



# What Are the Predictive Factors of Severe Conditions in Acute Obstructive Pyelonephritis?

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Acute obstructive pyelonephritis is a common urological infection, often requiring emergency drainage, which shows rapid progression to serious conditions, including severe sepsis or septic shock. Therefore, during an initial evaluation, knowledge of factors for prediction of severe conditions or mortality is important for immediate identification of patients requiring intensive care. Previous studies examining the characteristics of patients with acute obstructive or calculous pyelonephritis reported rates of septic shock and mortality of 20.8-33.3% and 0-7.4%, respectively. Thrombocytopenia, older age, low serum albumin, and bacteremia were relatively common predictors for septic shock. In contrast, age over 80 years, systemic inflammatory response syndrome, disseminated intravascular coagulation status, disturbance of consciousness, male gender, and having only one kidney were predictive factors for mortality.

**Keywords:** Pyelonephritis; Sepsis; Septic shock; Ureteral calculi; Ureteral obstruction

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## INTRODUCTION

Complicated urinary tract infection is defined as infection caused by an anatomical or functional abnormality of the urinary tract. Severe conditions sometimes occur in patients with acute complicated pyelonephritis, and bacteremia has been reported in 20-41% [1,2].

Acute obstructive pyelonephritis is acute pyelonephritis caused by upper urinary tract obstruction associated with ureteral calculi, ureteral structure, or extrinsic compression. It often shows rapid development into a life-threatening condition such as disseminated intravascular coagulopathy (DIC), multiple organ dysfunction, or septic shock, even with appropriate treatment including anti-microbial therapy, urological intervention, and intensive care [3]. The incidence of sepsis has increased over 30 years, although improved

management has led to decreased mortality associated with sepsis [4,5]. Therefore clarification of factors in acute obstructive pyelonephritis that are predictive of severe conditions and mortality is important for immediate identification of patients requiring intensive care. In the current study, we summarized the recent findings regarding patient characteristics associated with emergency drainage, septic shock, and mortality in acute obstructive pyelonephritis.

## METHODS

A systematic literature review was conducted using PubMed and a Urogenital Tract Infection website (<http://www.euti.org/main.html>). Terms including “obstructive,” “pyelonephritis,” “calculi,” and “septic shock” were used as keywords. Original articles and their references were

checked, and articles about pyelonephritis in pregnant or infant patients were excluded. Data from eight clinical studies discussing predictive factors for severe conditions and mortality in patients with acute obstructive pyelonephritis were summarized (Table 1) [6-13].

## 1. Definitions of Sepsis, Severe Sepsis, and Septic Shock

Sepsis is generally defined as a clinical syndrome involving both infection and a systemic inflammatory response [14], whereas the clinical manifestations of systemic inflammatory responses to infection are highly variable. Systemic inflammatory response syndrome (SIRS) includes two or more of the following conditions: 1) body temperature higher than 38°C or lower than 36°C, 2) heart rate greater than 90 beats per minute, 3) tachypnea, as manifested by a respiratory rate greater than 20 breaths per minute or hyperventilation, as indicated by a partial CO<sub>2</sub> pressure less than 32 mmHg, and 4) white blood cell count greater than 12,000/mm<sup>3</sup> or less than 4,000/mm<sup>3</sup>, or more than 10% immature neutrophils, and SIRS is often used as the diagnosis of sepsis [15]. Of eight studies summarized in this study, four studies adopted SIRS as the definition of sepsis [7,9-11], while the definitions of systemic inflammation response to infection were not specific or mentioned in the other four studies [6,8,12,13]. Severe sepsis and septic shock are generally defined as sepsis complicated by acute organ dysfunction and sepsis with acute circulatory failure characterized by persistent arterial hypotension despite adequate volume resuscitation, respectively [14]. However, the specific criteria for septic shock are unclear, and varied among studies [7,8,11].

## 2. Patients and Definitions of Severe Conditions

Of the eight studies, seven were retrospective, single-institutional studies, and one was a multicenter, nationwide survey of obstructive pyelonephritis caused by urolithiasis [13]. Of the seven single-institutional studies, five included only obstructive pyelonephritis with upper urinary tract calculi and one included obstructive pyelonephritis with any causes [6-11], and the other study targeted severe acute pyelonephritis and included non-obstructive cases [12].

Three studies defined a severe condition as septic shock, and one defined it as sepsis [6-8,11]. The need for intensive management was reported as a severe outcome in another

**Table 1.** Predictive factors for severe conditions and mortality in patients with obstructive pyelonephritis

Author, year	Number	Study patients	Diagnostic criteria	Definition of severe condition	Rate of			Risk factors for		
					Severe condition	Mortality		Severe condition		Mortality
Lim et al., 2015 [6]	73	Calculus pyelonephritis	SIRS	Sepsis	50.7	NE		Age, albumin, NLR	NE	NE
Tambo et al., 2014 [7]	69	Calculus pyelonephritis	Fever, pyuria	Shock	33.3	0		Thrombocytopenia, albumin	NE	NE
Yamamoto et al., 2012 [8]	101	Calculus pyelonephritis required drainage	Fever, inflammation	Shock	20.8	2.0		Age, paralysis	NE	NE
Angulo et al., 2010 [9]	110	Calculus pyelonephritis	SIRS	Drainage	26.4	0		CRP, age	NE	NE
Yoshimura et al., 2005 [10]	473	Calculus pyelonephritis	SIRS	Drainage	12.5	0.2		Age, female gender, poor PS	NE	NE
Kamei et al., 2014 [11]	54	Obstructive pyelonephritis required drainage	SIRS	Shock	37.0	1.8		Thrombocytopenia, bacteremia	NE	NE
Chung et al., 2014 [12]	68	Severe acute pyelonephritis	Mortality or ICU or intervention	Long hospital stay (> 14 days)	32.4	7.4		Bacteremia, shock, ICU, suppurative pyelonephritis	Male gender, DIC	
Hamasuna et al., 2015 [13]	1,363	Calculus pyelonephritis	Diagnosed by urologists	Undefined	NE	2.3		NE	Age, SIRS, DIC, single kidney, DOC	

SIRS: systemic inflammatory response syndrome, NE: not evaluated, NLR: neutrophil to lymphocyte ratio, CRP: C-reactive protein, PS: performance status, ICU: intensive care unit, DIC: disseminated intravascular coagulation, DOC: disturbance of consciousness.

study [10]. Two studies evaluated risk factors for emergency drainage in calculous pyelonephritis [9,10], and risk factors for mortality were assessed in two studies [12,13].

### 3. Rates of Severe Conditions and Mortality

The rates of septic shock reported in these studies were 20.8-33.3% [7,8,11,12]. Chung et al. [12], in evaluation of hospital stays of longer than 14 days as an outcome of severe acute pyelonephritis, reported a rate of 32.4%; however, the mortality rates were 0-7.4% [6-13], and the prognosis of severe obstructive pyelonephritis was good in most cases.

## 4. Risk Factors for Severe Conditions

### 1) Thrombocytopenia

Kamei et al. [11] and Tambo et al. [7], who reported thrombocytopenia as a risk factor for septic shock in obstructive or calculous pyelonephritis (odds ratios [ORs]: 23.90 and 5.43, respectively), defined thrombocytopenia as a blood platelet count of less than 120,000-150,000/ $\mu$ l. Yoshimura et al. [10], who performed univariate analysis for comparison of the characteristics of patients who received intensive management with those who received emergency drainage, reported that platelet counts of less than 100,000/ $\mu$ l were associated with intensive care. Even mild thrombocytopenia can be a risk factor for severe conditions. This is clinically useful information because blood platelet count testing can be performed rapidly in most institutes.

### 2) Older age

Older age was reported as a risk factor for septic shock or emergency drainage in four studies (OR, 1.07-1.15) [6,8-10]. Martin et al. [16] reported that the relative risk for sepsis was 13.1 times higher for patients older than 65, and the mortality rates for sepsis for those older than 65 years were also significantly higher than for younger people (27.7% vs. 17.7%; OR, 1.56).

### 3) Low serum albumin

Tambo et al. [7] and Lim et al. [6] reported that a lower serum albumin level (less than 2.8 and 3.5 g/dl, respectively) is a risk factor for septic shock in acute pyelonephritis associated with ureteral calculi (ORs: 5.88 and 4.27,

respectively). A systemic inflammatory response decreases serum albumin concentration by increasing protein catabolism and decreasing hepatic synthesis and increased vascular permeability during the process of inflammation leads to the escape of albumin into the extravascular space [17,18]. In a univariate analysis, Bossink et al. [19] reported that in febrile medical patients with a clinical infection, both the initial and lowest serum albumin levels were significantly lower in patients with shock than in those without shock,

### 4) Bacteremia

Bacteremia is detected in approximately 30-50% of cases of severe sepsis and septic shock [20,21]. Kamei et al. [11] reported that a positive blood culture is a risk factor for septic shock in patients with obstructive pyelonephritis (OR, 9.11), and bacteremia in severe acute pyelonephritis showed significant association with a hospital stay longer than 14 days (OR, 3.71) [12]. Hsu et al. [1] reported that patients with a positive blood culture in complicated acute pyelonephritis were likely to present with severe sepsis (OR, 4.76). However the results of a blood culture take at least 8-12 hours, therefore its use as a predictive factor may be difficult in routine clinical practice [22,23].

### 5) Poor performance status (paralysis)

Poor performance status, such as spinal cord injury, is a risk factor for renal calculi [24,25] and for symptomatic urinary tract infection [26]. Yoshimura et al. [10] reported that a poor performance status (Karnofsky performance status of 70% or less) is an independent risk factor for the requirement for emergency drainage in patients with urosepsis associated with upper urinary tract calculi (OR, 2.9). Yamamoto et al. [8] reported that patients with paralysis suffered from septic shock more frequently than those without paralysis (OR, 10.78).

### 6) Other factors

Several studies have reported other risk factors for severe sepsis and septic shock. Neutrophil to lymphocyte ratio (NLR), which is known to be associated with the prognosis of various cancers, has recently been identified as an additional marker of infection [27-29]. Zahorec [30] reported correlation of clinical course severity with NLR in patients with sepsis treated in an intensive care unit (ICU). Lim et al. [6] suggested that a higher NLR was associated with

urosepsis in patients with acute obstructive pyelonephritis (OR, 3.83).

Chung et al. [12] reported significant association of long hospital stays in patients with severe acute pyelonephritis with not only bacteremia but also with suppurative pyelonephritis, septic shock, and need for care in ICU. Yoshimura et al. [10] reported that female sex was a risk factor for emergency drainage, and Angulo et al. [9] reported a C-reactive protein (CRP) level higher than 28 mg/L as an independent risk factor for the requirement of an emergency ureteral drainage (OR, 1.013). However, no studies showing correlation between septic shock and female sex or CRP level using multivariate analysis have been reported; therefore, they may not be a useful predictive factor for septic shock associated with obstructive pyelonephritis [6-8,11].

## 5. Risk Factors for Mortality

Two studies evaluated predictive factors for mortality. In Japan in 2009, a retrospective nationwide survey was conducted of characteristics of patients with pyelonephritis caused by urolithiasis [13]. Hamasuna et al. [13] concluded that age over 80 years (OR, 4.752), SIRS (OR, 2.613), DIC status (OR, 3.131), disturbance of consciousness (OR, 11.281), and having only one kidney (OR, 4.369) were independent risk factors for mortality.

In another study, Chung et al. [12] reported DIC status (OR, 10.31) and male gender (OR, 11.75) as independent prognostic factors for mortality in severe acute pyelonephritis. DIC status was the common predictor for mortality across both studies. These data suggest that the risk factors for mortality are not the same as those for septic shock (Table 2).

## 6. Additional Comment

The limitation of these results is that most of the studies were retrospective, single-institutional studies with small sample sizes, and diagnostic criteria and definitions of severe conditions were not standardized. Prospective multicenter studies with larger cohorts of patients and specific diagnostic criteria and definitions should be conducted in order to clarify the predictors for emergency drainage, septic shock, and mortality.

**Table 2.** Predictive factors for emergency drainage, septic shock, and mortality

Predictive factors for emergency drainage
C-reactive protein
Female gender
Older age
Poor performance status
Predictive factors for septic shock
Bacteremia
Low serum albumin
Neutrophil to lymphocyte ratio
Paralysis
Thrombocytopenia
Predictive factors for mortality
Age over 80 years
Disseminated intravascular coagulation
Disturbance of consciousness
Male gender
Systemic inflammatory response syndrome
Solitary kidney

## CONCLUSIONS

Thrombocytopenia, older age, low serum albumin, and bacteremia were relatively common predictive factors for septic shock among the described studies. Reported predictors for mortality were age over 80 years, SIRS, DIC status, disturbance of consciousness, male gender, and having only one kidney.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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