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Original Article

Fever and systemic inflammatory response syndrome after retrograde intrarenal surgery: Risk factors and predictive model

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Abstract This paper investigates the characteristics of patients who underwent retrograde intrarenal surgery (RIRS) to determine the predictive factors for post-operative fever and systemic inflammatory response syndrome (SIRS) and to construct a predictive nomogram to help with risk-stratification. A retrospective study of 337 patients who underwent RIRS was performed. Fever and SIRS were defined according to a previous consensus. Multivariate logistic regression coefficients were used to generate nomograms. Post-operative fever was found in 59 patients (17.5%), and SIRS was found in 22 patients (6.5%). Septic shock developed in 2 patients (0.6%). Three patients (0.9%) suffered from obstructive hydronephrosis. By multivariate analysis, concomitant diabetes mellitus ($p = 0.015$), high pre-operative C-reactive protein (CRP) ($p = 0.015$), long surgical times ($p = 0.007$), high stone burden ($p = 0.004$) and positive stone culture ($p = 0.003$) were independent risk factors for fever. Only high pre-operative CRP ($p = 0.001$), long surgical times ($p = 0.001$) and high stone burden ($p = 0.001$) were found to significantly affect the occurrence of SIRS. Predictive nomograms were built for fever and SIRS and the c-statistics for the two predictive models were 0.766 and 0.887, respectively. All patients recovered well after proper treatment, which included antipyretics, antibiotics, and inotropic support and nephrostomy when needed. In conclusion, high stone burden, long surgical time, positive stone culture, high pre-operative CRP and the presence

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of diabetes mellitus was could increase the risk of fever or SIRS after RIRS for kidney stone. The constructed nomograms could help clinicians in evaluating the risk for post-operative infectious complications.

Introduction

The surgical approach for the treatment of kidney stones, a common urological disease with an incidence of approximately 3—15% [1], has dramatically improved in the past decades. Minimally invasive surgeries, including percutaneous nephrolithotomy (PCNL) and flexible retrograde intrarenal surgery (RIRS), have gained a greater acceptance [2]. PCNL has been challenged as a standard of care by the development of RIRS due to advances in the equipment and techniques used for a variety of surgical candidates, including patients with large stone size (over 2 cm in diameter), stone located in the lower pole of the kidney, and a solitary kidney [3,4].

There have been a number of studies comparing RIRS and PCNL for the management of kidney stones, and the general consensus has been that PCNL offers a higher stone-free rate (SFR), whereas RIRS was safer with lower complication rate [5]. The complications of PCNL have been reported and the risk factors for post-operative infectious complications including fever, systemic inflammatory response syndrome (SIRS) and sepsis. In contrast, the evidence concerning those predictive factors for RIRS remains scarce. Despite the developed equipment (e.g., ureteral access sheath) and peri-operative management, patients still have unpredictable post-operative systemic and sometimes fatal infections [6].

Thus, we have addressed this limitation and undergone this retrospective study to investigate the characteristics of this cohort of patients to identify the predictive factors for post-operative fever and SIRS and to develop a predictive nomogram to help with the risk-stratification of patients.

Methods

Patient enrollment

We retrospectively collected the data of 484 patients who underwent RIRS at our center between 2010 and 2017. Patients with incomplete data (62, mainly due to unknown urine or stone culture results), severe comorbidities (43, mainly severe cardiovascular or respiratory diseases), the presence of contralateral renal or ureteral stone (18) and renal failure (24) were excluded. Ultimately, 337 patients were enrolled for analysis. The study was approved by the local institutional review board, and written informed consent was obtained from all participants and all surgeries were performed by experienced urologists.

Patient treatment

The RIRS procedure was similar to that previously reported [4,7]. A 6-Fr ureteral catheter or double J stent was placed under cystoscopy 7—10 days before surgery (based on the judgment of the treating physician) to dilate the ureter. After the induction of general anesthesia and in the lithotomy position, guidewires were placed into the renal pelvis, after which a ureteral access sheath (UAS, Cook Medical Inc., USA) and a 7.5-Fr flexible ureteroscope (Olympus, Japan) or an 8.0/9.8-Fr (Karl Storz Endoscope, Tuttlingen, Germany) were implanted. The stones were fragmented by a 200-μm holmium laser (Coherent Power Suite, 60 Watts; Lumenis, Israel) until they were deemed small enough to pass spontaneously; and a stone basket was used to remove the fragments. A double-J stent was placed routinely at the end of the surgery.

A urine culture was collected sterilely in all patients before the surgery. Those with positive cultures (>100,000 cfu/ml) were treated with proper antibiotics for at least 7 days, and a re-evaluation for pre-operative urine was required. A single dose of intravenous prophylactic antibiotic was given in 100% patients when inducting anesthesia, which lasted 3—4 days after surgery. Body temperature, blood pressure, heart beat and respiratory rate were recorded daily after surgery, and a urine test or blood test was performed when indicated.

A KUB was performed on the 1st day after RIRS to assess the location of the double J stent and check for the presence of residual stone. Laboratory examination and KUB (or CT when indicated) were performed one or three months after surgery to assess the patients' status. The double-J stent was removed under local anesthesia when appropriate (usually 1 month after surgery). A "stone-free" status was defined as no evidence of stones or stones less than 2 mm on the one-month post-operative CT scan.

Patients evaluation

The covariates consisted of general information (age, gender, BMI, comorbidities), pre-operative laboratory tests (blood white blood cell-WBC including neutrophil/lymphocyte ratio-NLR, urine culture, C reactive protein-CRP), stone characteristics (stone burden, stone culture, location) and surgery-related information (operation time, complications). Blood samples were collected 1—7 days before surgery, and after antibiotic treatment for those with positive urine culture. CRP was measured using the BCG dye-binding method and a turbidimetric assay; the normal range at our institution was 0—10 mg/L. The stone burden was calculated by multiplying the longest diameter by the perpendicular diameter of the stone, and the sum of each stone as the total stone burden in cases of multiple stones [8].

The presence of post-operative fever was defined as a body temperature over 38 °C within hospital stay that persisted for 48 h [9,10]. Based on previous consensus, SIRS

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