Failure of initial superselective renal arterial embolization in the treatment of renal hemorrhage after percutaneous nephrolithotomy: A respective analysis of risk factors

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Abstract. Superselective renal arterial embolization (SRAE) is a well-established method for the treatment of severe hemorrhage following percutaneous nephrolithotomy (PCNL). However, there remains a significant rate of failures requiring repeat SRAE or nephrectomy. To identify risk factors for initial treatment failure of SRAE, the data of patients who had undergone SRAE for severe bleeding due to PCNL between August 2005 and June 2016 were retrospectively analyzed. A total of 98 patients required SRAE for bleeding control following PCNL. Renal arteriography revealed pseudoaneurysm in 65 patients, arteriovenous fistula in 6 patients, and a combination of both in 11 patients. Free extravasation was observed in 11 patients; 8 of these patients exhibited coexisting pseudoaneurysm. Vascular aberration/tortuosity was identified in 10 patients. A total of 17 patients (17.3%) experienced initial treatment failure and underwent repeat SRAE. Multivariate analysis identified percutaneous tract size, number of bleeding sites and vascular aberration/tortuosity as significant predictors of initial treatment failure. The results from the present study suggested that repeated SRAE is preferred for patients who have experienced initial treatment failure with recurrent hemorrhage following PCNL. Large tract size, multiple bleeding sites and renal vascular aberration/tortuosity were significantly associated with increased risk of initial treatment failure of SRAE. These data may assist interventional radiologists in the planning and execution of SRAE in the treatment of PCNL.

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Abbreviations: AVF, arteriovenous fistula; ESWL, extracorporeal shock wave lithotripsy; CTA, computed tomographic angiography; PCNL, percutaneous nephrolithotomy; SRAE, superselective renal arterial embolization

Key words: embolization, hemorrhage, kidney, nephrostomy, percutaneous nephrolithotomy, treatment failure

Introduction

Percutaneous nephrolithotomy (PCNL) is a common procedure for large-volume renal calculus disease (1). Due to the refinement of technology, improved surgical instrumentation and increasing experience, the safety and efficacy of PCNL has increased in the last two decades. However, the risk of significant complications, including renal hemorrhage remains a problem. The majority of the bleeding may be managed conservatively with bed rest and transfusion. However, massive or continuous renal hemorrhage often requires expeditious intervention (2,3). Surgical exploration as a therapeutic option to stop bleeding may lead to nephrectomy. Renal artery embolization has been used for controlling renal hemorrhage since the 1970s (4,5). This technique has advanced with the introduction of smaller delivery catheters and more precise embolic agents (6). It is now possible to perform superselective renal arterial embolization (SRAE), which minimizes the loss of renal function (7,8). However, when initial embolization fails, patients may require a second superselective embolization or surgical exploration, presenting a challenge for urologists and healthcare providers. A detailed examination of the literature revealed a relative paucity of studies focusing on the causes initial SRAE failure after PCNL. In the present study, clinical data was retrospectively analyzed to examine the incidence and management of the complication, and to identify any risk factors that may predict the possibility of this event.

Materials and methods

Patients. A total of 3,300 PCNL procedures were performed in The First Affiliated Hospital of Zhejiang University (Zhejiang, China) between August 2005 to June 2016. The records of patients who had undergone renal arteriography for renal hemorrhage following PCNL were respectively reviewed. The inclusion criterion was severe post-PCNL renal hemorrhage requiring SRAE. Exclusion criteria were no arterial lesion on renal arteriogram, and the use of anticoagulant drugs or abnormal blood coagulation. The study was approved by Research Ethics Committee of The First Affiliated Hospital of Zhejiang University (approval number, 2018-1056).

A total of 98 patients underwent SRAE due to uncontrolled renal hemorrhage following PCNL, including 15 patients transferred from other hospitals. There were 77 males and 21 females. The mean patient age was 51.9 years (26-77 years). The following variables were identified for each patient: Clinical presentation; comorbidities; hemoglobin concentration; requirement of pre-embolization blood transfusion; timing of embolization; embolization agents; injury mechanism and location; post-embolization transfusion requirement; and long-term outcome.

Techniques. The PCNL was performed by 3 specialists in The First Affiliated Hospital of Zhejiang University. The technique involved percutaneous puncture using an 18G gauge coaxial needle under ultrasound guidance. The nephrostomy track was dilated up to 26F using metal telescopic dilation, Amplatz serial dilation or a single-step balloon dilator. A smaller 16-18F tract was employed in patients with a small renal stone. A single tract or multiple tracts were used depending on the complex of stones. Pneumatic, holmium laser or ultrasonic lithotripsy was used for calculus disintegration at the discretion of the surgeon. A nephrostomy tube was placed at the end of the procedure. A KUB film was obtained 48 h after the procedure to confirm the stone clearance status. The tube was removed after 2 weeks if there were no complications or residual stones.

Mild bleeding is self-limiting and resolves with conservative measures, including bed rest, tamponade by clamping the nephrostomy tube and adequate hydration. If conservative treatment fails, patients with progressive decline of hemoglobin undergo a computed tomographic angiography (CTA) to define the optimal therapeutic strategy on the basis of the extent and origin of bleeding (arterial or venous). If renal artery injuries are confirmed, the patients proceed to renal arteriography with or without embolization.

The technical details of SRAE were described previously (8). Briefly, a 5F angiographic catheter was introduced into the renal artery via the transfemoral route. A global angiogram was performed to identify any lesions, which were additionally confirmed by selective renal arteriography. Embolic materials, metallic coils or polyvinyl alcohol (PVA) particles, were then deployed. Renal arteriogram was repeated to demonstrate a small avascular segment and patency of the rest of the vessels. All procedures were performed by 2 senior interventional radiologists.

Statistical analysis. To assess the risk factors for failure of initial SRAE, data from the patients requiring repeated SRAE were compared with those of the patients with successful initial SRAE using two-tailed t-tests for age, and χ^2 analysis for other variables. Multivariate logistic regression analysis were applied in a stepwise backward manner to verify the independent risk factors, with a significance level of $P<0.05$. Various clinical factors including patients age and sex, comorbidities (hypertension and diabetes), kidney side, percutaneous tract size, stone size, tract dilation methods, and the details of the angiographic data [number of bleeding sites, arteriovenous fistula (AVF) and vascular aberration/tortuosity] were assessed. All analyses were conducted using SPSS software v16 (SPSS, Inc.). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. All 98 patients had basically normal INR levels, and the platelet level was slightly decreased in 2 patients. A total of 43 patients exhibited bleeding from the left kidney, and 55 from the right. Blood transfusion was required for 42 patients prior to first embolization. The mean time between the surgery and first embolization procedures was 8.1 days (1-22 days). Of the 98 patients, 65 developed a pseudoaneurysm, 6 had an arteriovenous fistula, and 11 patients exhibited both. Free extravasation was observed in 11 patients; 8 of these patients exhibited coexisting pseudoaneurysm. Besides, renal vascular aberration or tortuosity were encountered in 10 patients. For embolization, metallic coils were used in all procedures, with the exception of 2 patients using PVA particles. Of the 15 patients from other hospitals, 5 patients had left kidney bleeding, and 10 had right. A total of 9 patients had a pseudoaneurysm, 2 had an arteriovenous fistula, 3 had both a pseudoaneurysm and an arteriovenous fistula, and 1 had free extravasation.

SRAE. Complete resolution of bleeding was observed in 81 patients, and initial SRAE failure occurred in 17 (17.3%) patients with recurrent hemorrhage. A second embolization was performed in 16 patients, and 1 patient had open exploration for deep suture of bleeding site due to renal rupture on CT image, but the bleeding did not cease following surgery until the second embolization was performed 7 days later. Of the 17 cases of SRAE failure, the angiography revealed a new bleeding site in 7 patients, while the arteries were incompletely occluded in 10 patients with metallic coils in place. Figs. 1 and 2 demonstrate the bleeding sites on initial and repeat renal arteriograms from 2 patients. Complete resolution of bleeding was observed in 16 patients following re-embolization. The remaining 1 patient, who had renal vascular tortuosity, with repeated embolization with metallic coils 5 times (the first 3 times were performed in other institutions and 2 times in The First Affiliated Hospital of Zhejiang University) was finally managed by conservative therapy with repeated transfusion. All the patients had blood transfusion following initial treatment failure.

Follow-up. The follow-up of 17 patients with repeated SRAE was presented in Table I. A total of 3 patients had low-grade fever, and 2 had flank pain. These symptoms disappeared 2-5 days after symptomatic treatment. The mean follow-up was 20 months (3-54 months). All had follow-up imaging of a renal ultrasonography or contrast CT, in addition to serum creatinine test. There was no global kidney atrophy or renal abscesses observed. There was no renovascular hypertension in any patient (5 patients had hypertension prior to embolization).

Risk factors for initial failure of SRAE. The univariate analyses results are presented in Table II, to compare between patients experiencing initial treatment failure and those who did not. Statistical significance was suggested in the univariate analyses for tract size, number of bleeding sites and renal vascular aberration/tortuosity. Patient age, sex, kidney side, hypertension, diabetes, stone size, tract dilation methods and AVF at initial SRAE were not potential risk factors for initial

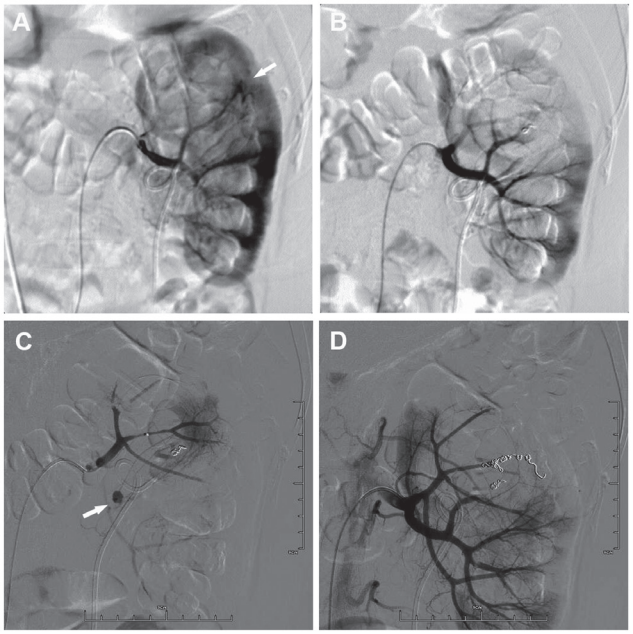

Figure 1. Bleeding sites identified on initial and repeat renal arteriograms from patient 1. (A) Initial angiography indicating left pseudoaneurysm with contrast medium exuding into renal subcapsule in a 32-year-old man following percutaneous nephrolithotomy (indicated by white arrow). (B) Superselective renal artery embolization of the damaged vessel with metallic coil. (C) The second renal angiography indicated 1 more pseudoaneurysm from an aberrant vessel (indicated by white arrow). (D) Repeated superselective embolization using microcoils.

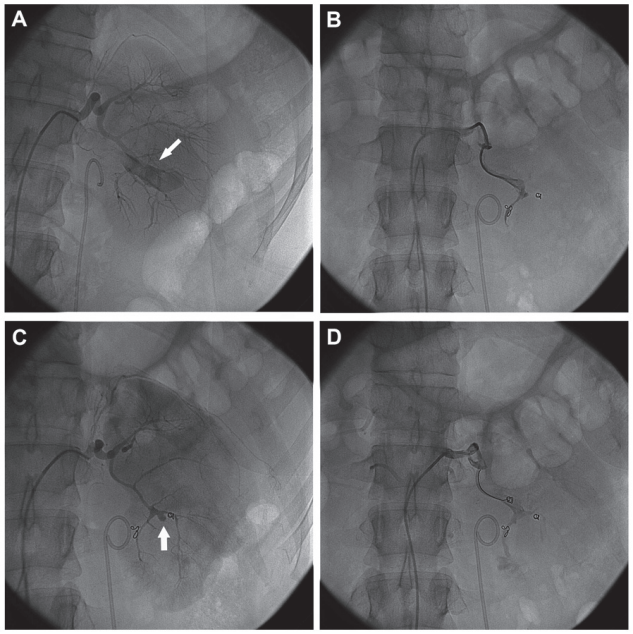

Figure 2. Bleeding sites identified on initial and repeat renal arteriograms from patient 2. (A) Initial angiography demonstrating a left renal arteriovenous fistula with early filling of renal vein following percutaneous nephrolithotomy (indicated by white arrow). (B) Selective embolization of the arteriovenous fistula with metallic coil. (C) The second renal angiography demonstrated a new pseudoaneurysm proximal to the coil (indicated by white arrow). (D) Repeated superselective embolization using an additional microcoil.

treatment failure. Multivariate analyses confirmed that the 3 factors identified in the univariate analysis were independent risk factors (Table III).

Table I. Follow-up of patients with repeated superselective renal arterial embolization.

Patients (n=17)	Count
Follow up, months [mean (range)]	20 (3-54)
Fever	3
Flank pain	2
Hypertension	0
Global renal atrophy	0
Renal abscess	0

Discussion

The introduction of smaller delivery catheters and more precise embolic agents has markedly improved the morbidity associated with SRAE (9), and it has continued to gain popularity as a minimally invasive approach for various urological conditions, including arteriovenous malformations, medical renal disease, angiomyolipomas and preoperative infarction of renal cell carcinoma (10). Although extracorporeal shock wave lithotripsy (ESWL) and flexible ureteroscopic stone removal are widely used treatment modalities for renal stones, PCNL is required for large and complex renal calculi (1). However, PCNL does carry a risk of post-operative renal bleeding (11-13). The iatrogenic renal artery injuries following PCNL now represent a significant proportion of the indications for SRAE (8,10,14). The present study describes the use of SRAE in 98 patients from The First Affiliated Hospital of Zhejiang University, with particular emphasis on the risk factors of initial treatment failure.

The reported incidence of post-PCNL bleeding requiring angiographic embolization is 0.8-2.4% (11,15-17). In the present study, out of the 3,300 PCNL procedures performed during the study period, 83 patients required SRAE (2.5%), and the incidence was slightly increased compared with previous studies (11,15-17). The discrepancy of incidence between studies may be attributed to the different indications for SRAE. For example, patients with severe hematuria with a fall in hematocrit fall in blood pressure, recurrent clot retention, and/or a requirement for inotropes to maintain hemodynamic stability, will undergo angiography and subsequent embolization. In the present study, if renal arterial injuries (pseudoaneurysm, arteriovenous fistula or free extravasation) were confirmed on CTA following severe hemorrhage, the patient was treated with SRAE immediately. However, spontaneous cessation of hemorrhage may occur for small renal arterial injuries, resulting in the relatively high rate of embolization in the present study cohort. Various risk factors have been proposed for predicting severe bleeding due to PCNL, including access needle size, number of punctures, staghorn stones, solitary kidney or history of urinary tract infection (16-19). Identification of risk factors affecting the incidence of hemorrhage recurrence following SRAE is also of the utmost importance, as failure of initial SRAE may be life threatening, resulting in significant pressure on the patient and surgical team. However, one study by Zeng *et al* (20) identified 3 risk factors for initial treatment failure, including multiple percutaneous access sites, >2 bleeding sites identified on renal

Table II. Univariate analysis of risk factors for initial failure of SRAE after PCNL.

Variable	Success	Failures	χ^2	OR (95% CI)	P-value
Sex					
Male	62	15		-	
Female	19	2	1.141	0.44 (0.09-2.08)	0.285
Kidney side					
Left	33	10		-	
Right	48	7	1.866	0.48 (0.17-1.39)	0.172
Hypertension					
No	56	11		-	
Yes	25	6	0.128	1.22 (0.41-3.67)	0.721
Diabetes					
No	75	16		-	
Yes	6	1	0.049	0.78 (0.09-6.94)	0.824
Stone size, cm					
<3	50	11		-	
≥3	31	6	0.053	0.88 (0.30-2.62)	0.818
Tract size					
Mini-PCNL	33	1		-	
Standard	48	16	7.536	11.00 (1.39-87.03)	0.006
Dilation method					
Telescopic/serial dilation	52	8		-	
Balloon dilation	29	9	1.739	2.107 (0.70-5.79)	0.187
No. of bleeding sites at initial SRAE					
1	76	12		-	
≥2	5	5	8.282	6.33 (1.59-25.20)	0.004
AVF at initial SRAE					
No	67	14		-	
Yes	14	3	0.001	1.03 (0.26-4.05)	0.971
Renal vascular aberration/tortuosity					
No	76	12		-	
Yes	5	5	8.282	6.33 (1.59-25.20)	0.004

CI, confidence interval; OR, odds ratio; PCNL, percutaneous nephrolithotomy; AVF, arteriovenous fistula; SRAE, superselective renal arterial embolization.

angiogram and gelatin sponge alone used as the embolic material. By contrast, the data from the present study revealed that large tract size, multiple bleeding sites and vascular aberration/tortuosity were significant predictors of initial treatment failure.

The degree of dilation of the tract is one of the factors responsible for bleeding. Previous evidence suggested that decreasing the tract size for PCNL may decrease blood loss and morbidity (21). Desai *et al* (22,23) even developed a 3.5-F ultra-thin telescope method, termed 'ultra-mini percutaneous nephrolithotomy'. In the present study, a significantly increased risk of repeated SRAE for patients who had undergone standard PCNL (26F) as compared with mini-PCNL (16F-18F) was observed. However, the most important disadvantages of mini-PCNL are the long surgery times and the more advanced technical skill required. It is difficult to determine exactly which tract size is most appropriate for PCNL. On the basis of the results of the present study, and the information from previous studies, we propose avoidance of large tract size for relatively small stone burden, in an attempt to decrease retreatment rate of SRAE, particularly in cases with non-hydronephrotic systems and those with a narrow infundibulum.

An additional risk factor for initial treatment failure observed in the present study was multiple bleeding sites. The renal arterial lesions may develop in a number of different sites, particularly in multi-tract PCNL, though all the patients with repeated SRAE underwent one-tract PCNL. In the patients in the present study, a global arteriogram was usually performed at the end of the procedure. However, it was possible that certain bleeding sites may have been omitted when the number of lesions was too high. In addition, temporary spasm of the involved artery, which is the first response of the blood vessel

Table III. Multivariate analysis of risk factors for initial failure of SRAE after PCNL.

Variable	OR (95% CI)	P-value
Tract size	12.23 (1.18-126.42)	0.036
No. of bleeding sites at initial SRAE	10.86 (1.90-62.03)	0.007
Renal vascular aberration/tortuosity	6.73 (1.37-33.15)	0.019

CI, confidence interval; OR, odds ratio; SRAE, superselective renal arterial embolization.

to injury, would be difficult to identify on an arteriogram. Therefore, a second session of SRAE was often required following this event.

In the present study, the vascular aberration or tortuosity was also a significant risk factor for the failure of initial SRAE. Vascular aberration or tortuosity would add time, complexity and risk to the procedure. Navigating a guiding wire across highly tortuous segments of the renal artery is challenging and requires multiple attempts, and tends to induce severe vasospasm and arterial dissections, particularly when the wire catches the wall of the vessel at an abrupt 180˚ or 360˚ turn. In certain cases, a distal position cannot be achieved and the operator is forced to attempt embolization from a more proximal parent artery, which increases the risk of treatment failure and complication.

Akman *et al* (24) demonstrated that the risk of major complications, in particular hemorrhage, was significantly increased during PCNL in patients with diabetes mellitus, hypertension, and the metabolic syndrome. Kukreja *et al* (18) evaluated factors affecting blood loss during PCNL in a prospective study. They identified that diabetes was one of the risk factors associated with significantly increased blood loss during PCNL. Associated arteriosclerosis in patients with diabetes and hypertension may make these patients more prone to iatrogenic arterial injuries secondary to endovascular treatment, and impair the self-healing properties of the arterial wall, due to the loss of its normal muscle and elastic layers (25), resulting in recurrent hemorrhage following initial SRAE. However, patients with comorbidities including diabetes mellitus and hypertension appeared to have no propensity to treatment failure in our series. Balloon dilation is generally considered to have an improved hematologic morbidity profile compared with the other dilation methods, as it is radial without the risk of perforation of any structures ahead or surrounding the tract, which is a risk of multi-incremental methods. In the present study, there was no significant difference of re-treatment rate between the balloon dilation and telescopic/serial dilation groups. There have been studies suggesting that the experience of the interventional radiologists is associated with endovascular procedural outcomes, and the risk of complications with coil embolization appears to decrease markedly in correspondence with the level of physician experience. However, all the procedures in the present study were performed by 2 senior interventional radiologists, who were highly experienced in other endovascular techniques at study onset; therefore, the physician experience was not considered to be as a risk factor in the analysis.

The present study has several limitations, including the nonrandomized and retrospective nature of the present study, the unequal patient number in the different groups, and procedures performed with different surgeon experience from different institutes. Due to limited samples within the subgroups, the power of statistical analyses for certain variables may have been low, and potentially relevant factors may have been overlooked. In addition, follow-up of differential renal function using radioisotope renal scan was not available. Therefore, other studies are required to address these limitations.

In conclusion, SRAE is recommended for patients who have uncontrolled hemorrhage following PCNL, and patients experiencing initial treatment failure may be successfully managed with repeated SRAE. The results of the present study indicated that tract size, number of bleeding sites and renal vascular aberration/tortuosity significantly predicted the occurrence of initial treatment failure of SRAE. No significant association was identified between the other variables. The results of the present study may assist interventional radiologists in the planning and execution of SRAE in the treatment of PCNL.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

QM was involved in acquisition, analysis and interpretation of the data. QM, CW and BS contributed to the design and the conception of the study and interpretation of the data. GC and FT conceived the study and participated in its design and coordination. QM and BS drafted the manuscript.

Ethics approval and consent to participate

The study was approved by Research Ethics Committee of The First Affiliated Hospital of Zhejiang University (approval number, 2018-1056).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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