International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 11, No. 2, 2025

Research Advances and Treatment of Risk Factors for Postoperative Urosepsis Following Percutaneous Nephrolithotomy

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Abstract: Percutaneous Nephrolithotomy (PCNL) is the preferred treatment for complex upper urinary tract stones and large-burden (diameter >2 cm) or multiple renal calculi, offering advantages such as higher efficacy, minimal invasiveness, and faster recovery compared to traditional surgery. However, it carries a significant risk of urosepsis. Currently, the incidence of urosepsis associated with urinary stones has not declined despite advances in diagnostic and therapeutic techniques, remaining one of the most critical complications in urology. Its high mortality rate poses significant challenges to clinicians. This article reviews the potential risk factors and therapeutic approaches for post-PCNL urosepsis.

Keywords: Percutaneous Nephrolithotomy (PCNL); Urosepsis; Risk Factors; Treatment.

1. Introduction

Urinary stones are among the most common diseases in urology. In China, the incidence varies across regions, ranging from 1.5% to 18%, with an overall higher prevalence in southern regions compared to the north [1]. The annual incidence is (150–200)/100,000, and approximately 25% of patients require hospitalization [2]. A safe and efficient treatment approach is therefore crucial for urinary stone disease. According to the EAU Guidelines [3], Percutaneous Nephrolithotomy (PCNL) is the preferred treatment for complex upper urinary tract stones, large-burden stones (>2 cm in diameter), or multiple renal calculi. PCNL is widely adopted in upper urinary tract stone management due to its advantages over traditional open surgery, including fewer postoperative complications, faster recovery, and lower residual stone rates [4,5]. This has also led to its widespread implementation in primary hospitals [4,5]. Infection is the most common complication of PCNL. Without timely and effective intervention in its early stages, it can rapidly progress to urosepsis, occurring in 0.3%–7.6% of cases. Studies indicate that urosepsis is the most frequent cause of death following PCNL [6,7], with mortality rates reported as high as 28.3%–41.4% [8].

2. Analysis of Causes for Post-PCNL Urosepsis

2.1. Preoperative Risk Factors

2.1.1. Age and Sex as Risk Factors

Some scholars propose that age-related decline in immune system function serves as a risk factor for both the occurrence and progression of urosepsis [9,10]. Current research widely recognizes female sex as a risk factor for postoperative infectious complications following PCNL [11-14]. The shorter female urethra facilitates easier colonization by perineal and rectal bacteria, leading to recurrent infections in female patients [15]. Furthermore, decreased estrogen levels in elderly women cause atrophy of the urinary tract mucosa, resulting in reduced glycogen content in epithelial cells. This decline in glycogen-dependent vaginal flora allows for increased colonization by Escherichia coli, elevating the risk of urinary tract infections [16,17]. For elderly female patients, preoperative risk of infection should be thoroughly evaluated to reduce postoperative complications.

2.1.2. Figures History of Diabetes

It is widely recognized that diabetic patients face significantly higher perioperative infection risks compared to non-diabetic individuals, primarily attributed to compromised immune function [18]. Studies demonstrate that hyperglycemia in diabetic patients promotes bacterial proliferation, leading to recurrent urinary tract infections [19]. Furthermore, chronic hyperglycemia impairs migration, chemotaxis, phagocytosis, and adhesion of leukocytes, monocytes, and macrophages, thereby weakening immune defenses [20]. Even with strict preoperative glycemic control, diabetic patients retain elevated risks of postoperative urosepsis [21,22].

2.1.3. Stone Burden

Stone size, location, and multiplicity are among the factors influencing post-PCNL urosepsis. Specifically, larger stones—particularly staghorn calculi—harbor greater bacterial loads and prolong operative duration [23]. Moreover, Nahas et al. [24] demonstrated that calculi >30 mm in diameter and multiple calyceal stones constitute significant risk factors for postoperative sepsis. Difficult-to-access calyceal stones, combined with excessive nephroscope manipulation and confined calyceal spaces, frequently cause renal mucosal injury, facilitating increased absorption of bacteria and endotoxins.

2.1.4. Preoperative Urinary Drainage as a Risk Factor

Patients may require preoperative indwelling catheters for various indications. The most common scenario involves secondary procedures, where a ureteral stent is placed in the affected ureter to facilitate stone passage. Additionally, patients presenting with oliguria/anuria or signs of infection (e.g., chills, fever) due to ureteral obstruction may undergo retrograde ureteral stenting or percutaneous nephrostomy, leaving drainage devices in situ. Studies identify preoperative ureteral stenting as an independent risk factor for post-PCNL infectious complications [11,25]. Foreign bodies in the urinary system provide scaffolds for microbial colonization and biofilm formation, serving as nidi for infection that exacerbate urothelial irritation and inflammatory responses [26-28]. Ureteral stents impair the anti-reflux mechanism, facilitating retrograde urine flow from the bladder to the renal collecting system along the stent [29,30]. Furthermore, stents reduce ureteral peristalsis, promoting bacterial ascension [31]. Bacteria within the collecting system may then enter renal parenchyma via collecting ducts in the renal calyces. Once in the parenchyma, they can access the renal circulation, leading to bacteremia.

2.1.5. Urinary Tract Infection as a Risk Factor

Even with adequate preoperative antibiotic therapy and negative follow-up tests, some patients with preexisting urinary tract infections (UTIs) complicated by diabetes, urinary obstruction, or infection stones still develop post-PCNL urosepsis [32]. Studies reveal inconsistencies between preoperative midstream urine cultures and postoperative stone cultures [33,34]. Despite occasional discordance, these cultures remain the primary method for identifying pathogens and guiding antimicrobial therapy. Patients with positive postoperative stone cultures demonstrate higher rates of infectious complications. Although stone cultures more accurately predict post-PCNL infections than urine cultures, their clinical utility for early prediction is limited due to prolonged turnaround times (typically 48–72 hours) [25]. Nevertheless, all admitted patients should undergo routine preoperative urine culture and postoperative stone culture to ensure adequate treatment of preexisting infections and prevent postoperative complications.

2.2. Intraoperative Risk Factors

2.2.1. Prolonged Operative Duration as a Risk Factor

Prolonged operative duration is a documented risk factor for post-PCNL urosepsis [35]. Stone size, morphology, location, and surgeon experience directly impact operative time. Studies demonstrate that PCNL exceeding 90 minutes significantly increases infection risk. Notably, PCNL with suction sheaths reduces operative time compared to standard PCNL [36]. Growing evidence supports the use of suction sheaths during PCNL to shorten procedure duration. For complex or staghorn calculi, clinicians may consider suction sheath systems [37-39]. Therefore, preoperative assessment of stone characteristics and renal anatomy is essential to select optimal access routes and lithotripsy devices, thereby improving surgical efficiency, minimizing operative time, and reducing postoperative complications.

2.2.2. Surgical Perfusion Pressure

Under physiological conditions, the pressure within a normally structured renal pelvis is approximately 5-10 mmHg. When renal pelvic pressure exceeds 30 mmHg, it may cause pyelovenous and pyelolymphatic backflow [40]. During surgery, continuous irrigation is required to maintain a clear visualization and flush out stone fragments. However, inadequate drainage or improper manipulation can easily elevate renal pelvic pressure beyond 30 mmHg. Scholars have observed that under continuous irrigation during surgery, renal pelvic pressure can reach 328 mmHg—nearly ten times the backflow threshold [41]. Research indicates that intraoperative renal pelvic pressure >40 mmHg is a risk factor for urosepsis following PCNL [42].The introduction of negative-pressure access sheaths in PCNL enables real-time suction of irrigation fluid, stone fragments, and blood throughout the procedure, effectively reducing renal pelvic pressure, improving intraoperative visualization, and accelerating surgical progress [43, 44]. This negative-pressure system significantly minimizes fluid backflow, thereby reducing the dissemination of infectious toxins and pathogens and correspondingly controlling the incidence of infectious complications.

2.3. Postoperative Influencing Factors

2.3.1. Postoperative Stone Culture

Multiple studies have identified stone culture as an independent risk factor for urosepsis, whereas urine culture is not [33, 34, 45]. Research indicates that both urine culture and stone culture serve as independent risk factors for urosepsis in patients with complex renal stones, with the coexistence of positive urine and stone cultures posing an even higher postoperative infection risk than either positive culture alone [46]. Although stone culture provides more accurate prediction of post-PCNL sepsis, its results require extended processing time and are primarily utilized postoperatively to guide antibiotic therapy.

2.3.2. Residual Stones

Approximately 15%-25% of patients with large stones exhibit residual fragments after initial PCNL [47]. Residual stones <4 mm (or occasionally <5 mm) without urinary tract infection or obstruction are typically classified as Clinically Insignificant Residual Fragments (CIRFs) and generally require no specific intervention. (1) Studies have identified the following risks associated with postoperative residual stones [48]. (2) Infection perpetuation: May cause and perpetuate urinary tract infections Nidus for recurrence: Can serve as a nucleus for new stone formation. (3) Obstructive complications: Migration may induce obstruction, triggering new symptoms. Research confirms that residual stones increase infection risk and constitute a risk factor for infectious complications post-PCNL [25, 49, 50]. In patients with positive preoperative urine or stone cultures, residual fragments may act as infectious foci, potentially driving postoperative infectious complications [7].

3. Treatment

The management of urosepsis primarily encompasses four key aspects [51]: (1) Supportive therapy (hemodynamic stabilization); (2) Early antibiotic administration;(3) Elimination of predisposing factors;(4) Adjunctive sepsis therapies.

3.1. Supportive Therapy

Maintaining fluid-electrolyte balance is critical in urosepsis management. During early sepsis, a cascade release of inflammatory mediators increases vascular permeability, causing significant fluid extravasation and eventual intravascular volume depletion. Without prompt fluid resuscitation, this may progress to hypovolemic shock and mortality [52]. Early Goal-Directed Therapy (EGDT) was previously advocated to reduce mortality in severe sepsis and septic shock [53]. However, recent large-scale randomized trials [54-56] demonstrate no mortality reduction with EGDT compared to conventional care. Fluid Management Principles: (1) Post-resuscitation reassessment of volume status and tissue perfusion is mandatory, as excessive fluid accumulation correlates with higher mortality [57]. (2) Crystalloids remain first-line, with balanced crystalloids (e.g., lactated Ringer's) preferred over normal saline due to superior survival outcomes [58, 59].

3.2. Antibiotic Therapy

Rational antibiotic use is decisive in treating urosepsis, with earlier initiation directly improving prognosis. Notably, patients receiving antibiotics within 30 minutes of hypotension onset exhibit significantly higher survival rates than those treated in the subsequent 30-minute window (82.7% vs. 77.2%), while each hour of delay reduces survival by 7.6% [60]. Given that urinary tract infections are predominantly caused by Gram-negative bacilli—including Escherichia coli, Proteus, Klebsiella, and Pseudomonas aeruginosa [61, 62]—empirical therapy should commence immediately using β-lactams or third-generation cephalosporins, escalating to aminoglycosides or carbapenems in severe cases. For patients with positive blood or stone cultures, antibiotics must be adjusted promptly based on susceptibility results. Per Chinese Urological Guidelines [2], the recommended duration is 7-10 days, extended for slow clinical responders.

Source Control

Urinary tract obstruction—most commonly caused by calculi—constitutes the primary infectious focus. Immediate decompression is essential, prioritizing minimally invasive techniques under local anesthesia: retrograde double-J stent insertion or percutaneous nephrostomy. Definitive management of underlying causes (e.g., stone removal, stricture repair) should be deferred until after obstruction relief and adequate antimicrobial therapy, proceeding only when surgical safety is assured.

3.3. Adjunctive Therapies

Adjunctive sepsis management encompasses corticosteroids, vasoactive agents, insulin, and thromboprophylaxis. While corticosteroid use remains controversial [63, 64], the 2016 Surviving Sepsis Campaign (SSC) guidelines [65] advise against intravenous hydrocortisone for septic shock if hemodynamic stability is achieved with fluids and vasopressors. Norepinephrine is the preferred vasopressor due to its potent vasoconstrictive effect on mean arterial pressure with minimal heart rate changes; whereas dopamine—though potentially beneficial in systolic dysfunction—carries higher risks of tachycardia and arrhythmias [66]. For glycemic control, insulin should initiate when blood glucose exceeds 180 mg/dL on two consecutive readings, maintaining levels below 180 mg/dL rather than targeting 110 mg/dL [65]. Thromboprophylaxis with low-molecular-weight heparin (LMWH) is recommended unless contraindicated, with mechanical prophylaxis as the alternative [65].

4. Conclusion

While urosepsis exhibits relatively low incidence, its atypical presentation, rapid progression, and high mortality demand vigilant clinical attention. Multiple perioperative risk factors (pre-, intra-, and postoperative) underscore the necessity for comprehensive perioperative management to mitigate occurrence. Upon diagnosis, immediate intervention—including prompt source control and targeted therapy—is critical to optimize patient outcomes.

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