

## Review article

### Urosepsis in adults

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**Abstract:** Urosepsis is defined as sepsis caused by urinary tract infection (UTI). Urosepsis represents a quarter of all cases of sepsis in adults. Complications of UTIs are the most common risk factor for urosepsis development. These infections, especially pyelonephritis, often occur in patients with structural or functional malformations that interfere with normal urine flow. The problem of a significant increase in UTIs with multiresistant bacteria should be emphasized, especially in patients with recurrent UTI and their frequent treatments. As the urogenital tract is one of the most common sources of infection in sepsis in general, a detailed assessment of the tract should be carried out in all septic patients. Even though urosepsis is associated with a relatively good prognosis and lower mortality than sepsis of another etiology, it occurs rapidly and progresses at a significant speed. Since urosepsis is mainly the result of obstruction of the urinary tract, the development of septic shock can most often be prevented by implementing early deobstruction. Knowledge of the most common causes of urosepsis and the category of high-risk patients will provide clinicians with the tools with which to prevent its occurrence.

**Keywords:** urosepsis; urinary tract infections; risk factors

## INTRODUCTION

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) defines sepsis as a life-threatening organic dysfunction arising from an irregular response of the host to infection. This response of the host involves not only systemic inflammation, but also the dysfunction of many systems, such as the hormonal, metabolic, coagulation, micro- and macrovascular and antiinflammatory systems [1,2]. Furthermore, sepsis is classified according to the level of severity and the development of associated organ dysfunction and shock, which exacerbate the outcome of treatment for patients. Patients with developed refractory septic shock have a mortality of about 50% [3].

Urosepsis is defined as sepsis caused by urinary tract infection (UTI). It represents about 25% of all cases of sepsis in adults, and the prognosis of these patients is more favorable with a mortality of patients from 20% to 40% [4,5]. Complicated urinary infections are the most common cause of sepsis in patients older than 65 years [6]. In patients with a nosocomial UTI in urological departments, the prevalence of urosepsis is about 12%, while in patients with a nosocomial urinary tract infection treated in other departments, the prevalence of sepsis is 2% [7].

## Etiology of urosepsis

The causes of urosepsis and urinary infections in general are numerous. UTIs are listed as the cause

of sepsis from 9% to 31% [8]. UTIs are one of the most common nosocomial infections. In a study of the European Center for Disease Prevention and Control, UTIs accounted for 19% of all nosocomial infections, especially in urology departments due to interventions on the urinary tract. The most common forms were asymptomatic bacteriuria (29%), cystitis (26%), pyelonephritis (21%) and urosepsis (12%) [9].

UTIs are often divided into uncomplicated and complicated. Uncomplicated UTIs represent low-risk infections for the development of urosepsis, while complicated are the most common risk factor for urosepsis development. The most commonly used classification is proposed by the European Association of Urology [10]. According to this classification, UTIs are divided into Uncomplicated, Complicated, Recurrent, Catheter-associated UTIs and Urosepsis. Uncomplicated UTIs are acute, sporadic or recurrent lower and/or upper UTIs, limited to non-pregnant women with no known relevant anatomical and functional abnormalities within the urinary tract or comorbidities. Complicated UTIs are all other UTIs not defined as uncomplicated. These infections occur in patients with an increased risk of a complicated course: patients with anatomical or functional abnormalities of the urinary tract, indwelling urinary catheters, renal diseases with immunocompromising diseases such as diabetes, etc. Recurrent UTIs represent uncomplicated or complicated infection that occur at least three times a year or two times in the last six months. Catheter-associated UTIs occur in a person whose urinary tract is currently catheterized or has had a catheter in place during the past 48 h. Urosepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection originating from the urinary tract and/or male genital organs [10].

Urosepsis typically starts with a UTI and the severity of urosepsis depends primarily on the host's response to the infection. The frequency of urosepsis has increased significantly in recent years, suggesting the need for a high level of caution in the treatment of urological patients [11,12]. The most common uropathogen is *Escherichia coli*, which is responsible for about 80% of uncomplicated UTIs [13]. In the case of complicated infections and in the pathogenesis of urosepsis, commonly isolated pathogens are *Escherichia*

*coli* (43%), *Enterococcus* spp. (11%), *Pseudomonas aeruginosa* (10%) and *Klebsiella* spp. (10 %) [11]. It has been shown that patients with Gram-negative bacteremia develop a stronger inflammatory response with higher serum C-reactive protein (CRP) values and interleukin-6 (IL-6) than patients with Gram-positive bacteremia. These patients develop septic shock more rapidly and have a mortality of about 40% versus Gram-positive infections with a mortality of about 28% [6].

The problem of the significant increase in UTIs with multiresistant bacteria should be emphasized, especially in patients with recurrent UTIs and their frequent treatments [14]. The incidence of resistance is greater in patients with urosepsis than in other nosocomial UTIs. The most common multiresistant pathogens involved in the pathogenesis of urosepsis are Enterobacteriaceae, which are resistant in about 45% of cases, and *Pseudomonas aeruginosa* that is multiresistant in 21% of cases [11]. Excessive and irrational use of antibiotics has certainly contributed to the occurrence of this problem. A special clinical problem among urological patients is the presence of asymptomatic bacteriuria. Asymptomatic bacteriuria is the presence of bacteria in properly collected urine in patients that present no signs or symptoms of an UTI. Asymptomatic bacteriuria is common in clinical practice and its incidence increases with age. This condition usually leads to the unnecessary use of antibiotics. Treatment of asymptomatic bacteriuria is generally recommended only in pregnant women and preoperatively in urological patients who will undertake surgical treatment [15].

The guidelines of the European Association of Urology state that asymptomatic bacteriuria does not represent a risk factor for the development of infection in diagnostic and therapeutic procedures that do not involve entering the urogenital tract, so its treatment is not advised. On the other hand, in procedures that involve entering the urogenital tract and possible trauma to the mucosa, especially in endoscopic surgery, bacteriuria presents a risk factor for the development of infection and should be treated [10]. Interesting data from literature suggest that the treatment of asymptomatic bacteriuria prior to orthopedic surgical implantation of joint prosthesis is not beneficial and is not recommended. Also, some authors suggest that

in open-heart surgery, in the absence of symptoms of UTI, urinalysis and urine culture did not show any benefits in the perioperative evaluation of these patients [10, 16, 17].

## Pathogenesis

The rapid inflammatory response of a host to the presence of bacteria in the urogenital system is characterized by the appearance of urosepsis. Pathogenesis of urosepsis is a complex process of a series interactions between the initial inflammatory response and the counterregulatory antiinflammatory response, and the overall response of the host includes the participation of the autonomic nervous system, the endocrine system and coagulation pathways [7].

Despite microbiological pathogens being the cause of the disease, it is the host that develops the disease. The bacteria bind to cellular receptors on the surface of macrophages, neutrophils, endothelial cells or urothelial cells. Intracellular signal transducers are activated and lead to transcription of cytokine mediators, primarily interleukins and tumor necrosis factor. These factors trigger the formation of chemokines, prostaglandins, thromboxanes, leukotrienes and nitric oxides. There is a development of a strong proinflammatory reaction involving neutrophils and macrophages, as well as T and B lymphocytes [7]. During the development of sepsis, cells of both the innate and acquired immune system uncover necrosis by releasing mediators that can also further alter the immune system. That is why both the pathogen-related and host immune systems are viewed together as patterns of sepsis development [18, 19].

## Risk factors

Risk factors for the occurrence of urosepsis are numerous. Some categories of patients, such as females and elderly patients, are at greater risk of developing urosepsis than men and younger individuals. All UTIs are more common in women. Bacteriuria has the highest prevalence among the older population, and its incidence in older women is about 50%. More than 60% of patients with sepsis are older than 65 years. The presence of urinary infection is the second most common form of infection in geriatric patients.

However, the classic symptoms of an infection in older patients may be masked by comorbidities, but as their body temperature is lower, it does not have to increase to indicate an infection [20].

Complicated UTIs, especially pyelonephritis as the most frequent precursor of urosepsis, most often occur in patients with structural or functional malformations that interfere with normal urine flow. The most common cause of urosepsis is an obstruction that impedes urine flow. Patients that are particularly sensitive are those with anatomical malformations of the urinary tract, neurogenic bladder, vesicoureteral reflux, chronically placed drainage systems such as urinary catheters, ureteral stents, percutaneous nephrostomy, as well as patients with a history of the presence of infection due to calculosis or with previous urological interventions [21]. Various structural and functional disorders of the genitourinary system associated with urosepsis are shown in Table 1.

**Table 1.** Disorders of the genitourinary system associated with urosepsis.

<p><b>Obstruction of normal urine flow</b></p> <ul style="list-style-type: none"> <li>• Congenital: Urethral or ureteral stricture, phimosis, ureterocele</li> <li>• Acquired: calculus, prostatic hypertrophy, urinary tract tumors, trauma, radiotherapy</li> </ul>
<p><b>Instrumentation</b></p> <ul style="list-style-type: none"> <li>• Urological procedures</li> <li>• Presence of urinary catheter</li> <li>• Nephrostomy tube</li> <li>• Ureteral stent</li> </ul>
<p><b>Impaired emptying</b></p> <ul style="list-style-type: none"> <li>• Neurogenic bladder</li> <li>• Cystocele</li> <li>• Vesicoureteral reflux</li> </ul>

Patients with chronic urinary catheters and stents have an increased predisposition to the development of bacteria as well as fungal infections. On the present drainage systems placed in the urinary tract, a biofilm is often formed by the accumulation of microbes. The presence of this biofilm leads to irritation of the urothelium, causing an inflammatory response. It was shown that colonization of a ureteral stent occurs in as much as 42-90% of patients [22]. Of greatest importance for the occurrence of infection is the duration of catheterization. The incidence of catheter-related bacteriuria increases by 3-8% with each day [10]. However, this colonization is most commonly

polymicrobial, while urinary system infections are most commonly the result of the development of a single bacterial species. This indicates that potential stent contamination occurs during its insertion [23].

A systematic review that included six major studies of urosepsis risk factors showed that chronic urinary catheter use was associated with a higher frequency of sepsis. It was shown that the presence of a urinary catheter was associated with Gram-positive bacteria more than with Gram-negative bacteria. Patients who have a catheter-related urine infection develop bacteremia three times more often than patients with asymptomatic bacteriuria associated with the catheter. Also, patients with UTI associated with a catheter are four-fold more likely to develop uroseptic shock [6].

### Interventions on the urogenital system

Particularly important for clinicians is urosepsis that has developed in a hospital after interventions on the urinary system. The main feature of this kind of urosepsis is its unpredictable and rapid development, and the importance of early recognition should be emphasized for its rapid and adequate treatment. Prior to surgical treatment, of essential importance is patient evaluation and categorization according to: general health status as per the American Society of Anesthesiology classification score (ASA score), the presence of risk factors such as age, diabetes mellitus, an impaired immune system, the presence of specific risk factors such as urogenital infection, catheter presence, recent urinary intervention, and the type of intervention and possible contamination of the surgical field.

Patients with a positive urinary culture are at highest risk of developing urosepsis following interventions on the urinary system. This correlation was demonstrated regardless of whether the patients received an antibiotic prior to intervention or were asymptomatic [24]. Postrenal obstructive uropathy is the cause in 78% of urosepsis. The most common causes of obstruction are urolithiasis (43%), prostate adenoma (25%) and malignancies (18%). Bacteremia occurs because of increased pressure in the renal collecting system due to impaired free urine flow. In endoscopic procedures, rapid perfusion and flushing with irrigation fluid leads to an additional increase in intrarenal pressure, thus allowing bacteria and toxins to enter the

small blood vessels of the convolutes. Trauma to the genitourinary system in the presence of bacteria in urine is associated with an increased risk of developing urosepsis. The development of urosepsis after UTI occurs usually after the use of instruments for stone treatment, prostate biopsies and transurethral resections, and there is a marked heterogeneity in reporting urosepsis rates in literature [25], as follows:

- transurethral resection of the prostate: 0-4%
- transrectal prostate biopsies: 0.5-0.8%
- shock wave lithotripsy: 1%
- ureteroscopy for stone treatment: 9% systemic inflammatory response syndrome (SIRS), 3% severe sepsis
- percutaneous kidney stone surgery: 23-27% SIRS, 1.4-7% sepsis, and
- endoscopic urethrotomy: 8%.

The published data indicate that the risk of infectious complications following ureteroscopy is in the range of 2.2% to as much as 20% [24,26,27]. Potential risk factors for urosepsis after ureteroscopy are preoperatively positive urine culture, the presence of stones and the presence of comorbidity. Prior to these interventions, patients with positive urine culture should be adequately treated, and these patients should be followed postoperatively. Several intraoperative precautions such as shortening the intervention time as well as the need for lowering irrigation pressure reduce perioperative complications [28].

Urosepsis is the most severe complication of interventions on the urinary system, such as percutaneous nephrolithotomy. The frequency of bacteremia after this intervention is 23%, of endotoxemia 34%, febrile reactions 25% and sepsis 0.3-2.5% [29]. One study showed that the overall complication rate after this procedure was 30% and that the most common complications observed were postoperative fever (9.52%) and bleeding [30]. A study involving 580 patients showed that three key factors correlated with the occurrence of sepsis. These are the size of a stone over 2.5 cm, the duration of an operation of more than 120 min, and significant bleeding that required transfusion [31]. In a similar study conducted on 405 subjects, diabetes mellitus, larger stones, longer

duration of surgery, increased irrigation speed and stone infection were identified as independent risk factors for the occurrence of sepsis following a single intervention [32].

It is important to note that some gynecological operations such as radical hysterectomy carry an increased risk of urological complications which, if not recognized and treated in time, can lead to urosepsis. Injuries of the ureter and bladder are the most serious complications in gynecological surgery. Ureteral injury leads to extraperitoneal or intraperitoneal accumulation of urine followed by vaginal leakage. Vesicovaginal and ureterovaginal fistulas are reported to develop after radical hysterectomy, and according to this study, the incidence of ureteric injuries during radical hysterectomy is 1.3% and of bladder injuries 1.49% [33].

A statistically significant association of urosepsis with the ASA score was demonstrated. Of the comorbidities present, the greatest risk factor for the occurrence of urosepsis is diabetes mellitus [24]. People with diabetes are at high risk of developing various complicated genitourinary system infections, including sepsis. Predisposing factors include poor glycaemic control, the presence of autonomic neuropathy, high glucose levels in the urine, diabetic cystopathy, increased bacterial adherence to uroepithelial cells, impaired immune function [34]. Some characteristics of UTIs in patients with diabetes mellitus are as follows: frequent asymptomatic bacteriuria, increased risk of recurrent infections, more common bilateral infections, and increased risk of renal insufficiency. Certain infections occur almost exclusively in diabetics, such as emphysematous pyelonephritis, renal papillary necrosis, renal abscess and prostatic abscess [34]. Special caution in the treatment of patients with diabetes is essential because they develop some of the most severe forms of the disease, including emphysematous pyelonephritis that is associated with high mortality, and renal abscess that develops in over 50% of diabetic patients [34].

### Clinical presentation and diagnosis

The signs and symptoms of the systemic inflammatory response that were previously considered for the diagnosis of sepsis today are warning symptoms. As the

urogenital tract is one of the most common sources of infection in sepsis in general, its assessment should be carried out in detail for all septic patients [28]. The presence of UTI should be confirmed. Diagnosis continues to rely on the recognition of a symptom constellation associated with sepsis. The presence of clinical symptoms, including a body temperature  $>38.5^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ , tachypnea, altered mental status; the presence of an inflammatory response: leukocytosis (WBC  $>11000$ ), leukopenia (WBC  $<4000$ ) or normal values of WBC and the presence of immature forms  $>10\%$ , hemodynamic changes: hypotension (systolic blood pressure  $<90\text{mmHg}$ , MAP  $<70\text{ mmHg}$ ) and tachycardia (heart rate  $>90/\text{min}$ ); the presence of signs indicating organic dysfunction: hypoxemia ( $\text{PaO}_2 / \text{FiO}_2 <300$ ), oliguria (urine output  $<0.5\text{ mL/kg/h}$  longer than 2 h despite sufficient fluid replacement), increased values of creatinine (increase  $>0.5\text{mg/dL}$  from baseline), coagulation disorder (INR  $>1.5$ , aPTT  $>60\text{ s}$ ); the presence of signs of insufficient tissue perfusion: elevated lactate ( $>2\text{ mmol/L}$ ), prolonged capillary refill time [28].

It is important to emphasize that urosepsis can rapidly progress to the most severe forms and must be treated aggressively. An early clinical presentation of urosepsis is most often elevated body temperature or hypothermia, tachycardia and altered mental status. It can be presented with various symptoms such as fever and tachypnea, but it can also be a rapid, acute multiorgan dysfunction and hypotension that requires pharmacological support.

The clinical assessment of the presence of genitourinary tract infection involves the presence of frequent urination, dysuria, hematuria, pyuria (in case of UTI), lumbar pain and fever (pyelonephritis), pain when sitting and during defecation, the presence of tumefaction during the digital rectal examination (prostatitis), scrotal pain (epididymo-orchitis) and postsurgical pain. Pain is a complex subjective experience with sensory-discriminative, emotional-affective and cognitive-evaluative components [35]. Diagnosis of sepsis of any etiology is a risk factor for developing chronic pain following Intensive Care Unit discharge [36].

Sepsis-2 proposes the use of the Sequential Organ Failure Assessment (SOFA) and quick SOFA (qSOFA) scoring system for quick bedside diagnosis. Organic

dysfunction is defined as an acute change in the overall SOFA score by 2 and more points, which is caused by infection. The new definition suggests a qSOFA score, which includes altered sensory, systolic pressure <100 mmHg and breathing frequency  $\geq 22$ /min. qSOFA can be used for fast screening as it does not require laboratory measurements or monitoring [1,2].

Even though urosepsis is associated with a relatively good prognosis and lower mortality than sepsis of another etiology, it should not be forgotten that it occurs and progresses very rapidly. It has been shown that organic dysfunction occurs much earlier in patients with urosepsis than in sepsis of another etiology. The WBC count and platelets drop significantly faster and procalcitonin rises significantly faster in the urosepsis group, but the need for mechanical ventilation is more common in sepsis of other etiology; in urosepsis the SOFA score is significantly associated with survival [37].

The most serious complication in patients with urosepsis is the development of shock. A recent study has shown that the occurrence of shock in uroseptic patients is more common in women and in patients with obstruction of the urinary system. In patients with uroseptic shock, Gram negative bacteria (70%) are most often isolated with a large proportion of multiresistant strains. In one multicenter study, high levels of CRP were shown to be an independent risk factor for the development of uroseptic shock [38]. Although this complication results in a high mortality rate, compared to a sepsis of another etiology, the mortality in septic shock caused by urinary infection is lower [37].

### **Analysis of urine and the presence of kidney stones**

Analysis of urine and urinary cultures must be carried out in all patients prior to antibiotic treatment. However, it should be emphasized that urinary cultures are of limited benefit in obstructive pyelonephritis, as urine with the highest pathogen concentration is above the obstruction. On the other hand, a negative urine culture has a high negative predictive value and is useful for excluding the presence of urinary infection [39].

Stone culture plays an important role in the identification of microbes as the cause of urosepsis. The presence of positive stone culture is associated with

an increased risk of urosepsis after endoscopic procedures. Positive stone culture can be followed by a negative preoperative urine culture. Therefore, microbiological stone treatment is recommended routinely in patients undergoing lithotripsy [40].

### **Biomarkers and urosepsis**

Biomarkers, together with clinical signs, significantly help in the identification of patients with sepsis and in monitoring the severity of the disease. Measurement of CRP values is routinely performed in patients with urosepsis. Although it has been used for more than ten years as an indicator of systemic inflammation caused by infection, the specificity of this biological marker is controversial. However, a large multicenter study has shown that high CRP values are an important and independent risk factor for shock [38].

Studies have shown that the values of procalcitonin (PCT) are more accurate predictors of bacterial infection than CRP and leukocyte values. The importance of PCT in assessing the course and outcome of sepsis as well as monitoring the effects of antibiotic therapy has been investigated in many studies. These studies (ProHOSP, PRORATA) have shown that the use of procalcitonin-guided causative therapy reduces the duration of antibiotic therapy but does not affect patient mortality. It is important to note that it is necessary to regularly measure the value of procalcitonin as an early marker of diagnosis and to distinguish between urosepsis and septic shock [41,42]. It has been shown that the values of procalcitonin are significantly different in patients with urosepsis and septic shock following percutaneous nephrolitholapaxia, while the leukocyte values were almost identical. Also, in patients with urosepsis who were adequately treated, the values of procalcitonin significantly decreased after two days, while the leukocyte values in the first two days did not change significant [43]. In the differential diagnosis of urosepsis and patients with febrile urinary infection, the ratio of procalcitonin/albumin can serve as an early diagnostic marker. This is a quick and relatively simple test. It has been shown that this ratio in patients with urosepsis is elevated, and it is an independent predictive risk factor. This ratio also has higher values in patients with septic shock than in those without [44].

A new biomarker, which is considered to be more specific and more sensitive in the diagnosis of sepsis, is presepsin (soluble CD 14-subtype-CD14-ST). However, there is still insufficient data in the literature on the prognostic significance of this biomarker in monitoring sepsis, or its significance in modeling antibiotic therapy [45].

### Treatment of urosepsis

Treatment of patients with urosepsis should be focused on the cause of infection (antibiotic therapy and the elimination of the focus of infection) and use supportive therapy (maintain hemodynamic stability) and additional therapy (glucocorticoids, insulin, etc.). Urosepsis treatment is subject to all the rules given in the Surviving Sepsis Campaign guidelines. The Surviving Sepsis Campaign proposes treatment of sepsis by implementing each treatment procedure within certain time frames. They suggest a set of measures to be applied within 3 h and within 6 h of diagnosing sepsis [2].

Within 3 h of suspected sepsis: take blood culture before using antibiotics, apply a broad-spectrum antibiotic, measure lactate concentration, apply 30 ml/kg of crystalloid when there is hypotension or lactate >4 mmol/L [2].

Within 6 h of suspected sepsis: apply vasopressor if the patient has hypotension that does not respond to initial fluid replacement (maintain mean arterial pressure (map) >65 mmHg), reconsider the volume status and tissue perfusion, monitor vital parameters, cardiopulmonary status, capillary filling, register central venous pressure (CVP), central venous oxygen saturation (ScvO<sub>2</sub>), perform cardiovascular ultrasound, examine dynamic response to volume through a bolus fluid (fluid challenge) or a passive foot test; check the lactate value again [2].

Urine output rate should be kept at >0.5 mL/kg/h. The onset of oliguria is a poor prognostic sign indicating the impending onset of acute kidney injury. A recent large cohort study found that the presence of oliguria on admission in the ICU was not independently associated with an increased risk of death, but the persistence of oliguria during ICU stay was associated with higher ICU and hospital mortality rates [46].

Intravenous fluid administration is an essential component of sepsis management, but fluid replacement in these patients must be carefully performed. Excessive fluid balance may adversely affect the outcome of treatment [47]. One study showed negative effects on patient mortality of higher cumulative fluid balance on day three; however, fluid replacement and cumulative fluid balance on the first day after admission was not associated with an increased risk of death [48].

Patients exhibiting symptoms should be urgently sampled for urine and blood. Urosepsis due to a large residual urine volume or acute urinary retention is best managed by rapid administration of a transurethral urinary catheter. Immediately after placement, urine should be sampled.

Any delay in initiating antibiotic therapy increases the mortality rate [49]. As soon as urinary culture and blood culture are taken, it is necessary to start antibiotic therapy empirically with a broad spectrum of antibiotics. The use of an adequate dose of the appropriate antibiotic is of crucial importance to the outcome of patients with urosepsis and septic shock. In cases of infection with multidrug-resistant bacteria, an infectious disease specialist should be consulted [50]. Adequate life-support measures and appropriate antimicrobial treatment provide the best conditions for improving patient survival. The European Association of Urology guidelines contain clear recommendations for antibiotic use in urosepsis [10]. Beta-lactamase-producing bacteria are the most common cause of urosepsis, while on the other hand, Enterobacteria that produce carbapenemases are still rare. Empirical therapy includes beta-lactam antibiotics of a wide spectrum. Piperacillin/tazobactam, carbapenems and the new cephalosporin/beta-lactamase inhibitor are given as monotherapy, while cephalosporins should be combined with aminoglycosides or fluoroquinolones. Adequate antibiotic therapy in the first hour of treatment of a septic patient or a patient with a serious urogenital infection significantly improves the outcome of the treatment. All diagnostic procedures must be carried out as soon as possible [51]. UTIs caused by multiresistant Gram-negative bacteria are a major problem due to limited therapeutic options. Aminoglycosides, colistin and tigecycline present alternatives in the case of multiresistant Gram negative infections [52].

The urosepsis treatment algorithm involves taking hemocultures and urine cultures (minimum two sets). In the first h, use of wide-spectrum antibiotics and urgent implementation of diagnostic procedures to determine the causes of infection (usually ultrasound or scanner). In the first 6 h, early administration of fluid and vasopressor if the response to fluid is poor, and control of glycemia. In the first 12 h, source control: drainage or debridement to eradicate or limit a focus of infection. Decompression of the urinary tract using stents, probes and urinary catheters is most important for a patient with urosepsis. Starting with oral or enteral nutrition as soon as possible, in the first 48 h.

Ultrasound is the first and the fastest method for examining the urogenital tract. Ultrasound detection of kidney renal dilation is easily established. Also, the urinary bladder and prostate should be examined. If an ultrasound scan is suspected of causing urosepsis, detailed imaging methods should be carried out [7].

A recent study showed an interesting result that the use of vitamin D in urosepsis patients shows a significant improvement in leukocyte, urea and creatinine values, as well as a reduction in the number of hospitalization days [53].

## Prevention

Prevention of urosepsis implies the identification of patients with predisposing factors such as certain comorbidities or malformations of the genitourinary tract. The main strategy for urosepsis prevention is the correction of genitourinary disorders that affect normal urine flow. As long as these disorders exist, patients are at risk of recurrent UTIs and urosepsis. Since urosepsis is mainly the result of obstruction of the urinary tract, development of septic shock can most often be prevented by early deobstruction [7]. Ureteroscopic lithotripsy is a method that postoperatively results in a much higher and statistically significant improvement of the quality of life of patients with urolithiasis [54]. Patients with diabetes mellitus as well as immunocompromised patients must be monitored closely both during the operative period and postoperatively. The risk is particularly high in the case of positive urinary culture, the presence of foreign bodies in the urinary system and obstructions. Therefore, adequate antibiotics must be carefully used

perioperatively [55]. Also, urinary catheters should be used only when there is clear clinical indication, they should be placed under sterile conditions and removed immediately after the need for them has ceased.

## CONCLUSION

Urosepsis is the most severe complication of urinary tract infection. It can usually be recognized at an early stage. Despite the association of urosepsis with a relatively good prognosis and lower mortality than sepsis of other etiology, urosepsis occurs and progresses rapidly. By knowing the most common causes of urosepsis and the category of high-risk patients, clinicians can prevent its occurrence. Quick diagnosis and early recognition of the focus of infection is crucial.

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