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# Elevated serum uric acid after injury correlates with the early acute kidney in severe burns

Juan Liang [a], Ping Zhang [a], Xinlei Hu [b], Lizhu Zhi [b,*]

[a] The Children's Hospital of Zhejiang University School of Medicine, Department of Internal Medicine, Hangzhou, China

[b] Second Affiliated Hospital of Zhejiang University School of Medicine, Department of Burn Surgery, Hangzhou, China

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ABSTRACT

*Objective:* Early acute kidney injury (AKI) is one of the most serious and common complications in the early stage of severe burns, but the pathological mechanisms still need to be elucidated. High uric acid (UA) has been found to be correlated with renal dysfunction in some experimental and clinical studies; however, the study of the dynamic correlation between AKI and UA in severe burns is still lacking.

*Methods:* The diagnosis and classification of AKI were performed according to RIFLE criteria, UA, serum creatinine (Scr), estimated glomerular filtration rate (eGFR), C-reactive protein (CRP) and lactic acid (LA) were dynamically monitored within 2 days after injury in 59 severely burned patients.

*Results:* Within 2 days after injury, AKI occurred in 23 of 59 patients (risk in 12 cases, injury in seven cases and failure in four cases), UA level in AKI patients was significantly higher than that in No-AKI patients, and referring to the cutoff level of UA (375.5 μmol/l) from ROC curve for predicting AKI, the abnormal increase of UA levels was earlier than acute deterioration of renal function in most of the AKI patients after injury. Among AKI patients, the Scr/eGFR levels were closely related to UA levels for 2 days after injury. Moreover, UA level in cases with severe grade of AKI was significantly higher than that in those with less severe grade of AKI. Furthermore, there was a positive correlation between UA and CRP for 2 days after injury in AKI patients, and a significant correlation between CRP and Scr/eGFR was found 1 day after injury. The positive correlation was also found between LA and UA after injury in AKI patients.

*Conclusion:* The results suggest that elevated serum UA after injury due to hypoxia is closely correlated with early AKI after severe burns, and UA-related aberrant inflammation also appears to be one of the pathogenic factors, providing the useful information for potential therapy.



* *Corresponding author*. Tel.: +86 0571 87783661.
E-mail address: zlizhu@yahoo.com (L. Zhi).

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## 1. Introduction

Early AKI is one of the most serious and common complications in the early stage of severe burns, and is associated with both short and long term adverse events [1–3]. As the pathogenesis and guidelines for the treatment of AKI are not well defined, the prevention is still the key strategy for dealing with AKI. Thus, it is of great importance to identify the potentially modifiable risk factors for developing AKI in the early stage of severe burns.

Recently, some animal experiments and clinical studies have shown that elevated serum UA was associated with the AKI by activating the renin–angiotensin system, suppressing nitric oxide to lead to systemic vasoconstriction and early saltresistant hypertension [4], impairing renal blood autoregulation, decreasing single nephron GFR, and inducing inflammatory and anti-angiogenic properties, etc. [5]. It was reported that preoperative serum UA $\geq$ 7 mg/dl was associated with a 35-fold increased risk for AKI in patients undergoing cardiovascular (CV) surgery [4], and in an animal model of AKI, lowering of UA has shown to decrease tubular injury and inflammatory response [6]. Therefore, although the detailed dynamic pathogenesis is still not clear, elevated serum UA was proposed as a novel risk factor for AKI [7].

The increase of UA level has also been found soon after severe burns in our previous reports, which was also closely related to the prognosis [8], but the study of the possible association between UA level and early AKI in severe burns has not been reported, and the continuously, dynamically clinical observation in severe burns is still lacking.

The purpose of this study is to investigate the possible correlation and its clinical implications between UA level and AKI in the early stage of severe burns, by monitoring the dynamic changes of blood UA and common indicators of renal function (Scr and eGFR). And the relevant mechanisms (related to hypoxia and inflammation, which were proposed to contribute to early AKI [9]) involved were also discussed: that is the dynamic monitoring of LA [10] (as an indice for overall tissue perfusion) and CRP (as a marker for inflammatory reaction) in the early stage of severe burns.

RIFLE criteria was used for the diagnosis and classification of AKI: The RIFLE acronym quantifies various elements of renal dysfunction into five categories: risk (R), injury (I), failure (F), loss (L) and end-stage kidney disease (E). In the first three categories, the RIFLE criteria define three grades of increasing severity of AKI by stratifying patients based on the changes in serum creatinine (SCr) and/or urine output (UOP) from the baseline condition (Table 1) [11]. Because AKI was defined as an absolute increase in SCr $>$ 0.3 mg/dl from baseline within 48 h after injury in accordance with the Acute Kidney Injury Network's criteria [12], dynamic monitoring were performed within 2 days after burn.

## 2. Patients and methods

### 2.1. Patients

We performed a prospective study in a cohort of severe burn patients. Considering the influence of gender on UA level, only men participated in this study.

Patients with more than 40% TBSA (total body surface area) burns (grades II–III°) caused by flame or scalds and admitted to the hospital 6–8 h after burn were enrolled into this study between January 2009 and November 2014. All patients were formerly healthy men, from the Department of Burn Surgery of the Second Affiliated Hospital of Zhejiang University School of Medicine, ranging from 20 to 50 years old.

Exclusion criteria were: electrical or chemical burn lesions, severe inhalation injury, decompensated heart failure, uremia, neoplasia, urolithiasis, gout, autoimmune disorders, recent cardiovascular events, vascular active drugs were used within 2 days after injury, combined with fracture or severe soft tissue injuries (creatine kinase $>$ 1000 u/l), with obvious abnormal liver function and apparent clinical manifestations of systemic infection or wound infection within 2 days after injury, and died within 2 days after injury.

Finally, 59 patients with severe burns were included for analysis. All of the clinical diagnoses and treatments were in accordance with Chinese Medical Association criteria [13]. Patients were treated in a uniform way. Routine anti-shock fluid therapy was administered after admission, approximately 6–8 h after injury. The resuscitation protocol in 48 h after burn was derived from crystalloid–colloid combinations method (the ratio of the crystalloid and colloid was about 2:1, and fresh frozen plasma was used as the colloid, Lactated Ringer's Solution was used as the crystalloid), and fluid administration was adjusted hourly to maintain stable hemodynamics and adequate urine output (>0.5 ml/kg/h). Sometimes, small doses of osmotic diuretic (20% mannitol) was used for a short time because of the need for treatment, but the mean arterial pressure (MAP) was not obviously changed. The patients' blood sugar levels were controlled

**Table 1 – RIFLE criteria for acute kidney injury.**

| Class | Glomerular filtration rate criteria | Urine output criteria |
|---|---|---|
| Risk | Serum creatinine × 1.5 | <0.5 ml/kg/h for 6 h |
| Injury | Serum creatinine × 2 | <0.5 ml/kg/h for 12 h |
| Failure | Serum creatinine × 3, or serum creatinine ≥4 mg/dl with an acute rise ≥0.5 mg/dl | <0.3 ml/kg/h for 24 h, or anuria for 12 h |
| Loss | Complete loss of kidney function >4 weeks | |
| ESKD | End-stage kidney disease >3 months | |

RIFLE: risk, injury, failure, loss, ESKD.
ESKD: End-stage kidney disease.