Int J Clin Exp Med 2019;12(9):11831-11836
www.ijcem.com /ISSN:1940-5901/IJCEM0096478

Original Article

The application value of using sera levels of c-reaction protein (CRP) and procalcitonin (PCT) in serum to predict the occurrence of systemic inflammatory response syndrome (SIRS) after lithotripsy guided by flexible ureteroscope

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Received May 5, 2019; Accepted August 6, 2019; Epub September 15, 2019; Published September 30, 2019

Abstract: To investigate the occurrence of systemic inflammatory response syndrome (SIRS) after ureteroscopy (URS)-guided lithotripsy and the application value of c-reaction protein (CRP) and procalcitonin (PCT) in serum to predict the occurrence of SIRS. We retrospectively summarized 86 cases of patients with urinary calculi who were treated with URS-guided lithotripsy. The patients were divided into two groups after operation, including the SIRS group (n = 22) and non-SIRS group (n = 64). On the first day after operation, the levels of CRP and PCT in serum in the SIRS group were significantly higher than those in the non-SIRS group. We performed ROC analysis and found that the diagnostic accuracy of CRP level was 0.864 (95% CI = 0.812 to 0.965, p = 0.009), the sensitivity was 86.9%, the specificity was 76.5% and the cutoff value was 8.3 mg/L. The diagnostic accuracy of PCT level was 0.881 (95% CI = 0.823 to 0.958, p = 0.005), the sensitivity was 88.2%, the specificity was 83.6% and the cutoff value was 7.5 μg/L. The results showed that levels of CRP and PCT in serum on the first day after operation could improve the diagnostic accuracy, sensitivity and specificity, and predict the occurrence of SIRS.

Keywords: Ureteroscopy (URS)-guided lithotripsy, systemic inflammatory response syndrome, C-reaction protein, procalcitonin

Introduction

With the wide application of flexible ureteroscopy (URS) guided lithotripsy in the treatment of renal calculi and ureteral calculi, various studies have confirmed that URS guided lithotripsy is safer and more effective [1, 2]. For renal calculus, the calculus clearance rate of URS-guided lithotripsy can be equivalent to that of percutaneous nephrolithotomy (PCNL), but with fewer complications [3]. Whereas, for ureteral calculus, the calculus clearance rate of URS-guided lithotripsy is superior to that of extracorporeal shock wave lithotripsy (ESWL), and there is no increase in the incidence of complications [4]. The working principle of URS-guided lithotripsy is that URS can pass through the body's natural openings, such as the urinary tract, bladder or ureter, to the location of the calculus and provide the physicians with direct vision, with which physicians can perform lithotripsy using holmium laser and collect the calculus using a mesh basket.

Therefore, there are many advantages to improving the efficiency of lithotripsy and collecting calculus, such as no surgical incisions, less trauma, and rapid recovery. However, the incidence of systemic inflammatory response syndrome (SIRS) has increased to about 10-40%, with an increasingly frequent application and severe infection, or even death [5]. This is associated with the displacement of macroflora colonization in the urinary system, injury of the

urinary tract and stress responses [6]. Regular bacterial detection and prophylactic antibiotics cannot effectively prevent the occurrence of SIRS [7]. Thus, searching for detection indicators with higher sensitivity and specificity has important clinical significance for the prediction and intervention in SIRS. C-reaction protein (CRP), as an important indicator of acute inflammatory response *in vivo*, and it has a better correlation with the occurrence of SIRS and a higher sensitivity [8]. Procalcitonin (PCT) shows great application value in the treatment of various infective diseases, such as bacterial infection, septicopyemia, respiratory tract infection and meningitis [9, 10]. This is consistent with the trend of inflammatory indexes, such as IL-6 and TNF-α [11]. In the current study, we aimed to analyze the application value of dynamic monitoring of serum CRP and PCT levels in predicting the occurrence of SIRS.

Subjects and methods

Subjects

We retrospectively analyzed 86 patients with urinary calculi who were admitted to the Fifth Affiliated Hospital of Guangzhou Medical University for URS-guided lithotripsy. This study was approved by the ethics committee of the Fifth Affiliated Hospital of Guangzhou Medical University and conducted in accordance with the principles of the Helsinki Declaration II. All participants provided written informed consent.

Inclusion criteria: a) patients aged between 18 and 70 years old; b) patients with URS-guided lithotripsy indications and calculus treatment indications that were expected to achieve an effective outcome; c) patients without any infection in the urinary system and without primary and secondary renal diseases before operation.

Exclusion criteria: a) patients who had complications with autonomous immune diseases, tumor or respiratory tract infections; b) patients with insufficient clinical data; c) patients with a temperature above 38°C or below 36°C; d) patients with a heart rate higher than 90 beat/min; e) patients with a respiratory rate faster than 20 time/min or $PaCO_2$ lower than 4.3 kPa; f) patients whose white blood cell count in the peripheral blood was higher than 12×10^9/L or lower than 4×10^9/L, or the proportion of immature cells was not less than 10%.

Methods

Eighty-six patients were divided into two groups, i.e. the SIRS group (n = 22) and non-SIRS group (n = 64) as per the diagnostic criteria of SIRS. Operations were carried out by the same physician and nursing team. Regular administration of antibiotics was carried out before and after the operation. Operations conformed to aseptic principle: after epidural anesthesia, the lithotomy position was confirmed, where the Zebra urological guidewire was placed under F8/9.8WOLF rigid ureteroscopy to detect the position of ureter and then guided to the pelvis and the rigid ureteroscope was withdrawn; after successfully placing the soft sheath of Cook F12/14 ureteroscope and Storz Flex X27.5F flexible cystoscope, a fiber optic cable (200 μm) was inserted to connect the Holmium laser lithotripter (Litho) to break the calculi into pieces (2 to 3 mm in diameter) which were excreted autonomously and the fragments of calculi of larger sizes were collected by a basket extractor and then taken out; 6F double J catheters were placed in the body, the urinary catheter was removed on the second day after operation, and the double J catheters were removed in the 4^{th} week after operation. The treatment of SIRS after operation was carried out with the following procedures: drug susceptibility test for bacteria cultured from blood and midstream urine were carried out; individual therapies, such as anti-infection, infusions, lowering of temperature, oxygen inhalation, administration of vasoactive drugs and glucocorticoids, were also performed; patients with severe conditions were transferred to ICU.

The levels of CRP and PCT in serum were detected at 1, 3 and 7 days after the operation using ELISA. The reagents were purchased from Jiangsu Beyotime Biotech Co., Ltd (CHINA), and all the procedures were carried out strictly in accordance with the instructions.

Observation indexes

We compared the surgery duration, intraoperative bleeding, positive rate of urinary bacterial culture after operation and the levels of CRP and PCT in serum between the two groups.

Table 1. Comparisons of the surgery duration, intraoperative bleeding, positive ratio of culture of urinary bacteria after surgery between the two groups

Group	Cases	Surgery duration (min)	Intraoperative bleeding amount (ml)	Positive ratio of culture of urinary bacteria after surgery [case (%)]
SIRS group	22	46.5 ± 7.6	25.9 ± 5.7	3 (13.6)
Non-SIRS group	64	44.7 ± 7.3	23.6 ± 6.2	8 (12.5)
t/χ^2		0.265	0.193	0.000
P		0.867	0.924	1.000

Table 2. Comparison of CRP level in serum (mg/L)

Group	Before operation	1 d	3 d	7 d
SIRS group	5.3 ± 1.2	10.8 ± 3.5	12.4 ± 4.2	4.5 ± 2.1
Non-SIRS group	4.6 ± 1.0	7.9 ± 3.3	5.3 ± 1.6	3.6 ± 1.3
t	0.096	4.554	6.127	0.185
P	0.952	0.021	0.006	0.869

Statistical methods

SPSS 20.0 software was used for the statistical analysis. Measured data were presented as mean ± standard deviation (SD). Independent sample t test was performed for comparison between groups. Variance analysis of repeated measurement data was performed for intragroup comparison. Counting data were presented in cases or proportion (%). Chi-square test was performed for comparison between groups. The diagnostic value of predicting the incidence of SIRS using the levels of CRP and PCT in serum was analyzed by receiver operating characteristic curve (ROC). $p < 0.05$ was considered as a statistically significant difference.

Results

Clinical characteristics of patients

In the SIRS group, there were 12 males and 10 females with an average age of (46.5 ± 13.4) years, and the postoperative onset time of SIRS ranged from 6 to 32 h with an average of (16.7 ± 10.5) h. Preoperative bacterial culture from the urinary system was positive in 4 patients. There were 13 patients with renal calculi and 9 patients with ureteral calculi, with an average number of calculus (1.5 ± 0.6) and an average diameter of calculus (1.6 ± 0.7) cm. Five patients underwent ESWL for treatment. In the non-SIRS group, there were 36 males and 28 females with an average age of (44.8 ± 15.5) years. Preoperative bacterial culture from the urinary system was positive in 8 patients. There were 42 patients with renal calculus and 9 patients with ureteral calculus, with an average number of calculus (1.6 ± 0.8) and an average diameter of calculus (1.5 ± 0.7) cm. Twelve patients underwent ESWL for treatment. The baseline data of both groups were comparable.

Comparisons of surgery duration, intraoperative bleeding, positive ratio of culture of urinary bacteria after surgery between groups

There was no significant difference in operation time, intraoperative bleeding volume and positive rate of urinary bacterial culture after surgery between the two groups ($p > 0.05$) (**Table 1**).

Comparison of CRP level in serum

On the first day after operation, the levels of CRP in serum of both groups were increased compared to those before operation, in which the levels in the SIRS group were significantly higher than those in non-SIRS group ($p < 0.05$). Such a high level lasted for 3 days and began to recede in the 7th day. The levels in the non-SIRS group decreased on the 3rd day and were equal to those in the SIRS group on the 7th day (**Table 2**).

Comparison of PCT levels in serum

On the first day after operation, the levels of PCT in serum of both groups were increased compared to those before operation, in which the levels of PCT in the SIRS group were significantly higher than those in the non-SIRS group ($p < 0.05$). Such a high level lasted for 3 days and began to recede on the 7th day; the levels in

Table 3. Comparison of PCT level in serum (μg/L)

Group	Before operation	1 d	3 d	7 d
SIRS group	1.5 ± 0.6	11.4 ± 3.6	13.5 ± 4.7	1.9 ± 0.8
Non-SIRS group	1.3 ± 0.4	6.9 ± 2.4	3.5 ± 1.2	1.1 ± 0.6
t	0.122	5.854	7.628	0.235
P	0.906	0.012	0.000	0.854

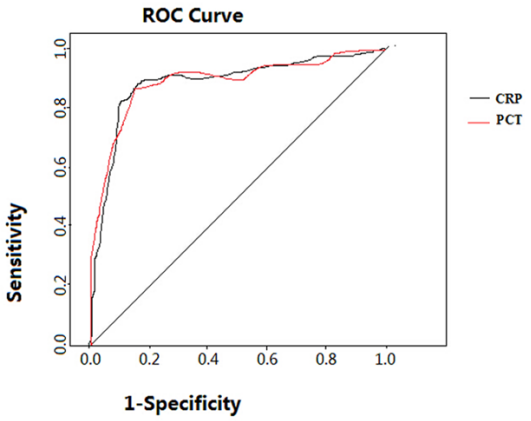

Figure 1. ROC analysis of the occurrence of SIRS predicted by the levels of CRP and PCT in serum.

the non-SIRS group were decreased on the 3rd day and equal to those in the SIRS group on the 7th day (**Table 3**).

ROC analysis of the occurrence of SIRS predicted by the levels of CRP and PCT in serum

The levels of CRP and PCT in serum on the first after operation served as the diagnostic indexes, and the SIRS after operation as the diagnostic results, for which we performed the ROC analysis (Area under the curve, AUC) and found that the diagnostic accuracy through CRP level in serum was 0.864 (95% CI = 0.812 to 0.965, p = 0.009), sensitivity was 86.9%, specificity was 76.5% and cutoff value was 8.3 mg/L; and the diagnostic accuracy through PCT level in serum was 0.881 (95% CI = 0.823 to 0.958, p = 0.005), sensitivity was 88.2%, specificity was 83.6% and cutoff value was 7.5 μg/L (**Figure 1**).

Discussion

The flexible URS rises through the urinary tract to the upper ureter, pelvis and renal calices to perform lithotripsy, which not only enlarges the indication range of treatment of calculi in the upper urinary tract, but also expands the infection range of the urinary system, which has become an important factor for the postoperative occurrence of SIRS [12]. The hydrostatic pressure caused by perfusion will lead to blood contamination by bacteria and endotoxin, thus causing a systemic inflammatory response [13]. Some studies [14] have indicated that the concordance rate of bacterial cultures using the bacteria collected from the preoperative midstream urine and calculi collected during the operation can be as high as 70%.

In addition, some studies [15] have also revealed that nearly 70% of patients with negative preoperative urine culture showed positive results in bacterial culture of calculi collected during operation. CROES studies [16] also have shown that the risk of infection-related complications is 2.2% in patients with negative results of bacterial culture in the preoperative midstream urine who received the operation. Based on these results, we can infer that there is a certain limitation in the use of bacterial culture in urine to predict the occurrence of SIRS.

The first step in SIRS treatment is to rapidly diagnose and identify infections. It has been confirmed [17] that CRP participates in various processes, such as lipid accumulation, complement activation, the synthesis and release of cytokines, chemotaxis of inflammatory factors and cell signal transduction. PCT, a propeptide of hormone-free active glycoprotein calcitonin, can be increased in the first 2 to 4 h after infection and reach a peak in 8 to 24 h. The half-life of PCT is 25 to 30 h, indicating that it can stably exist *in vivo* [18]. For patients with severe infection, the levels of PCT in the serum have acutely increased, but can be rapidly decreased after treatment with antibacterial drugs [19]. The occurrence of SIRS is a series of waterfall-like cascade releases of inflammatory mediums, result in an imbalance between the levels of anti-inflammatory factors and pro-inflammatory factors, further causing the complex network effects of systemic inflammation, which involves disordered immune functions, coagulation disorders, tissue injury, and abnormal responses of the host to pathogenic microorganisms and toxins [20]. In our study, the levels of CRP and PCT in serum in the SIRS group were significantly higher than those in the non-SIRS group on the first day after operation. Such a high level lasted for 3 days and began to recede on the 7th day. An increase was identi-

fied in the augmentation amplitude of levels of CRP and PCT in serum in the SIRS group, and the peak time was also prolonged. The diagnostic accuracy through CRP levels in serum was 0.864, sensitivity was 86.9%, specificity was 76.5% and cutoff value was 8.3 mg/L. The diagnostic accuracy through PCT levels in serum was 0.881, sensitivity was 88.2%, specificity was 83.6% and cutoff value was 7.5 μg/L. The results suggested that better accuracy, sensitivity and specificity to predict the occurrence of SIRS can be achieved by using the levels of CRP and PCT in serum on the 1st day after operation. As well, the application of antibiotics and the control of early infection sources are also important for the treatment of SIRS. Bochud and his colleagues [21] believed that the administration of cefoperazone/sulbactam or piperacillin/tazobactam should be prioritized after the patient's urine sample was acquired for culture, and evaluation of the efficacy of treatment should be carried out after 48 to 72 h. Additionally, the types and doses of antibiotics should be adjusted accordingly to alleviate the drug tolerance and reduce adverse reactions. In addition, the treatment cycle usually lasted 7 to 10 d.

In this study, we proposed the value of serum CRP and PCT levels in predicting the occurrence of SIRS after surgery. The reliability of these two indicators can be improved by further expanding the sample and increasing the risk stratification of SIRS in patients after operation.

Disclosure of conflict of interest

None.

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