

## Original Research Article

# Systemic inflammatory response syndrome in ureteroscopy: frequency, risk factors, and implications for prevention

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## ABSTRACT

**Background:** Systemic inflammatory response syndrome (SIRS) is a preventable cause of morbidity and mortality in patients undergoing ureteroscopy for urinary stone treatment. Multiple factors, including diabetes, hypertension, positive urine cultures, prophylactic antibiotics, and procedure duration, may influence SIRS risk, but their individual roles remain unclear.

**Methods:** A descriptive, retrospective, and prospective cross-sectional study was conducted at Hospital General Dr. Manuel Gea González from January 2021 to December 2024. Inclusion criteria encompassed patients aged  $\geq 18$  years undergoing ureteroscopy. Data were collected on comorbidities, stone characteristics, procedural details, and outcomes. Statistical analyses were performed using logistic regression to identify risk factors. Ethical approval was obtained.

**Results:** Among 351 patients, 60 (17.09%) developed SIRS. Factors associated with higher SIRS rates included flexible ureteroscopy (73.33%), ureteral access sheath use (50%), postoperative stents (60%), and preoperative positive urine cultures (33.33%). Patients with harder stones ( $\geq 1175$  HU) experienced longer operative times ( $\geq 75$  minutes).

**Conclusions:** Flexible ureteroscopy, ureteral access sheaths, postoperative stents, and positive urine cultures are significant risk factors for SIRS.

**Keywords:** SIRS, Ureteroscopy, Kidney stones, Ureteral stones

## INTRODUCTION

Urinary tract infections (UTIs) include infections in the bladder (cystitis) and upper urinary tract (pyelonephritis). These infections are commonly caused by the colonization of the urethral meatus or vaginal introitus by fecal flora pathogens that ascend to the bladder and upper urinary tract. Other causes include hematogenous spread from infectious foci outside the genitourinary system, which

travel to the kidneys via the bloodstream or lymphatic system, usually caused by *Staphylococcus aureus*, often leading to more severe infections with tissue necrosis and abscess formation in the kidneys or perirenal spaces.<sup>1</sup>

Systemic inflammatory response syndrome (SIRS) is defined as the body's response to severe injury or infection, characterized by an excessive activation of the immune cascade aimed at localizing and eliminating

endogenous or exogenous injury.<sup>2,3</sup> This process activates and releases acute-phase reactants, which directly mediate alterations through autonomic, endocrine, hematological, and immunological pathways, potentially leading to widespread oxygen delivery reduction, reversible or irreversible organ dysfunction, and even death.<sup>2</sup>

Several statistical analyses have been conducted on the incidence of these cases, showing an average of 437 cases per 100,000 patients in developed countries. However, global statistics reveal much higher numbers, with a study reported in 2017 estimating 48.9 million cases worldwide, including 11 million deaths, representing 19.7% of all global deaths. The admission rate with SIRS criteria ranges from 12.8 to 18.6 per 1,000 admissions.<sup>4-6</sup>

When SIRS is suspected to have an infectious origin, it is referred to as sepsis. Sepsis is characterized by two or more of the following signs: temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ , heart rate  $>90$  beats per minute, respiratory rate  $>20$  breaths per minute or  $\text{pCO}_2 <32$  mmHg, white blood cell count  $>12,000/\text{mm}^3$  or  $<4,000/\text{mm}^3$ , or  $>10\%$  immature forms.<sup>7</sup>

There are different degrees of sepsis severity, ranging from infection and bacteremia to sepsis and septic shock, which can progress to multiple organ dysfunction and death. Early identification of infection and bacteremia, the initial stages of this spectrum, involves recognizing the invasion of microorganisms in sterile tissues, which leads to infection. When a bacterial presence is confirmed via blood culture, it is classified as bacteremia.<sup>8</sup>

Early sepsis detection can reduce the incidence of sepsis and its potentially fatal consequences by using appropriate tools. The most commonly used score is the quick sequential organ failure assessment (qSOFA), which is easy to calculate and is based on three components quickly identifiable at the patient's bedside, particularly in non-intensive care settings: respiratory rate  $\geq 22$  breaths per minute, altered mental status, and systolic blood pressure  $\leq 100$  mmHg.

Each of these components adds one point, and a score of  $\geq 2$  points indicates a higher likelihood of poor outcomes due to sepsis.<sup>3</sup> The qSOFA is a modification of the SOFA score, which assesses six organ systems: pulmonary evaluation through  $\text{PaO}_2/\text{FIO}_2$  ratio, considering patients on mechanical ventilation; coagulation evaluation based on platelet count; liver function evaluation through total bilirubin levels; cardiovascular evaluation through mean arterial pressure and vasopressor use in different doses; neurological evaluation using the Glasgow coma scale; and renal function evaluation based on serum creatinine levels.<sup>9</sup>

There are various risk factors for developing sepsis and/or septic shock, including intensive care unit admission, advanced age ( $\geq 65$  years), bacteremia, immunosuppressive treatments, diabetes, obesity, any type of cancer, previous hospitalizations, and genetic factors.

Risk factors specifically associated with urological procedures, particularly those identified in studies by the Clinical Research Office of Endourological Society (CROES), which evaluated 11,885 patients with complications in 7.4% of cases, include the following.

#### ***Previous urinary catheterization with ureteral stents***

This is related to urinary complications following ureteroscopy procedures in up to 22.3% of cases.<sup>10</sup>

#### ***Positive urine cultures prior to the procedure***

Positive urine cultures were associated with SIRS in 76.2% of cases.<sup>16</sup>

#### ***Use of ureteral access sheaths during flexible ureteroscopy and their size***

A higher incidence of SIRS was reported with 12/14 Fr sheaths compared to 14/16 Fr sheaths, which, having a larger diameter, allow for lower intrarenal pressure and better urine drainage. SIRS occurred in 81% versus 19%, respectively.<sup>11</sup> Overall, sheath use was associated with 28.8% of complications, regardless of size.<sup>12</sup>

#### ***Prolonged operative time***

The average operative time for patients with complications, including SIRS, was longer than those without complications, averaging 50 minutes (range 33-75 min) compared to 40 minutes (range 25-60 min).<sup>13</sup>

#### ***Stone location and size***

Ureteral stones were associated with more complications (62.9%) than renal stones (23.9%), though SIRS was more prevalent in the treatment of renal stones (42.9%) compared to ureteral stones (33.3%).<sup>14-17</sup>

The incidence of SIRS following flexible ureteroscopy has been reported to range from 6.9% to 9.1%, with no clear understanding of unique or isolated causes.<sup>9-13</sup> These factors should be evaluated collectively, as initially reported in studies from 2014.

#### ***Objectives***

The general objective was to identify the frequency of SIRS in patients undergoing ureteroscopy for the treatment of urinary stones and to evaluate the known factors associated with its development. The specific objectives were to report the frequency of SIRS based on the use of antibiotic prophylaxis, the presence of positive preoperative urine cultures, the composition of the urinary stones, the use of ureteral access sheaths, the use of postoperative ureteral stents, the presence of comorbidities, and the duration of the surgical procedure.

## METHODS

### Study design and setting

This descriptive, retrospective, and prospective cross-sectional study was conducted at the Department of Urology, Hospital General Dr. Manuel Gea González, from January 2021 to December 2024.

### Patient selection

Inclusion criteria included patients aged  $\geq 18$  years undergoing flexible or rigid ureteroscopy for ureteral or renal stone treatment. Exclusion criteria included active infections, recent antibiotic use ( $< 2$  weeks), and incomplete medical records.

### Procedures

All patients underwent preoperative evaluation, including urine culture, imaging (CT or ultrasound), and risk assessment. Prophylactic antibiotics were administered based on culture results. Ureteroscopy procedures followed standard protocols using 11/13 Fr access sheaths for flexible ureteroscopy and stent placement as indicated.

### Statistical analysis

Descriptive statistics summarized demographic and clinical variables. Logistic regression identified risk factors for SIRS. Statistical significance was set at  $p < 0.05$ .

### Sample size calculation

Sample size was calculated to detect a 10% difference in SIRS rates with 80% power and  $\alpha = 0.05$ , requiring a minimum of 300 patients.

## RESULTS

A total of 351 patients met the inclusion criteria (male or female patients aged 18 years or older who underwent

flexible or rigid ureteroscopy for the treatment of ureteral and renal stones).

The average age of the 351 patients was 46 years, with a minimum age of 18 years and a maximum age of 86 years. Of these, 175 patients (49.85%) underwent flexible ureteroscopy, 109 patients (31.05%) underwent rigid ureteroscopy, and 67 patients (19.1%) underwent a combination of flexible and rigid ureteroscopy. A preoperative positive urine culture was found in 51 patients (14.52%), with *Escherichia coli* being the predominant organism in 32 of these cases (62.74%) (16). Antibiotic prophylaxis with third-generation cephalosporins (ceftriaxone) or selective antibiotics based on preoperative urine culture and antibiogram was administered in 100% of cases.

Comorbidities included diabetes mellitus type 2 (DM) and systemic arterial hypertension (SAH) in 32 patients (9.11%), DM alone in 30 patients (8.54%), and SAH alone in 32 patients (9.11%). A ureteral access sheath (11/13 Fr) was used in 197 procedures (56.12%) (16, 17), and a postoperative ureteral stent was placed in 146 patients (41.59%) (17). The mean stone density was 916 Hounsfield units (HU), with a minimum density of 100 HU and a maximum of 1900 HU (14, 15). Stones were subdivided into those with densities less than 1000 HU (264 stones, 54.2%) and those greater than 1000 HU (223 stones, 45.8%). The average duration of the procedure was 60 minutes, with a minimum of 15 minutes and a maximum of 260 minutes.

Among the 351 patients, 60 (17.09%) developed SIRS. The average age of these patients was 46 years (range: 19-68 years). In these patients, flexible ureteroscopy was performed in 44 cases (73.33%), while rigid ureteroscopy was performed in 16 cases (26.67%). A positive preoperative urine culture was found in 20 patients (33.33%), with *Escherichia coli* being the predominant organism in 10 of these cases (50%).<sup>16</sup> Comorbidities included both DM and SAH in 8 patients (13.33%), DM alone in 10 patients (16.66%), and SAH alone in 8 patients (13.33%).

**Table 1: Comparison of clinical outcomes in ureteroscopic procedures: SIRS versus non-SIRS patients.**

Variables	Total (n=351)	SIRS patients (n=60) (%)	Non-SIRS patients (n=291) (%)
Number of patients	351	60 (17.09)	291 (82.91)
Average age (min-max) in years	46 (18-86)	46 (19-68)	46 (18-86)
Flexible ureteroscopy	175	28 (16)	147 (84)
Rigid ureteroscopy	109	16 (14.67)	93 (85.33)
Flexible + rigid ureteroscopy	67	16 (23.88)	51 (76.12)
Preoperative positive urine culture	51	20 (39.21)	31 (60.79)
Use of ureteral access sheath	197	30 (15.22)	167 (84.78)
Postoperative ureteral stent	146	36 (24.65)	110 (75.35)
Stone density (average HU)	916	1175	940
Operative time (minutes)	60	75	60

In patients who developed SIRS, a ureteral access sheath was used in 50% of the cases, with its use being more prevalent in flexible ureteroscopy procedures (68.18%).<sup>16</sup> No ureteral access sheath was used in rigid ureteroscopy procedures. Postoperative ureteral stents were placed in 36 procedures (60%), with 24 stents (54.54%) placed after flexible ureteroscopy and 12 (75%) placed after rigid ureteroscopy. The average stone density in these patients was 1175 HU, with a minimum of 218 HU and a maximum of 1519 HU. The average procedure duration was 75 minutes, with a minimum of 15 minutes and a maximum of 180 minutes, with a mode and median of 60 minutes (Table 1).<sup>16</sup>

## DISCUSSION

In our study, a total of 60 out of 351 patients developed SIRS, representing 17.09% of the studied population. This incidence is higher than what has been reported in multiple international studies, where the incidence ranges from 7.4% to 9.7%.<sup>9,11,16</sup>

Among these 60 patients, it is important to highlight that the majority underwent flexible ureteroscopy with the use of ureteral access sheaths. They had positive urine cultures prior to the procedure, longer operative times (greater than 75 minutes), and required the placement of a postoperative ureteral stent. These results are similar to those obtained by Mi et al.<sup>16</sup>

In our SIRS population, the predominance of stones with higher densities (average of 1175 HU) reflects harder stone composition, which impacts the duration of the procedure (average of 75 minutes). The combination of positive urine cultures and higher stone densities presents a set of risk factors predisposing patients to the development of SIRS. However, our data are still limited to confirm a direct relationship between stone density and the development of SIRS as an isolated factor.

These findings align with studies conducted by the Clinical Research Office of Endourological Society (CROES), where the use of ureteral access sheaths, positive urine cultures, and prolonged operative times were significantly associated with an increased risk of SIRS following ureteroscopy.<sup>16,17</sup>

However, there are still gaps in understanding the specific roles of stone density and composition in the development of SIRS. Some studies suggest that higher-density stones, particularly those above 1000 HU, often require more laser energy and longer operative times, leading to increased intrarenal pressure and a higher likelihood of residual fragments, which may explain the association with higher SIRS rates.<sup>14,15</sup> Nevertheless, further prospective studies are needed to explore the independent role of stone density in SIRS development.

This study's retrospective nature limits causal inferences. Potential biases include incomplete records and

heterogeneity in procedural techniques. The single-center design limits generalizability, and prospective multicenter studies are needed to validate findings.

## CONCLUSION

The findings of this study demonstrate an increased frequency of SIRS in patients undergoing flexible ureteroscopy, particularly associated with the use of ureteral access sheaths, postoperative stents, and positive preoperative urine cultures. These results highlight the need for a comprehensive understanding of the interplay between procedural factors and patient characteristics. Addressing these factors through optimized surgical techniques and tailored perioperative management can contribute to improved patient safety and reduced complications in ureteroscopy.

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