Endourology and Stones

Failure of Angiographic Management in Cases of Postrenal Intervention Bleed: Risk Factors and Management Approach

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OBJECTIVE	To evaluate the factors predicting the risk for failed angiographic management (AM), we retrospectively studied cases of digital subtraction angiography (DSA) and superselective angiography (SSA) to control severe/delayed bleeding following renal interventions, which may otherwise be life threatening and often require nephrectomy.
METHODS	We have retrospectively evaluated the data of 154 patients who underwent DSA and or SSA during January 2006 to June 2016. Twenty-one patients (Group A) with failed AM were compared to patients with success AM (n = 133, Group B).
RESULTS	Out of 21 patients in whom AM failed, 20 should be managed with subsequent sessions of DSA/SSA and only 1 had to undergo nephrectomy. On univariate analysis, low hemoglobin (P = .025), multiple tracts (n > 1) during percutaneous nephrolithotomy (P = .01), multiple bleeding site (>1 = 0.01 and >2 = 0.001) and patients, who needed inotropes (P = .008) were found to predict risk for failure. On multivariate analysis, multiple bleeding site >2 (P = .003, odds ratio 5.23, 95% confidence interval = 1.3-22.5) and patients on inotropes (P = .02, odds ratio 2.56, 95% confidence interval = 2.15-4.75) were found to independently predict the failure.
CONCLUSION	Patients with multiple bleeding lesions and who are on inotropic (leading to intrarenal vasoconstriction) are at high risk for failure of AM. Most of them can be successfully managed by subsequent session AM. UROLOGY 125: 40−45, 2019. © 2019 Elsevier Inc.

S evere as well delayed persistent bleeding following renal intervention or renal surgery is always a challenging event faced by an urologist. Digital subtraction angiography (DSA) has been traditionally used to diagnose the culprit vessels, and superselective angioembolization (SSA) is effective in controlling the bleeding in most of the cases.[1,2] Existing literature have reported a success rate of 70%-95% for initial (first session) DSA and SSA.[2-4] Failure of initial DSA and SSA may be life threatening for the patients and present a challenging situation for the urologist. There is only 1 retrospective study available in literature, which addresses this issue in patients with percutaneous nephrolithotomy (PCNL). In the prospect of various renal interventions, this issue has not been discussed adequately in literature. As a consequence, there are no guidelines to manage failure of embolization. We evaluated the factors predicting failure of initial angiographic management for

bleeding secondary to vascular complications after various renal interventions. We have also proposed a management protocol based on our experience to deal with such situations.

MATERIALS AND METHODS

We conducted a retrospective analysis of 154 patients who underwent DSA and SSA at our center from January 2006 to June 2016 for severe or persistent, delayed bleeding (indications noted below). Only those who could maintain their blood pressure to a mean BP of 70 mm of Hg on ionotropic support were included in the study. Flowchart with inclusion and exclusion criteria of our patients is given in Figure 1. Study subjects were either primarily operated at our center or referred from other centers for management of bleeding complications following various renal interventions. The study protocol was according to the guidelines of the institutional review board. Twenty-one patients (Group A) with severe bleeding following renal intervention with initial failed angiographic management were compared to those who had initial successful management (n = 133, Group B). The various base line parameters, operative details, and angiographic findings of the patients were analyzed and compared (Table 1). Intrarenal vasoconstriction (IRV) secondary to global vasoconstriction as noted in patients

on inotropic support or local vasoconstriction due to renal artery catheterization were also noted and compared in both the groups. The assessment of IRV was subjective as no objective criteria exist. It can be suspected when the blush of renal artery is less than expected (as in Fig. 2), especially if the patient is on ionotropes and no bleeding vessel is seen. To differentiate between global vasoconstriction and IRV secondary to renal artery manipulation, we used femoral artery as a marker. Stone size and type (staghorn and nonstaghorn) was defined according to Guidelines by European Association of Urology and Soucy et al.[5,6]

Indications for DSA

1. Any postoperative severe arterial bleeding with hemodynamic instability with concomitant significant fall in hemoglobin.
2. Recurrent or persisting bleeding requiring multiple transfusions in early postoperative period.
3. Delayed recurrent or intermittent significant bleeding (>7 days postoperatively) irrespective of hemodynamic status.

All the DSA were performed under local anesthesia by 2 interventional uroradiologists with experience of more than 10 years in presence of the treating urology team. The femoral artery was accessed and a 4-6 Fr sheath was placed. After DSA, SSA was performed as indicated.

Nonionic contrast was used in all patients with normal renal function, and isotonic medium was selected for those with renal insufficiency. Gelatin sponges were rarely used only for very small vascular lesions like simple contrast extravasations. Polyvinyl alcohol (PVA) particles/beads, cyanoacrylate glue, microcoil, or combination of 2 materials was used in cases of arteriovenous fistula (AVF) or pseudoaneurysm (PA). DSA was repeated to confirm that bleeding was completely controlled. Finally, a compression dressing was applied on the patient's groin and maintained for 12 hours to prevent hematoma.

Patients who were on inotropic support with evidence of IRV or evidence of local vasospasm due to arterial catheterization with lack of demonstrable vascular lesion on DSA received intravenous vasodilators like nitroglycerine or calcium channel blocker to induce renal vasodilatation with continuous monitoring of hemodynamic parameters.

A successful DSA/SSA was defined as no further evidence leakage of contrast from the PA or AVF and complete disappearance of PA sac. Clinically, success was defined as no evidence further fresh bleeding, including fresh hematuria, perinephric bleeding, and homodynamic instability. If there was further evidence of fresh bleeding episodes, DSA was repeated. Consideration for surgical intervention was planned following 3 successive failed DSA as in Figure 1.

Statistical analyses were carried out by using MS excel 2011 for mac and SPSS version 23 for mac. Normality of data was assessed using Shapiro-Wik test and Q-Q plots. For continuous variables, normally distributed data were described as mean ± SD (standard deviation) and analyzed using t test. Else median and range with Mann-Whitney U test was used. Categorical data was analyzed using chi-square univariate test. Significant parameters on univariate analysis were then evaluated by
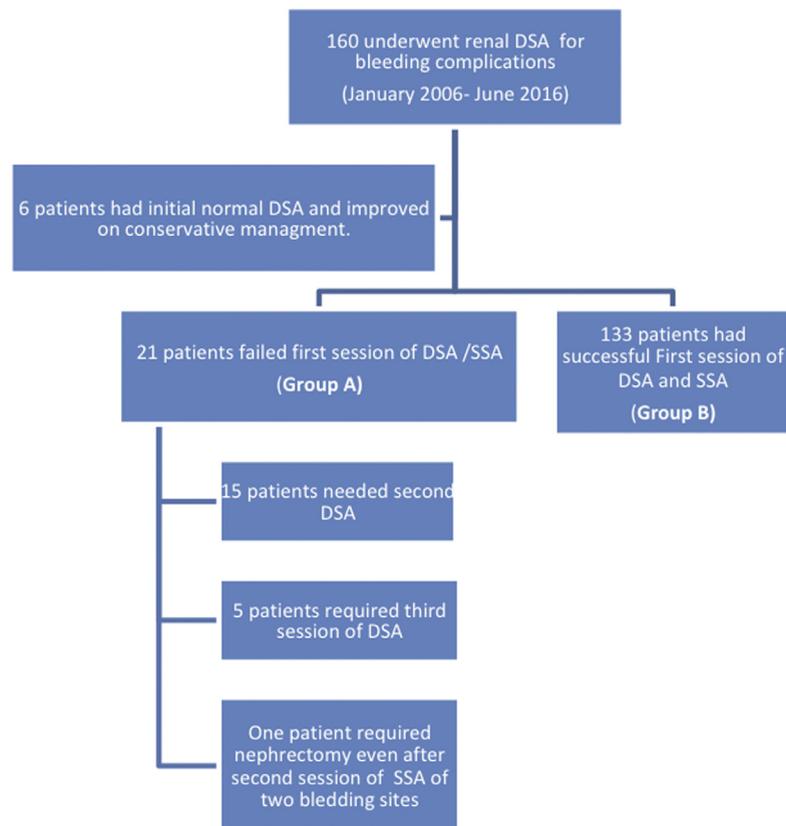

Figure 1. Study populations. (Color version available online.)

Table 1. Results of univariate analysis

Variables		Group A n = 21	Group B n = 133	P Value
Sex	Male	13	81	.85
	Female	8	52	.85
Mean age in years	42.6 ± 12.5	44.4 ± 11	0.45	
Diabetes		3	21	.22
Hypertension		5	28	.34
Mean hemoglobin level in g/dl		6.7 ± 1.46	7.8 ± 1.85	.025
Mean serum creatinine in mg/dl	<1.5	15	98	.26
	>1.5	06	35	.26
Hydronephrosis	None or mild	10	65	.35
	Moderate /severe	11	68	.42
Mean time gap in days from primary surgery to first DSA/SSA		9.2	11.5	.14
Intrarenal vasoconstriction	Yes	07	14	.008
	No	14	119	.008
Intervention	PCNL	17	107	.20
	PLT	1	14	.46
	PCN	1	7	.32
	Biopsy	1	3	.30
	PN	1	2	.25
Stone burden horn	Staghorn	12	67	.63
	Nonstaghorn	9	66	.78
	<3 cm	07	38	.36
	>3 cm	14	95	.24
Number of PCNL puncture tracts	n > 1	13	45	.01
Bleeding site	n = 1	6	98	.01
	n = 2	7	24	.03
	n > 2	8	11	.0001
Vascular lesions	PA (66.6%)	12	91	.25
	AVF (15.3%)	4	18	.42
	CEV (11.8%)	3	17	.33
	PA + AVF (6.25)	2	7	.09
Site of vascular lesion	Upper pole	4	29	.56
	Middle pole	6	35	.42
	Lower pole	11	69	.22
Material used	Gelatin	5	15	.36
	Coils	4	30	.25
	PVA particles	2	18	.45
	Cyanoacrylate glue	1	09	.38
	Combinations	9	61	.23

AVF, arteriovenous fistula; CEV, contrast extravasations; PA, pseudo aneurysm; PCN, percutaneous nephrostomy; PCNL, percutaneous nephrolithotomy; PLT, pyelolithotomy; PN, partial nephrectomy; PVA, polyvinyl alcohol.
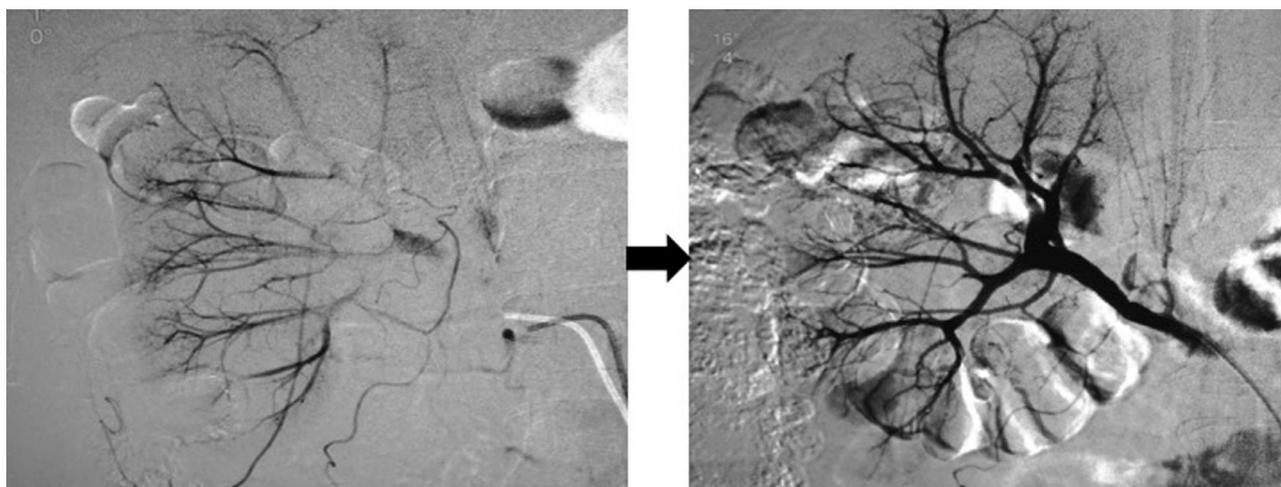

Figure 2. Initially, DSA did not reveal any lesions due to vasospasm but lower polar PA were detected when vasoconstriction resolved (after 12 hours).

multivariate analysis using logistic regression. In all analyses, we have used 2-sided hypothesis testing and probability values (P) <.05 were considered significant.

RESULTS

One hundred fifty-four patients who underwent DSA and or SSA between January 2006 and June 2016 for severe bleeding or persistent delayed bleeding following renal intervention were studied. Pertinent baseline demographic data are tabulated in Table 1. First DSA was successful in 133 patients (Group B, 86.9%) and failed in 21 (Group A, 13.1%) patients. In Group A, initial angiography failed to detect any bleeding site in 6 patients. In the other 15 patients of Group A, DSA did detect a site and SSA was carried out satisfactorily but they had persistent hematuria. Subsequently, they needed a second session of DSA and SSA. Out of these 15, 5 patients required third session and 1 had to undergo nephrectomy.

Mean duration between renal intervention (which lead to the hematuria/perinephric bleed) and first DSA was 10.2 ± 4.5 days (range 1-25 days). The mean gap between the first and second DSA in Group B was 5.6 ± 2.3 days (range 0-14). The base line hemoglobin was significantly lower in Group A vs Group B with P value of .02. In patients, who had presented with bleeding after PCNL, use of more than 1 puncture sites was significantly higher in Group B. Group B also had a significantly higher number of vascular lesions on the initial DSA (Table 1).

The most common vascular lesion was PA (101, 66.66%), followed by AVF in 22 (15.3%), simple contrast extravasations and a combination of above in 10 (6.25%).

During angiography, evidence of IRV was found in 8 (31.5%) patients of Group A and 12 (8%) patients of Group B. The etiology of IRV likely to be related to inotropic support in 11 (56.25%) and local vasospasm due to renal artery manipulation in 9 (43.75%) patients. IRV was found to independently predict the risk of failure of initial angiography.

On repeat DSA, in 18 cases, the site of bleed was different from the site embolized during the first DSA/SSA. In 3 cases, the embolized site had rebled. One patient with transplanted kidney had persistent bleeding after biopsy required graft nephrectomy due to refractory hemodynamic instability after 3 failed DSA/SSAs. In both groups, there was no recurrence on follow-up (median 45 months, range 22-128 months).

Among various factors assessed, on univariate analysis, low base line hemoglobin (P = .025), multiple tracts (n > 1) during PCNL (P = .01), multiple bleeding site (more than one = 0.01 and more than 2 = 0.001) and patients with IRV (P = .008) were found to be risk factors for failure but on multivariate analysis more than 2 bleeding sites (P = .003, 95% confidence interval = 5.23 [1.3-22.5]) and evidence of IRV (P = .02,95% confidence interval = 2.56 [2.15-4.75]) were found to independently predict the risk of failure (Table 2 Electronic Supplement Material).

DISCUSSION

Severe bleeding requiring arterial angioembolization is relatively uncommon events following various renal interventions.[4,7,8] Most of the reported series[1,4,5,7] related to such events has traditionally been focused on post-PCNL bleeding. Few studies have recently focused on such bleeding complications following partial nephrectomy.[8-10] While including these common indications, we have attempted to have a holistic outlook and have also included bleeding following pyelolithotomy, percutaneous nephrostomy, and renal biopsy. DSA and SSA have been established as standard care for such cases.[1-4,6,7] First session of angiographic management has been reported to be successful in 70%-95% of patients.[1-4,9] Failure of initial angiographic management could be a distressing event to the patient as well as to the urologist. It mandates urgent intervention, including repeat DSA or nephrectomy. Till date only 1 study has predicted risk factors for failure of initial DSA and SSA for bleeding complications following PCNL.[4] Risk factors of failure of DSA/SSA following other renal interventions have not been described until now. Understandably due to dearth of data, no guidelines exist regarding the management of failure of angiographic management of postrenal intervention bleed.

In this study, we have found that multiple vascular lesions following multiple segmental arterial injuries secondary to multiple PCNL tracts or from other major interventions possess significant risk of missing of one of the bleeding site during angiography if not carefully looked for. This factor was found as independent predictor for failure of initial DSA in our study. Zengemail et al have reported similar findings in their series.[4]

We also noted that other factors like multiple PCNL tracts, low hemoglobin, h/o of shock with need of inotropic support were also found to be significant predictors of failure of initial DSA on univariate analysis but none of them were found to be an independent predictor on multivariate analysis. This can be explained by the fact that these factors are not independent of each other. Multiple PCNL tracts could lead to increased number of vascular lesions, which could mean more bleeding, low hemoglobin, and even need of ionotropic support.

SSA can employ numerous options, including temporary agents like gelatin sponge and permanent materials like microcoils, cyanoacrylate glue, PVA particles.[10-12] PVA is an effective material for use in larger luminal catheters as it can form a plug inside the microcatheter lumen.[11] Microcoil is a popular agent due to its long-term efficacy.[10] Gelatin sponges are easy to handle and inexpensive. They are commonly used in many centers due to easy availability and low cost. It has the advantages of being biodegradable and it can be used repeatedly for SSA until the arteries are occluded.[13] Sofocleous et al and Farmer et al have reported high success rate with Gel foam.[14,15] In our study too, we have found gelatin to be acceptable for small lesions. We have used different materials and there was no significant difference among the 2 groups.

Our study has found that renal vasoconstriction had significant impact on DSA to diagnose the vascular lesions correctly. During DSA, evidence of IRV was found in 8 (31.5) and 12 (8%) patients of Groups A and B, respectively. The etiology of IRV was as a part of global effect of inotropic support in 11 (56.25%) and local vasospasm due renal artery manipulations or contrast load in 9 (43.75%) patients respectively support. When there was evidence of IRV and no identifiable bleeding site, vasodilation was
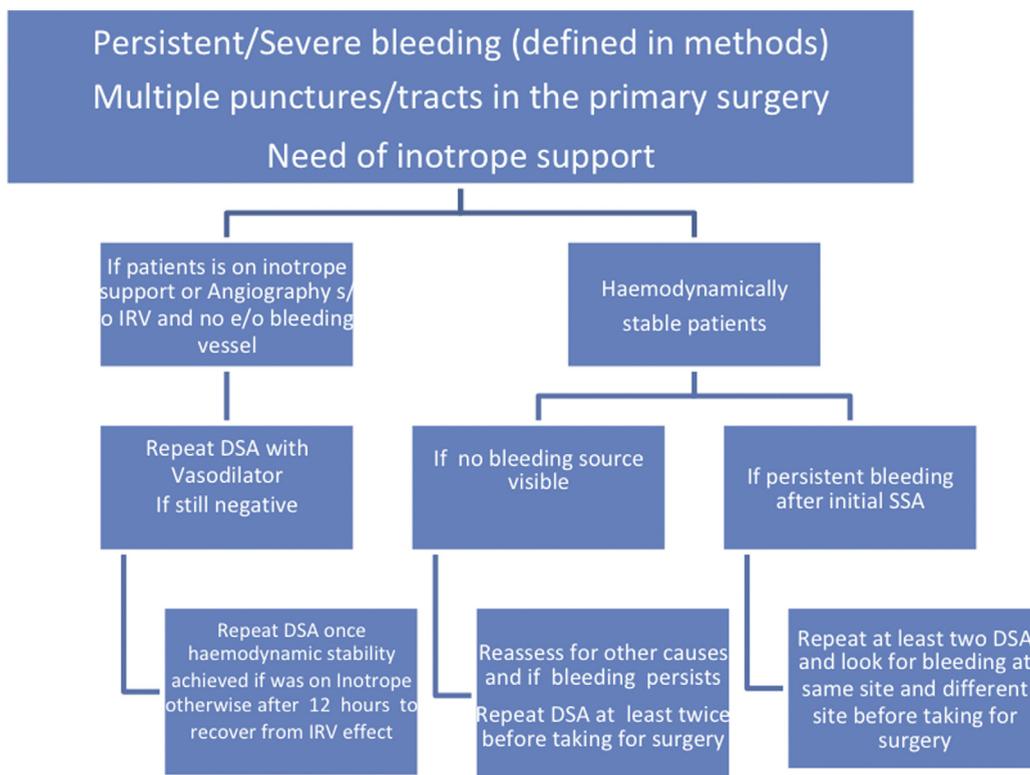
Figure 3. Management protocol. (Color version available online.)

induced pharmacologically and angiography was repeated. If repeat angiography failed to detect any vascular lesion, DSA was repeated after improvement of hemodynamic status and discontinuation of inotropes wherever feasible. Local vasospasm due to arterial catheterization improved with use of vasodilators in 4 patients. Three patients who failed to respond with vasodilator required repeat DSA with nonionic contrast after 12 hours. We successfully identified bleeding sites in all these patients after disappearance of vasoconstriction effect (Fig. 2).

It is evident that IRV can be a significant risk factor for failure of DSA/SSA. It is difficult to objectify IRV but the radiologist should suspect it in all patients, who are on ionotropic support. In such cases, it can be helpful to observe the femoral artery as even it will be seen to have a small caliber due to global vasoconstriction. In patients who do not have global vasoconstriction and IRV is suspected, the femoral artery will appear normal but the renal artery will not. In these cases, the cause of IRV is most likely to be manipulation of the renal artery. While it is not possible to completely avoid it, minimizing such manipulation is helpful in our experience.

We also identified other possible etiopathogenesis of initial failure of angioembolization in other patients in this current study. One important factor was not doing superselective angiography of all segmental arteries individually when we already identified and embolized 1 bleeding site detected during initial selective angiography. Thus, small PA or contrast extravasations may be missed in cases of multiple bleeders if we do not perform superselective angiogram of all segmental arteries routinely. Second

etiology of failure was incomplete occlusion of bleeding vessels with microcoils. This may be due to local vasospasm after initially placed coils it often appeared that the bleeding sites had sealed but bleeding restarted after sometimes. So we suggest use of combinations of 2 materials or multiple coils when there are large PA or AVF and repeat angiography for confirmation after an interval of 30 minutes.

In our study, 20 (95%) out of 21 patients of Group A were successfully managed with second (n = 15) or third sessions (n = 5) of angiography. Only 1 patient required graft nephrectomy to due persistent hemodynamic instability with a nonfunctional graft in situ.

On basis of our experience, we have formulated a management protocol to deal with cases of initial failed angiographic management (Fig. 3).

Limitations

The sample size and retrospective nature of this study might have had some impact on our results. However, it is hard to obtain a large sample of failed initial DSA cases, and it is not practical to design a prospective study. Many of our patients had primary surgery done elsewhere before being referred to our center. So, there may be some shortcomings in standardization of operative technique and reporting of intraoperative findings, though it was unlikely to make a difference to our results since the management of bleeding was standardized.

CONCLUSION

Patients with multiple bleeding lesions and those who are on inotropic support or evidence of IRV are at high risk

for failure of initial DSA and SSA. Careful search for multiple bleeders and understanding the impact of IRV can prevent such failure. Most of these patients can be successfully managed by subsequent sessions of DSA and open surgical intervention including nephrectomy is usually avoidable.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.urology.2018.12.018.

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