased postoperative urosepsis risk—preoperative stent placement (odds ratio=3.94, $p<0.001$, 6 studies), positive preoperative urine culture (odds ratio=3.56, $p<0.001$, 6 studies), ischemic heart disease (odds ratio=2.49, $p=0.002$, 2 studies), older age (mean difference=2.7 years, $p=0.002$, 6 studies), longer procedure time (mean difference=9 minutes, $p=0.02$, 1 study), and diabetes mellitus (odds ratio=2.04, $p=0.04$, 6 studies).

Conclusions: Current evidence suggests that among patients undergoing URS for treatment of stone disease, the risk of postoperative urosepsis was 5.0%. Older age, diabetes mellitus, ischemic heart disease, preoperative stent placement, a positive urine culture, and longer procedure time were associated with increased postoperative urosepsis risk. These results will assist urologists with preoperative risk stratification before ureteroscopic procedures.

Keywords: kidney stone, lithiasis, renal calculi, ureteroscopy, urosepsis

Introduction

APPROXIMATELY 10% TO 12% OF ADULTS will receive a diagnosis of kidney stone disease during their lifetime, with the probability of having a stone varying according to age, gender, race, and geographic location.¹ Patients with symptomatic ureteral or renal stones are typically initially managed with pain control, medical expulsive therapy, and

serial imaging to monitor stone position and assess for hydronephrosis. However, persistent complications such as pain, nausea, and renal insufficiency are indications for definitive stone treatment. Several surgical options are available for treatment of stone disease, including ureteroscopy (URS), shockwave lithotripsy, and percutaneous nephrolithotomy. Treatment selection is largely dictated by patient preference, symptomology, and stone size/location.

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URS is the most common interventional treatment for ureteral and renal stones. Ureteroscopic treatment options include using a basket to extract stone fragments and/or using a laser to dust stone fragments. Due in part to high success rates with these techniques,² URS is increasingly being used in higher-risk patients, which may increase procedural risk and the likelihood of postprocedural infectious complications. Previous meta-analyses have identified risk factors for infectious complications after URS for stone disease.^{3,4} However, the definition of infectious complications in these reviews included a spectrum of diagnoses ranging from isolated fever or urinary tract infection (UTI) to urosepsis. Since patient prognosis and therapeutic strategies differ by diagnosis where urosepsis confers the greatest patient risk with potential for extended hospitalization, unplanned intensive care admission, or death,⁵ identification of risk factors specifically for postoperative urosepsis may assist with risk stratification before URS. The purpose of this systematic review with meta-analysis was to identify potential risk factors specifically for urosepsis after URS for stone disease.

Methods

This systematic review and meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).⁶ A protocol was developed for our review and prospectively registered at research registry website (reviewregistry996).

Two researchers (L.M. and D.F.) experienced in systematic reviews performed searches of Medline, Embase, and the Cochrane Central Register of Controlled Trials from inception to September 30, 2020 to identify studies of patients undergoing URS for renal stones. Manual searches were performed using the Directory of Open Access Journals, Google Scholar, and the reference lists of included articles and systematic reviews. The search strategy was initially developed for Medline (Table 1) and subsequently adapted for the other databases. During screening, we excluded review articles, editorials, commentaries, conference proceedings, case series with <10 patients, gray literature, and studies that reported outcomes from mixed urologic procedures. No language or publication date restrictions were used.

The same reviewers independently reviewed study records and a final list of studies for full-text review was determined after record comparisons and discussion. We included both cohort and case-control studies that provided data to determine the association between at least one prospectively defined risk factor and the postoperative urosepsis rate. Studies that only reported rates of isolated fever, UTI, or pooled infectious complications were excluded. We pilot-tested a database to align our data extraction methods with data typically reported in the literature. We extracted article meta-data, study characteristics, patient characteristics, procedural outcomes, and postoperative urosepsis rates. The risk factors that were evaluated in this systematic review were age, sex, body mass index, diabetes mellitus, ischemic heart disease, recent UTI, pyuria, hydronephrosis, stone history, stone size, preoperative stent placement, preoperative positive urine culture, and procedure time. The risk of bias among included studies was assessed using the Newcastle-Ottawa scale.⁷

A statistician author (L.M.) performed a random effects meta-analysis with inverse variance weighting where the

TABLE 1. MEDLINE SEARCH STRATEGY

Treatment indication search terms
1. Kidney stone
2. Lithiasis
3. Renal calculi
4. Stone disease
5. Ureteral calculi
6. Ureteral obstruction
7. Ureterolithiasis
8. Urinary calculi
9. Urolithiasis
Procedural search terms
10. Lithotripsy
11. Ureterolithotripsy
12. Ureterorenoscopy*
13. Ureteroscopia*
14. ECLS
15. Shockwave lithotripsy
16. Percutaneous nephrolithotomy
Postoperative diagnostic search terms
17. Infectious complication
18. Sepsis*
19. Septicemia
20. SIRS
21. Systemic inflammatory response syndrome
22. Urosepsis
Combination terms
23. or/1–9
24. or/10–13
25. not/14–16
26. or/17–22
27. and/23–26

“*” represents a wildcard symbol used in a search query to represent end truncation.

statistic of interest was the odds ratio for dichotomous variables and the mean difference for continuous outcomes. Individual study results and pooled meta-analysis data for key outcomes were displayed with forest plots. We used the I^2 statistic to estimate heterogeneity of effects across studies with values of $\leq 25\%$, 50% , and $\geq 75\%$ representing low, moderate, and high inconsistency, respectively.⁸ We were unable to assess the potential for publication bias or to explore sources of heterogeneity with metaregression owing to an insufficient number of available studies. All tests were two sided and the threshold for statistical significance was $p < 0.05$. Statistical analyses were conducted using Stata v. 16.1 and Review Manager v5.3.

Results

Among 251 articles identified in the searches, 13 met the eligibility criteria and were included in the systematic review.^{9–21} A PRISMA flow diagram depicting the study identification and selection results is shown in Figure 1. Among 13 studies (5 prospective) with 5597 patients, mean patient age ranged from 43 to 77 years (median 51 years) and 64% were men. Patient characteristics and risk factors were reported inconsistently among studies (Table 2). Seven studies were judged to have low risk of bias and six were intermediate risk. The most commonly identified risks of bias among studies were attributable to retrospective patient

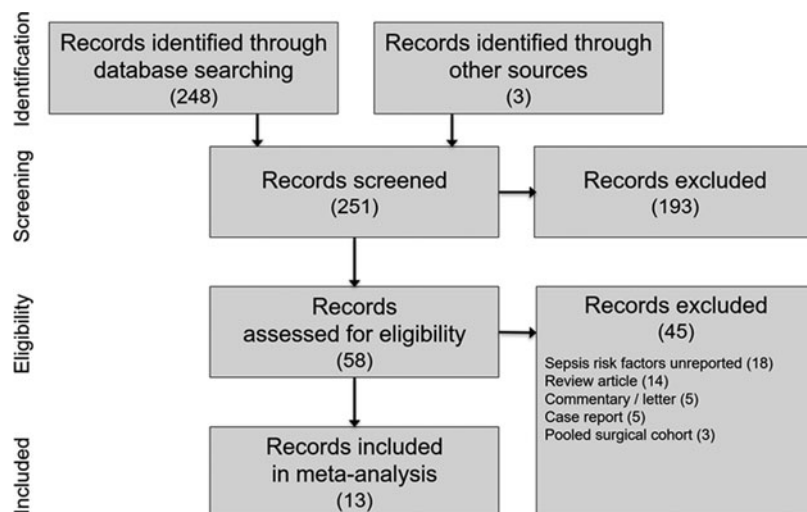


FIG. 1. CONSORT flow diagram.

enrollment, inconsistent risk factor reporting, and variability in postoperative urosepsis diagnostic criteria (Table 3).

Mean procedure time ranged from 24 to 97 minutes among studies; length of hospitalization was rarely reported. Postoperative urosepsis rates ranged from 0.2% to 17.8% (Table 4) and urosepsis diagnostic criteria varied among studies (Table 5). The pooled incidence of postoperative urosepsis was 5.0% (95% confidence interval: 2.4–8.2) (Fig. 2). Among three studies reporting urosepsis severity, the pooled incidence was 71% for urosepsis, 5% for severe urosepsis, and 24% for septic shock. Among 13 risk factors evaluated, 6 were statistically associated with increased postoperative urosepsis risk—preoperative stent placement (odds ratio = 3.94, $p < 0.001$, 6 studies), positive preoperative urine culture (odds ratio = 3.56, $p < 0.001$, 6 studies), ischemic heart disease (odds ratio = 2.49, $p = 0.002$, 2 studies), older age (mean difference = 2.7 years, $p = 0.002$, 6 studies), longer procedure time (mean difference = 9 minutes, $p = 0.02$, 1 study), and diabetes mellitus (odds ratio = 2.04, $p = 0.04$, 6 studies) (Table 6). Forest plots displaying the association of patient risk factors with postoperative urosepsis rates are provided for the variables reported in two or more studies (Figs. 3–7).

Discussion

Because of the considerable clinical and economic burden of urosepsis, identification of risk factors for this complication after URS would be particularly informative to patients, physicians, and health care policy makers. Although others have reported risk factors for generalized infectious complications,^{3,4} this is the first systematic review with meta-analysis to specifically investigate risk factors for postoperative urosepsis after URS. The overall risk of postoperative urosepsis was 5.0% in this review. Older age, comorbidities such as diabetes mellitus and ischemic heart disease, preoperative stent placement, positive urine culture, and longer procedure time were independently associated with increased postoperative urosepsis risk. This information is important for urologists as it can assist with preoperative risk stratification to provide individualized treatment recommendations for each patient as

well as to inform postoperative surveillance regimens. Furthermore, it is plausible that early identification and appropriate management of high-risk patients may decrease postoperative morbidity and reduce health care utilization, a hypothesis deserving of further study.

The current systematic review is unique in that we identified risk factors for urosepsis after URS, whereas others have reported risk factors for generalized infectious complications that included less severe complications such as isolated fever or UTI.^{3,4} However, the risk factors for urosepsis identified in this review are similar to those previously identified for generalized infectious complications. Sun and colleagues⁴ reported that a positive preoperative urine culture was the strongest risk factor (odds ratio = 2.95, $p < 0.01$) for generalized infectious complications after URS, with female sex, diabetes mellitus, preoperative stent placement, and longer procedure time also demonstrating statistical significance. Ma and colleagues³ performed a similar review where they identified female sex, preoperative stent placement, diabetes mellitus, positive preoperative urine culture, and longer procedure time as the key determinants of postoperative urosepsis risk. In our review, positive urine culture, preoperative stent placement, and older age were the strongest determinants based on reporting in the greatest number of studies and without influence by significant heterogeneity. Based on the collective results of these three reviews, positive preoperative urine culture and preoperative stent placement appear to be key determinants of generalized infectious complications as well as for urosepsis specifically. Although ischemic heart disease, procedure time, and diabetes mellitus were also associated with increased postoperative urosepsis risk in this review, the strength of this evidence was low because of a limited number of studies for ischemic heart disease and procedure time, and the presence of significant heterogeneity for diabetes mellitus.

Patients with a positive urine culture often received targeted microbial therapy followed by confirmation of a second negative culture before URS; however, reporting among studies in this review was inconsistent. Based on this limited evidence, it is plausible that prior antibiotic exposure may confer antibiotic resistance and greater infection risk after URS. In addition, a second negative test may not indicate

TABLE 2. STUDY AND PATIENT CHARACTERISTICS AMONG INCLUDED STUDIES

Study	Design	N	Age	Male sex	BMI	IHD	DM	Recent UTI	Stone history	Positive urine	Prior stent	HN	Pyuria	Cumulative stone size (mm)
Bai et al. ⁹	R	1421	59	62% (880/1421)	22	—	18% (259/1421)	—	11% (156/1421)	19% (266/1421)	3% (42/1421)	89% (1431/1599)	51% (729/1421)	11
Blackmur et al. ¹⁰	P	462	[55] ^a	—	[28] ^a	10% (47/462)	17% (80/462)	18% (81/462)	—	11% (52/462)	39% (182/462)	—	—	—
Bloom et al. ¹¹	R	345	50	50% (173/345)	29	—	18% (63/345)	17% (58/345)	—	9% (24/269)	53% (184/345)	—	—	9
Dessyn et al. ¹²	R	497	51	60% (299/497)	26	—	—	—	—	—	64% (316/497)	—	—	9
Hu et al. ¹³	R	332	43	56% (185/332)	—	—	—	0% (0/332)	—	—	—	—	—	10
Hughes et al. ¹⁴	P	37	50 ^a	65% (24/37)	—	—	—	—	—	—	—	—	—	9
Nevo et al. ¹⁵	P	1256	[57] ^a	69% (870/1256)	—	13% (161/1256)	20% (249/1256)	—	—	15% (193/1256)	48% (600/1256)	—	—	[8] ^a
Ogreden et al. ¹⁶	R	72	44	78% (56/72)	—	—	—	—	—	—	—	100% (72/72)	—	8
Perez et al. ¹⁷	R	246	52	63% (155/246)	—	—	—	—	—	33% (32/97)	36% (88/246)	—	—	—
Prattley et al. ¹⁸	P	110	77	75% (85/110)	—	—	—	—	—	26% (32/110)	26% (32/110)	—	—	17
Wood et al. ¹⁹	P	227	60	61% (193/281) ^d	—	—	22% (61/281) ^d	—	—	32% (90/281) ^d	100% (227/227) ^c	—	—	—
Xu and Guo ²⁰	R	305	51	47% (144/305)	22	—	10% (32/305)	—	—	0% (0/305) ^b	—	—	—	8
Zisman et al. ²¹	R	287	51	74% (211/287)	—	—	—	—	—	—	63% (180/287)	—	—	—

^aMedian.

^bPatients with positive urine culture were excluded from the study.

^cPatients without preoperative stent were excluded from the study.

^dReported using number of procedures in denominator.

BMI = body mass index; DM = diabetes mellitus; HN = hydronephrosis; IHD = ischemic heart disease; P = prospective; R = retrospective; UC = ureteral calculi; UTI = urinary tract infection.

TABLE 3. RISK OF BIAS ASSESSMENT WITH NEWCASTLE-OTTAWA SCALE AMONG INCLUDED STUDIES

<i>Study</i>	<i>Selection (4)</i>	<i>Comparability (2)</i>	<i>Outcome (3)</i>	<i>No. of stars (9)</i>	<i>Risk of bias</i>
Bai et al. ⁹	★★	★★	★★★	7	Low
Blackmur et al. ¹⁰	★★★	★★	★★★	8	Low
Bloom et al. ¹¹	★★	★★	★★★	7	Low
Dessyn et al. ¹²	★★		★★	4	Intermediate
Hu et al. ¹³	★★★		★★	5	Intermediate
Hughes et al. ¹⁴	★★★		★★	5	Intermediate
Nevo et al. ¹⁵	★★★	★★	★★★	8	Low
Ogreden et al. ¹⁶	★★		★★	4	Intermediate
Perez et al. ¹⁷	★★	★★	★★	6	Low
Prattley et al. ¹⁸	★★★		★★	5	Intermediate
Wood et al. ¹⁹	★★★	★★	★★	7	Low
Xu and Guo ²⁰	★★	★★	★★	6	Low
Zisman et al. ²¹	★★		★★	4	Intermediate

Selection comprised representativeness of exposed cohort, selection of nonexposed cohort; ascertainment of exposure, and demonstration that outcome of interest was not present at start of study. Comparability comprised study controls for baseline comorbidities and disease severity. Outcome comprised assessment of outcome, was follow-up long enough for outcomes to occur, and adequacy of follow-up of cohorts. Studies classified as high (1–3 stars), intermediate (4–5 stars), or low (6–9 stars) risk of bias.

absence of infection since negative midstream urine cultures are possible where infected urine is present proximal to the obstructing stone.²² Although infectious stones (struvite) may play an important role in this specific patient population, stone treatment may lower UTI risk even in nonstruvite stones.²³ In higher-risk patients, it may be prudent to tailor preoperative antibiotics to cover both gram positive and

multidrug-resistant organisms and also to employ intraoperative stone cultures since they may more accurately determine bacterial pathogens in infectious complications after endourologic procedures.²⁴ Although preoperative stent placement facilitates endoscopic management of stones, improves stone-free rates, and reduces intraoperative complications,²⁵ bacterial colonization and bacteriuria is an

TABLE 4. PERIOPERATIVE DETAILS AMONG INCLUDED STUDIES

<i>Study</i>	<i>Preoperative antibiotic</i>	<i>Stone location</i>	<i>Procedure time (minutes)</i>	<i>Hospital stay (day)</i>	<i>Urosepsis rate</i>
Bai et al. ⁹	(+) urine: 5–7 days targeted treatment	Ureteral	62	—	0.8% (12/1421)
Blackmur et al. ¹⁰	(+) urine: 7 days targeted treatment	Ureteral or renal	[38] ^a	—	7.4% (34/462)
Bloom et al. ¹¹	(+) urine: antibiotic regimen based on provider preference	Ureteral or renal	84	—	4.3% (15/345)
Dessyn et al. ¹²	—	Upper ureteral or renal	97	—	0.2% (1/497)
Hu et al. ¹³	Not reported; patients with recent UTI/antimicrobial prophylaxis were excluded from study	Ureteral	—	—	17.8% (59/332)
Hughes et al. ¹⁴	—	Renal	57 ^a	—	2.7% (1/37)
Nevo et al. ¹⁵	(+) urine: 5–7 days targeted treatment	Ureteral or renal	[42] ^a	1.0	2.9% (36/1256)
Ogreden et al. ¹⁶	(+) urine: appropriate empirical treatment	Ureteral	—	—	11.1% (8/72)
Perez et al. ¹⁷	(–) urine: IV cefazolin	Ureteral or renal	[63]	—	7.3% (18/246)
Prattley et al. ¹⁸	(+) urine: “appropriately treated”	Ureteral or renal	50	2.1	0.9% (1/110)
Wood et al. ¹⁹	(–) urine: IV cefazolin	—	—	—	5.7% (13/227)
	(+) urine: 3 days appropriate oral antibiotics				
Xu and Guo ²⁰	Not reported; patients with (+) urine culture were excluded from study.	Ureteral	24	—	14.8% (45/308)
Zisman et al. ²¹	Ciprofloxacin or gentamycin+ampicillin 12 hours before treatment, regardless of urine culture results	Ureteral or renal	—	—	3.1% (9/287)

^aMedian.

IV = intravenous.

TABLE 5. UROSEPSIS DIAGNOSTIC CRITERIA USED IN INCLUDED STUDIES

Study	Minimum No. of criteria met	Temperature (°C)	Heart rate (bpm)	Respiration rate, or PaCO ₂	WBC (mm ³)	SBP (mm/Hg)	Consciousness (GCS)	Reporting window
Bai et al. ⁹	2	<36 or >38	>90	>20 bpm, or <32 mm Hg	<4000, or >12,000	—	—	2 days
Blackmur et al. ¹⁰	2	<36 or >38	>90	>20 bpm, or <32 mm Hg	<4000, or >12,000	—	—	28 days
Bloom et al. ¹¹	2	>38	>90	—	>12,000	—	—	1 day
Dessyn et al. ¹²	2	>38	>90	b	b	b	b	b
Hu et al. ¹³	2	c	c	c	c	c	c	1 day
Hughes et al. ¹⁴	2	b	b	b	b	b	b	b
Nevo et al. ¹⁵	2	>38 ^a	>90	>20 bpm, or <32 mm Hg	<4000, or >12,000	—	—	2 days
Ogreden et al. ¹⁶	2	<36 or >38	>90	>20 bpm, or <32 mm Hg	<4000, or >12,000	—	—	In-hospital
Perez et al. ¹⁷	2	>38 ^a	>90	>20 bpm	<4000, or >12,000	—	—	30 days
Prattley et al. ¹⁸	2	>38	>90	>20 bpm	b	b	b	In-hospital
Wood et al. ¹⁹	2	<36 or >38	>90	>20 bpm, or <32 mm Hg	<4000, or >12,000	—	—	7 days
Xu and Guo ²⁰	2	—	—	≥22 bpm	—	≤100	≤13	1 day
Zisman et al. ²¹	2	c	c	c	c	c	c	1 day

^aMandatory criterion.^bData unreported.^cUrosepsis defined as documented or suspected infection in addition to other criteria set forth by the 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. GCS = Glasgow Coma Scale; SBP = systolic blood pressure; WBC = white blood cell.

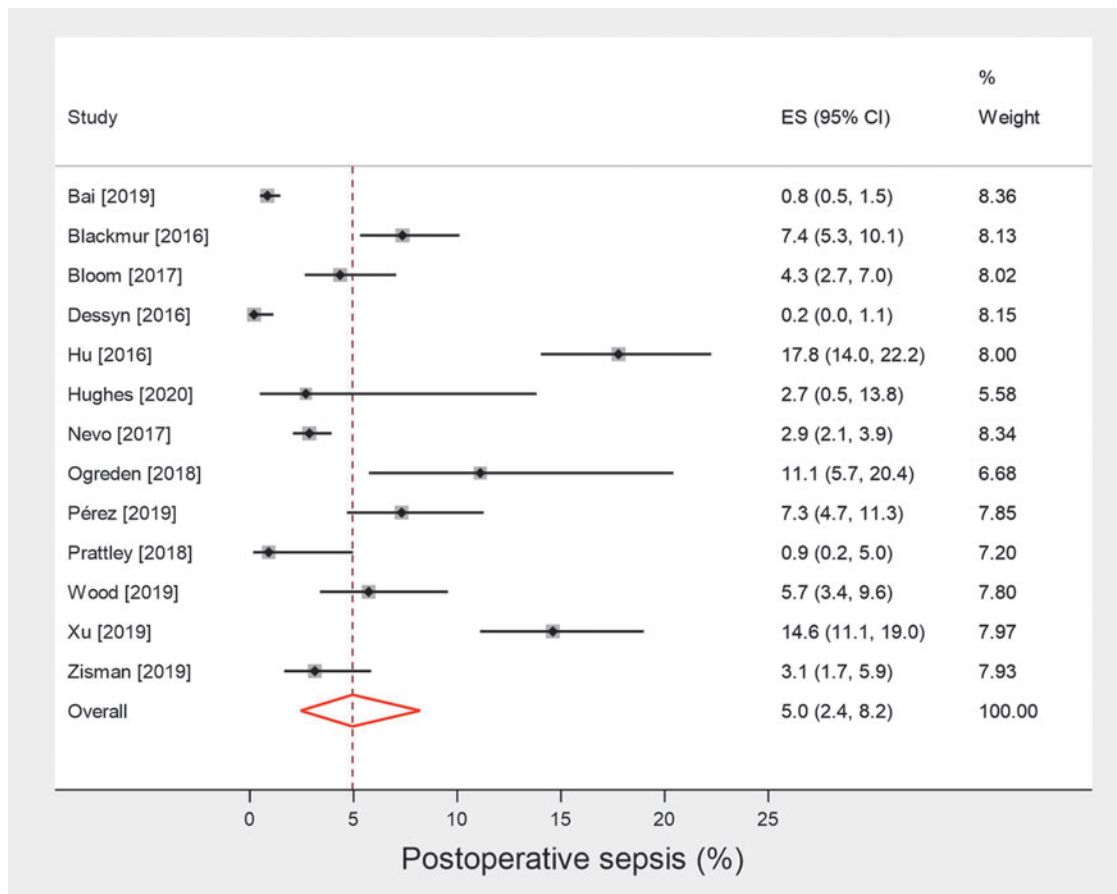


FIG. 2. Forest plot of postoperative urosepsis risk in patients undergoing ureteroscopy. The postoperative urosepsis rate and 95% CI are plotted for each study. The pooled mortality rate (diamond apex) and 95% CI (diamond width) are calculated using a random effects model. Pooled urosepsis risk=5.0%. Heterogeneity: $I^2=95\%$; $p<0.001$. CI=confidence interval; ES=effect size.

TABLE 6. SUMMARY OF RISK FACTORS FOR POSTOPERATIVE UROSEPSIS IN PATIENTS UNDERGOING URETEROSCOPY FOR STONE DISEASE

Risk factor	No. of studies	Unit of measure	Statistic	Effect size		p ^a	Heterogeneity	
				Value	95% CI		I ²	p
Preoperative stent	6	Yes vs no	Odds ratio	3.94	2.36 to 6.60	<0.001	0%	0.59
Positive preoperative urine culture	6	Yes vs no	Odds ratio	3.56	2.11 to 6.01	<0.001	32%	0.19
Ischemic heart disease	2	Yes vs no	Odds ratio	2.49	1.38 to 4.48	0.002	0%	0.51
Age	6	Years	Mean difference	2.7	1.0 to 4.4	0.002	44%	0.11
Procedure time	1	Minutes	Mean difference	9	2 to 16	0.02	b	b
Diabetes mellitus	6	Yes vs no	Odds ratio	2.04	1.04 to 4.03	0.04	64%	0.02
Stone size	4	Millimeters	Mean difference	10	-1 to 20	0.07	48%	0.12
Recent UTI	2	Yes vs no	Odds ratio	2.74	0.55 to 13.66	0.22	82%	0.02
Male sex	8	Yes vs no	Odds ratio	0.63	0.28 to 1.44	0.27	75%	<0.001
Stone history	1	Yes vs no	Odds ratio	1.63	0.35 to 7.51	0.53	b	b
Pyuria	1	Yes vs no	Odds ratio	1.33	0.42 to 4.22	0.63	b	b
Hydronephrosis	1	Yes vs no	Odds ratio	1.53	0.20 to 11.78	0.68	b	b
BMI	3	kg/m ²	Mean difference	0.2	-1.2 to 1.6	0.78	15%	0.31

^aSorted from lowest to highest p -value for effect size, with statistically significant risk factors in bold font.

^bNot calculable because of insufficient number of studies.

CI=confidence interval.

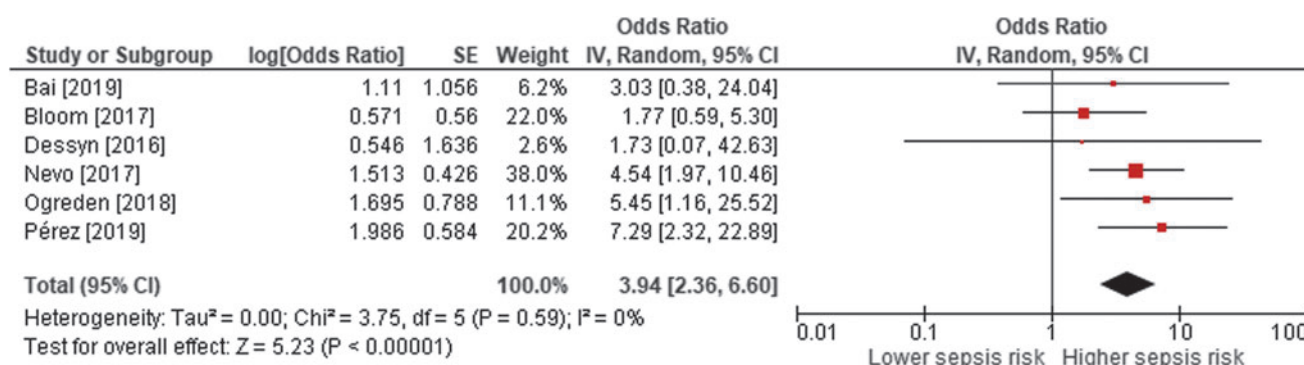


FIG. 3. Forest plot of the association between postoperative urosepsis risk in patients undergoing ureteroscopy with preoperative stent. The odds ratio and 95% CI are plotted for each study. The pooled odds ratio (diamond apex) and 95% CI (diamond width) are calculated using a random effects model. Pooled odds ratio=3.94; $p < 0.001$. Heterogeneity: $I^2 = 0\%$; $p = 0.59$. IV = intravenous.

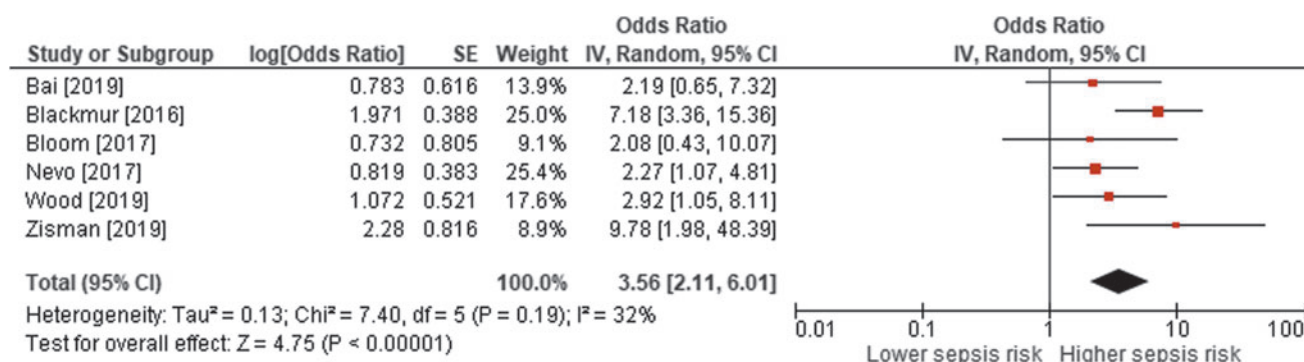


FIG. 4. Forest plot of the association between postoperative urosepsis risk in patients undergoing ureteroscopy with preoperative positive urine culture. The odds ratio and 95% CI are plotted for each study. The pooled odds ratio (diamond apex) and 95% CI (diamond width) are calculated using a random effects model. Pooled odds ratio=3.56; $p < 0.001$. Heterogeneity: $I^2 = 32\%$; $p = 0.19$.

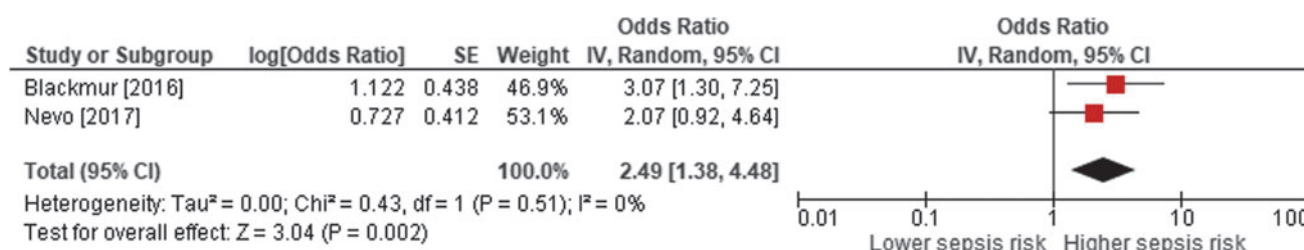


FIG. 5. Forest plot of the association between postoperative urosepsis risk in patients undergoing ureteroscopy with ischemic heart disease. The odds ratio and 95% CI are plotted for each study. The pooled odds ratio (diamond apex) and 95% CI (diamond width) are calculated using a random effects model. Pooled odds ratio=2.49; $p = 0.002$. Heterogeneity: $I^2 = 0\%$; $p = 0.51$.

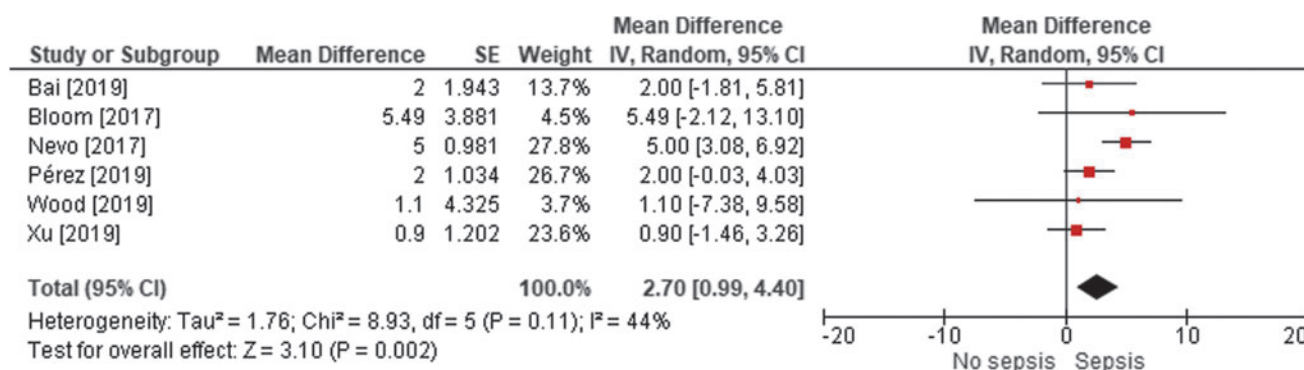


FIG. 6. Forest plot of the association between postoperative urosepsis risk in patients undergoing ureteroscopy with patient age. The mean difference and 95% CI are plotted for each study. The pooled mean difference (diamond apex) and 95% CI (diamond width) are calculated using a random effects model. Pooled mean difference=2.7 years; $p = 0.002$. Heterogeneity: $I^2 = 44\%$; $p = 0.11$.

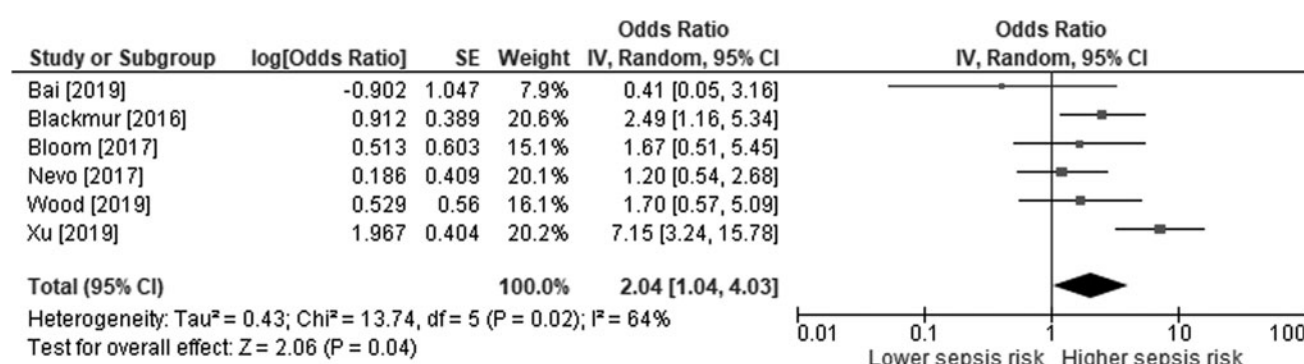


FIG. 7. Forest plot of the association between postoperative urosepsis risk in patients undergoing ureteroscopy with diabetes mellitus. The odds ratio and 95% CI are plotted for each study. The pooled odds ratio (diamond apex) and 95% CI (diamond width) are calculated using a random effects model. Pooled odds ratio = 2.047; $p = 0.04$. Heterogeneity: $I^2 = 64\%$; $p = 0.02$.

inevitable process that begins once a stent is inserted and progresses with prolonged stent dwelling time, particularly when stent dwelling times exceed 30 days.¹⁵ These findings suggest that patients with a recent positive urine culture or ureteral stent may benefit from enhanced intraoperative and postoperative surveillance and, if infectious symptoms arise, early institution of broad-spectrum antibiotics followed by targeted therapy pending specific pathogen identification from culture specimens. Although older age, ischemic heart disease, diabetes mellitus, and longer procedure time were also associated with increased postoperative urosepsis risk, a clear explanation for these associations and implications for patient risk stratification remain unclear.

This meta-analysis has certain limitations pertaining to the quality of studies available for analysis that may influence interpretation. First, patient characteristics were reported inconsistently and, consequently, the number of studies that adequately reported urosepsis risk factors was limited. Second, the definitions of postoperative urosepsis varied somewhat among studies and symptom surveillance ranged from 1 to 30 days. Third, we were unable to evaluate the potential for publication bias, perform multivariate analyses, or perform metaregression to determine whether study-level factors may have influenced the observed associations between risk factors and urosepsis rates owing to an insufficient number of studies. Fourth, preoperative stent placement indications and average dwell times were rarely reported, which hindered our ability to analyze these data in greater detail. Finally, studies that used shockwave lithotripsy or percutaneous nephrolithotomy were excluded from this review; thus, the risk factors for postoperative urosepsis after URS identified in this review may not be relevant to other urologic procedures for stone disease.

Conclusion

Current evidence suggests that among patients undergoing URS for treatment of stone disease, the risk of postoperative urosepsis was 5.0%. Older age, diabetes mellitus, ischemic heart disease, preoperative stent placement, a positive urine culture, and longer procedure time were associated with increased postoperative urosepsis risk. These results may assist urologists with preoperative risk stratification before ureteroscopic procedures.

Authors' Contributions

N.B., L.M., S.B., and B.C. conceived and designed the study; L.M. and D.F. (acknowledged) performed the database search, study selection, and data extraction; L.M. conducted the statistical analysis and drafted the article; N.B., L.M., S.B., B.C., and B.H.C. reviewed and revised the article; all authors interpreted data for the study, read, and approved the final article.

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Author Disclosure Statement

Drs. Bhojani, Miller, and Chew report consultancy with Boston Scientific. Dr. Bhattacharyya and Mr. Cutone report employment with Boston Scientific.

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References

1. Abufaraj M, Xu T, Cao C, et al. Prevalence and trends in kidney stone among adults in the USA: Analyses of National Health and Nutrition Examination Survey 2007–2018 Data. *Eur Urol Focus* 2020. PubMed PMID: 32900675. Epub 2020/09/10.
2. Humphreys MR, Shah OD, Monga M, et al. Dusting versus basketing during ureteroscopy—Which technique is more efficacious? A Prospective Multicenter Trial from the EDGE Research Consortium. *J Urol* 2018;199:1272–1276.
3. Ma YC, Jian ZY, Yuan C, Li H, Wang KJ. Risk factors of infectious complications after ureteroscopy: A systematic review and meta-analysis based on adjusted effect estimate. *Surg Infect (Larchmt)* 2020.PMID: 32286933
4. Sun J, Xu J, OuYang J. Risk factors of infectious complications following ureteroscopy: A systematic review and meta-analysis. *Urol Int* 2020;104:113–124.
5. Cindolo L, Castellan P, Scoffone CM, et al. Mortality and flexible ureteroscopy: Analysis of six cases. *World J Urol* 2016;34:305–310.

6. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ* 2009;339:b2700.
7. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603–605.
8. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–560.
9. Bai T, Yu X, Qin C, et al. Identification of factors associated with postoperative urosepsis after ureteroscopy with holmium: Yttrium-aluminum-garnet laser lithotripsy. *Urol Int* 2019;103:311–317.
10. Blackmur JP, Maitra NU, Marri RR, Housami F, Malki M, McIlhenny C. Analysis of factors' association with risk of postoperative urosepsis in patients undergoing ureteroscopy for treatment of stone disease. *J Endourol* 2016;30:963–969.
11. Bloom J, Fox C, Fullerton S, Matthews G, Phillips J. Sepsis after elective ureteroscopy. *Can J Urol* 2017;24:9017–9023.
12. Dessyn JF, Balssa L, Chabannes E, et al. Flexible ureterorenoscopy for renal and proximal ureteral stone in patients with previous ureteral stenting: impact on stone-free rate and morbidity. *J Endourol* 2016;30:1084–1088.
13. Hu W, Zhou PH, Wang W, Zhang L, Zhang XB. Prognostic value of adrenomedullin and natriuretic peptides in uroseptic patients induced by ureteroscopy. *Mediators Inflamm* 2016;2016:9743198.
14. Hughes SF, Moyes AJ, Lamb RM, et al. The role of specific biomarkers, as predictors of post-operative complications following flexible ureterorenoscopy (FURS), for the treatment of kidney stones: A single-centre observational clinical pilot-study in 37 patients. *BMC Urol* 2020;20:122.
15. Nevo A, Mano R, Baniel J, Lifshitz DA. Ureteric stent dwelling time: A risk factor for post-ureteroscopy sepsis. *BJU Int* 2017;120:117–122.
16. Olgren E, Oguz U, Demirelli E, Benli E, Ozen O. The impact of ureteral Double-J stent insertion following ureterorenoscopy in patients with ureteral stones accompanied by perirenal fat stranding. *Arch Ital Urol Androl* 2018;90:15–19.
17. Perez DD, Garcia IL, Guerrero CS, et al. Urinary sepsis after endourological ureterorenoscopy for the treatment of lithiasis. *Actas Urologicas Espanolas* 2019;43:293–299.
18. Prattley S, Voss J, Cheung S, Geraghty R, Jones P, Somani BK. Ureteroscopy and stone treatment in the elderly (≥ 70 years): Prospective outcomes over 5-years with a review of literature. *Int Braz J Urol* 2018;44:750–757.
19. Wood B, Habashy D, Mayne DJ, Dhar A, Purvis C, Skyring T. The utility of preoperative and intraoperative cultures for guiding urosepsis empirical treatment. *J Clin Urol* 2020;13:132–139.
20. Xu CG, Guo YL. Diagnostic and prognostic values of BMPER in patients with urosepsis following ureteroscopic lithotripsy. *Biomed Res Int* 2019;2019:8078139.
21. Zisman A, Badaan S, Kastin A, Kravtsov A, Amiel GE, Muller M. Tailoring antibiotic prophylaxis for ureteroscopic procedures based on local resistance profiles may lead to reduced rates of infections and urosepsis. *Urol Int* 2020;104:106–112.
22. Mariappan P, Smith G, Bariol SV, Moussa SA, Tolley DA. Stone and pelvic urine culture and sensitivity are better than bladder urine as predictors of urosepsis following percutaneous nephrolithotomy: A prospective clinical study. *J Urol* 2005;173:1610–1614.
23. Omar M, Abdulwahab-Ahmed A, Chaparala H, Monga M. Does stone removal help patients with recurrent urinary tract infections? *J Urol* 2015;194:997–1001.
24. Eswara JR, Sharifabrizi A, Sacco D. Positive stone culture is associated with a higher rate of sepsis after endourological procedures. *Urolithiasis* 2013;41:411–414.
25. Rubenstein RA, Zhao LC, Loeb S, Shore DM, Nadler RB. Pretesting improves ureteroscopic stone-free rates. *J Endourol* 2007;21:1277–1280.

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Abbreviations Used

BMI = body mass index
CI = confidence interval
DM = diabetes mellitus
ES = effect size
GCS = Glasgow Coma Scale
HN = hydronephrosis
IHD = ischemic heart disease
IV = intravenous
P = prospective
PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
R = retrospective
SBP = systolic blood pressure
UC = ureteral calculi
URS = ureteroscopy
UTI = urinary tract infection
WBC = white blood cell