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RESEARCH

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Negative renal angiography with subsequent denied angioembolization: findings in a series of 180 patients at a tertiary interventional uroradiology unit

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Abstract

Background: Renal arterial embolization (RAE) is considered to be a safe and effective method for treating a variety of renal lesions and pathology. It is the optimal method not only to stop bleeding, but to preserve renal parenchyma and renal function. Patients who are scheduled to RAE who showed negative catheter angiography with the procedure subsequently denied have a special concern because they are subjected to unnecessary procedure with its complications and didn't get its benefits. This circumstance is infrequently reported in the literature, and that compelled us to identify the predictors of negative renal angiography findings that would result in a failure to undertake RAE.

Results: The study included 180 patients (126 males; 70%) with a mean ± SD age of 44 ± 14 years. Iatrogenic causes were the most common indication for RAE (108 of 180; 60%), while spontaneous unknown reasons constituted (17 of 180 patients; 9%). Angiography showed various lesions in 148 patients: pseudoaneurysm (80 of 148; 54%), tumours (28 of 148; 19%), arteriovenous (AV) fistulas (22 of 148; 15%) and both pseudoaneurysm and AV fistulas (18 of 148; 12%). However, in the remaining 32 of 180 patients (18%) no lesions were identified on renal angiography and RAE procedures were not undertaken. On bivariate analysis, neither gender, side of the lesions, haematuria prior to RAE, or renal artery anatomy were predictors for negative angiography. However, the indication for RAE (spontaneous unknown reasons) of renal haemorrhage was the only predictor for negative angiography (9/17 (53%), $P = 0.001$).

Conclusion: Patients scheduled for RAE may show negative findings with no lesions on renal angiography. Among the different indications for RAE, patients with spontaneous (unknown) have the highest probability (53%) of being associated with negative renal angiography findings, however, those with renal tumours and post-traumatic causes have a low probability. In those patients with spontaneous (unknown), conservative management should be the initial treatment of choice in order to avoid unnecessary RAE and its associated complications.

Keywords: Renal arterial embolization, Renal angiography, Renal angioembolization, Negative catheter angiography, Spontaneous haematuria

Introduction

Renal arterial embolization (RAE) has been introduced as a minimally invasive procedure for treating emergent renal trauma and to control renal haemorrhage [1, 2]. With the recent advances in imaging, more experience in interventional radiology and the availability of

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more refined embolic materials, RAE has been frequently used to treat a wide variety of elective renal tumours and lesions [3, 4].

Despite all of the advantages as a minimally invasive procedure, RAE is not free of complications such as vascular injuries as well as contrast or radiation exposure [5]. This matter compelled investigators to identify predictors in repeated trials to avoid unnecessary procedures [6]. However, little is known regarding patients with negative catheter angiography that were subjected to unjustified RAE with the procedure subsequently denied. This circumstance is infrequently reported in the literature. For example, a previous study reported only two of 21 (10%) patients with negative angiography [7]. Another study reported six of 41 (15%) patients with no further details provided [8].

This current study aimed to identify the predictors of negative renal angiography findings and to identify patients that might be denied RAE.

Patients and methods

Patient population

This retrospective study enrolled consecutive patients in the Department of Urology, Urology and Nephrology Centre, Mansoura University, Mansoura, Egypt between January 2006 to June 2018. The series of patients included both local patients as well as those referred from other hospitals for immediate intervention. The inclusion criteria were as follows: (1) those patients with an indication for RAE; (2) patients with recurrent attacks of haematuria; (3 patients with a significant haemoglobin reduction. The exclusion criteria were as follows: (1) patients with non-significant renal haemorrhage; (2) patients that refused to be included in the study. The indications for RAE were classified into four main categories as follows (1) post-traumatic; (2) iatrogenic; (3) renal tumours; (4) unknown (spontaneous). Post-traumatic included both blunt and penetrating trauma. Iatrogenic included post-percutaneous nephrolithotomy (PCNL), percutaneous nephrostomy (PCN) and renal biopsy. Renal tumours included angiomyolipoma (AML) and renal cell carcinoma (RCC), both before radical surgery and as a palliative therapy. Unknown (spontaneous) cases were those that presented with significant haematuria or concealed renal bleeding with no identifiable cause (trauma, iatrogenic or tumours).

Basic laboratory, physical examinations and imaging investigations were undertaken as standard throughout the medical history. Abdominal ultrasound and Doppler ultrasound were used as the initial imaging tools using a Philips iU22 xMatrix-DS ultrasound system (Philips Healthcare, Best, the Netherlands) and Acuson-sequoia 512 (Acuson, Mountain View, CA, USA).

Table 1 Demographic and clinical characteristics of patients ($n = 180$) that underwent renal arterial embolization (RAE)

Characteristic	**Study cohort $n = 180$**
Age, years	44 ± 14
Body mass index, kg/m^2	22 ± 3
Sex	
Male	126 (70)
Female	54 (30)
Presentation	
Haematuria	133 (74)
Pain	42 (23)
Other	5 (3)
Indication for RAE	
Iatrogenic	108 (60)
PCNL	76
Open surgery	24
PCN, biopsy	8
Trauma	21 (12)
Blunt	15
Penetrating	6
Tumour	34 (19)
AML	23
RCC	11
Spontaneous	17 (9)
Laboratory parameters	
Pre-procedural haemoglobin, g/dl	9.0 ± 2.2
Platelet count, 10^3/μl	260 ± 100
Prothrombin level, %	85 ± 15
Pre-procedural creatinine, mg/dl	1.2 (0.6–8.2)
Blood transfusion units	3 (0–10)
Total number of RA trials	1 (0–4)

Data presented as *n* of patients (%) for categorical data, mean ± SD for normally distributed continuous data and median (range) for continuous data that were not normally distributed

PCNL post-percutaneous nephrolithotomy, *PCN* percutaneous nephrostomy, *AML* angiomyolipoma, *RCC* renal cell carcinoma, *RA* renal angiography

Non-contrast computed tomography (CT) imaging was used to detect the actual size of the intrarenal or perinephric haematoma and to detect any other associated abdominal organ injury. CT angiography was performed after intravenous (i.v.) administration of 1–2 ml/kg of non-ionic contrast media (Omnipaque™ 350 mg/ml, Schering, Berlin, Germany; Optiray 320 mg/ml, USP; Iodixanol 270 ml/kg; Visipaque, GE Healthcare, Amersham, England and Ultravist, Bayer Healthcare, Berlin, Germany) using a 64-multislice helical CT scanner (Brilliance, Philips, The Netherlands) (Philips Healthcare); light-speed plus scanner (General Electric, Milwaukee, Wis). When the administration of contrast media was contraindicated, or in cases of compromised renal

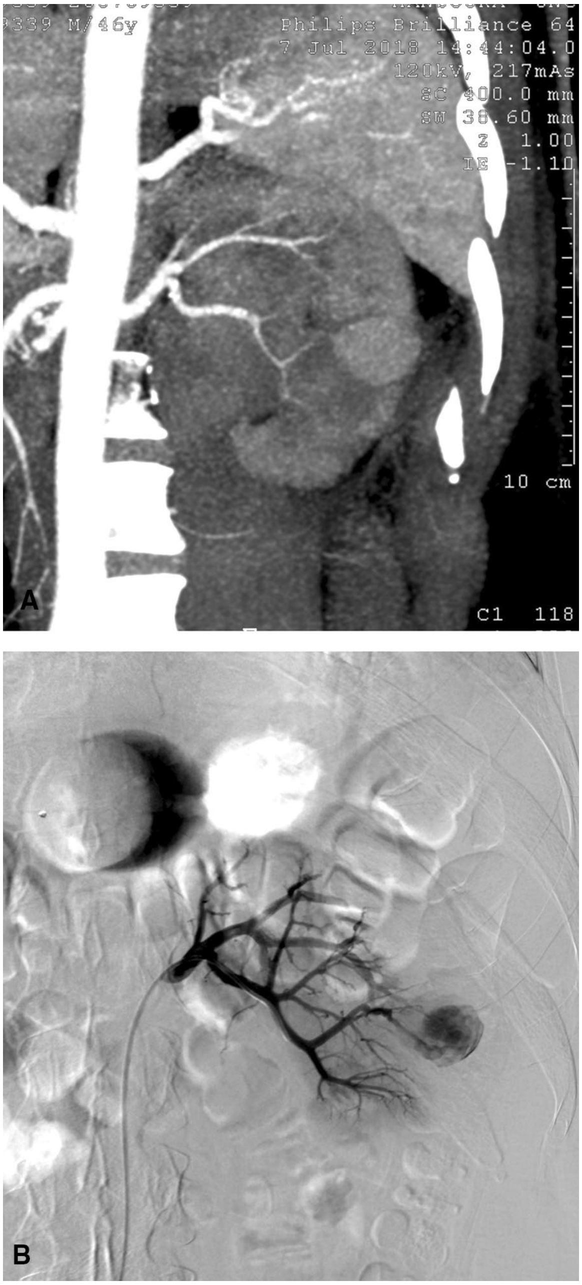

Fig. 1 Coronal CTA of left kidney in a 46-year-old male patient with hematuria after PCNL showing pseudoaneurysm from segmental lower branch (**A**). Selective left renal angiography of the same patient revealed the same findings (**B**)

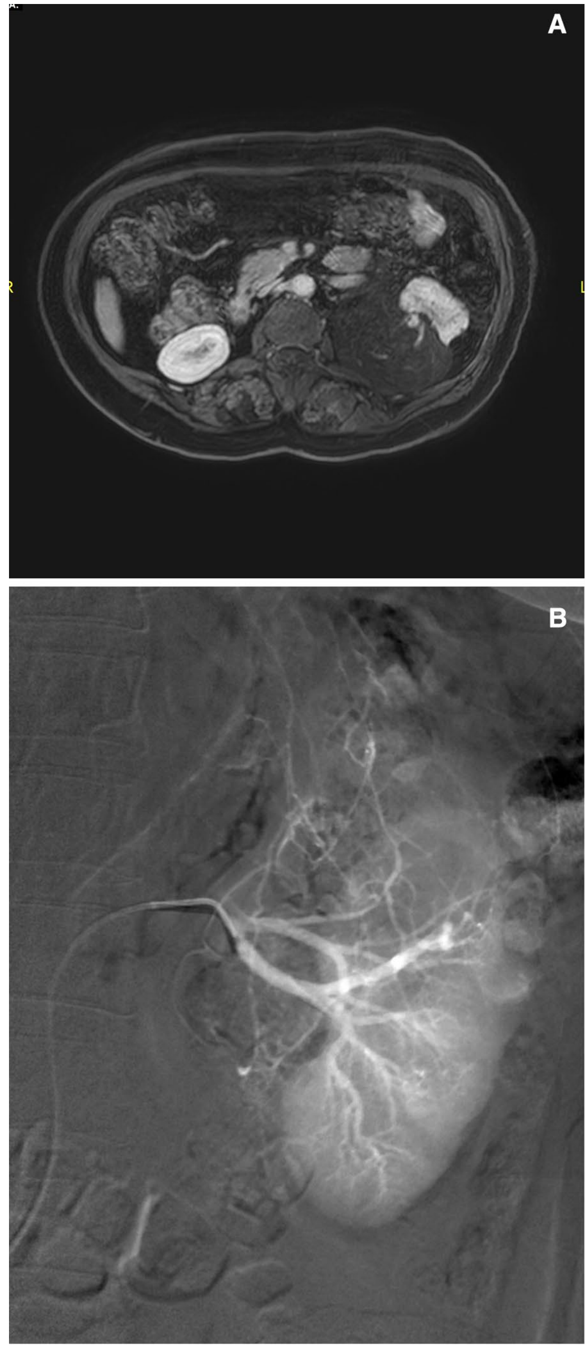

Fig. 2 Axial MRA in 43-year-old female patient with spontaneous hematuria showing a large left renal fat containing mass displacing the kidney anteriorly with evidence of micro-aneurysm inside the lesion (**A**). Selective left renal angiography of the same patient revealed the same findings (**B**)

function, magnetic resonance angiography (MRA) was undertaken using two MRI machines; 1.5-T MRI (SIGNA Horizon, General Electric Medical Systems, Milwaukee, WIS), and 3 Tesla MRI scanner (Phillips, Ingenia 3 T, Best, The Netherlands) after using gadolinium enhanced MRA with i.v. administration of 0.2 mmol/kg of Gadolinium; DOTAREM@ 0.5 mmol/ml (Guerbet, Princeton, NJ, USA), Gadodiamide (Omniscan 0.5 mmol/mL Gd-DTPA-BMA, Gadopentetate dimeglumine (0.2 mmol/kg of Magnevist; Schering Health Care, USA).

Table 2 Bivariate analysis of demographic and clinical characteristics of patients ($n=180$) that underwent renal arterial embolization (RAE) stratified according to the renal angiography results

	Abnormal angiography group *n* = 148	Negative angiography group *n* = 32	Statistical analyses[a]
Sex			NS
Male	105 (81)	24 (19)	
Female	43 (84)	8 (16)	
Side of the lesion			NS
Right	64 (84)	12 (16)	
Left	82 (80)	20 (20)	
Bilateral	2 (1)	0 (0)	
Haematuria prior to RAE			NS
No	32 (82)	7 (18)	
Yes	116 (82)	25 (18)	
Indication of RAE			$P=0.001$
Trauma	19 (91)	2 (9)	
Iatrogenic	88 (82)	20 (18)	
Tumour	33 (97)	1 (3)	
Spontaneous	8 (47)	9 (53)	
Renal artery anatomy			NS
Single	132 (82)	29 (18)	
With accessory	16 (84)	3 (18)	
Nephrectomy			NS
No	131 (81)	30 (19)	
Yes	17 (89)	2 (11)	
Haemoglobin, g/dl			NS
Pre-procedure	8.8 ± 2.4	9.3 ± 2.3	
Post-procedure	10.0 ± 1.9	10.4 ± 1.5	

Data presented as mean ± SD or *n* of patients (%)

Percentages given for rows and decimals deleted for simplification

[a] χ^2-test was used for categorical data and paired sample *t* test was used for normally distributed continuous data; *NS* not significant ($P \geq 0.05$)

In terms of patient management, this was initially conservative in stable patients that presented with haematuria. Conservative patient management included bed rest, serial recording of vital signs and haemoglobin levels, i.v. fluid administration and blood transfusion (if required). RAE was the next step if conservative management failed. Emergency RAE was performed for those that presented with severe renal bleeding and shock.

The study protocol was approved by the Institutional Review Board of Mansoura University, Mansoura, Egypt (no. R/18.04.218). This observational study has followed the STROBE guidelines for reporting observational studies [19]. All personal data were anonymized. All patients were counselled and provided written or verbal consent to treatment.

Angiographic technique

Vascular access was obtained via femoral artery puncture while the patient was in the supine position and under local anaesthesia. In all patients, the renal artery was selectively catheterized using a 5F cobra head catheter (Cordis, Santa Clara, CA USA) using the Seildinger technique. Non-ionic contrast media (Omnipaque™ 350 mg/ml. Schering, Berlin, Germany; Optiray 320 mg/ml, USP; Iodixanol 270 ml/kg, iopromide 300 mg/ml and Visipaque, GE Healthcare, Amersham, England) was used for arteriography in all patients.

In selective angiography, manual injection was used to administer a dose of 8–10 ml of contrast media in each injection. Digital subtraction angiography was carried out using a Toshiba Medical Angiography System (Toshiba, Tokyo, Japan) and Philips biplane flat-detector angiography system (Philips Healthcare, Best, the Netherlands) with a standard DSA program. The runs were finished after the renal vein was clearly visualized and then the same amount of saline as contrast media was administered. Sub-selective catheterization of the injured vessel was then performed using either the standard catheter or a microcatheter. Microcoils, sized 3–5 mm

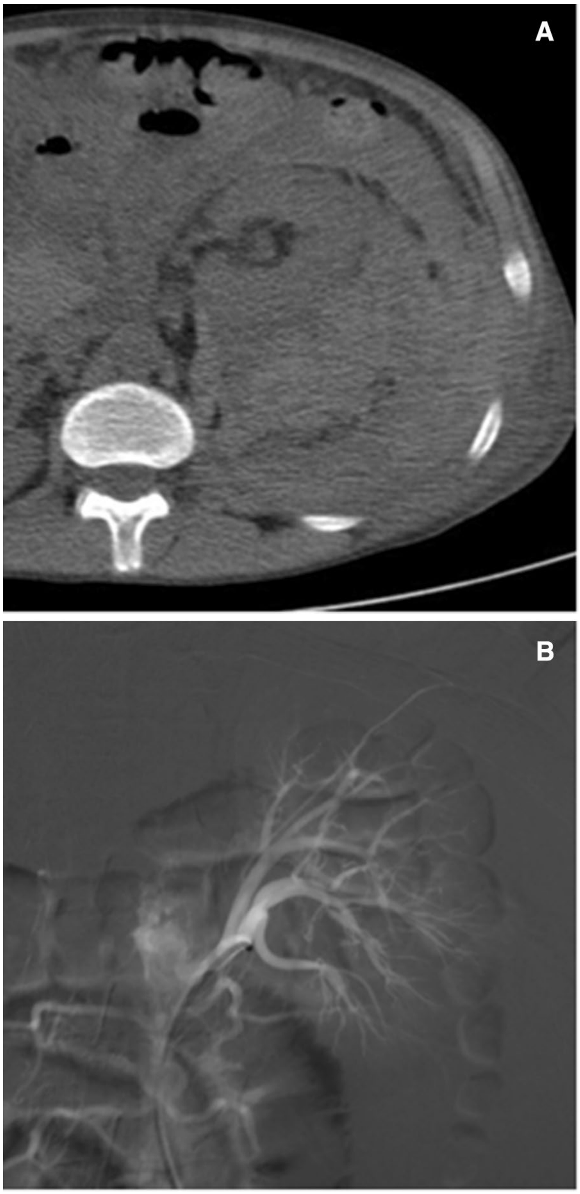

Fig. 3 Axial non-contrast computed tomography imaging of a 42-year-old male patient with spontaneous haematuria showing a large posterior left perinephric haematoma displacing the kidney anteriorly (**A**). Selective left renal angiography of the same patient revealed normal intrarenal arteries with no vascular lesions (**B**)

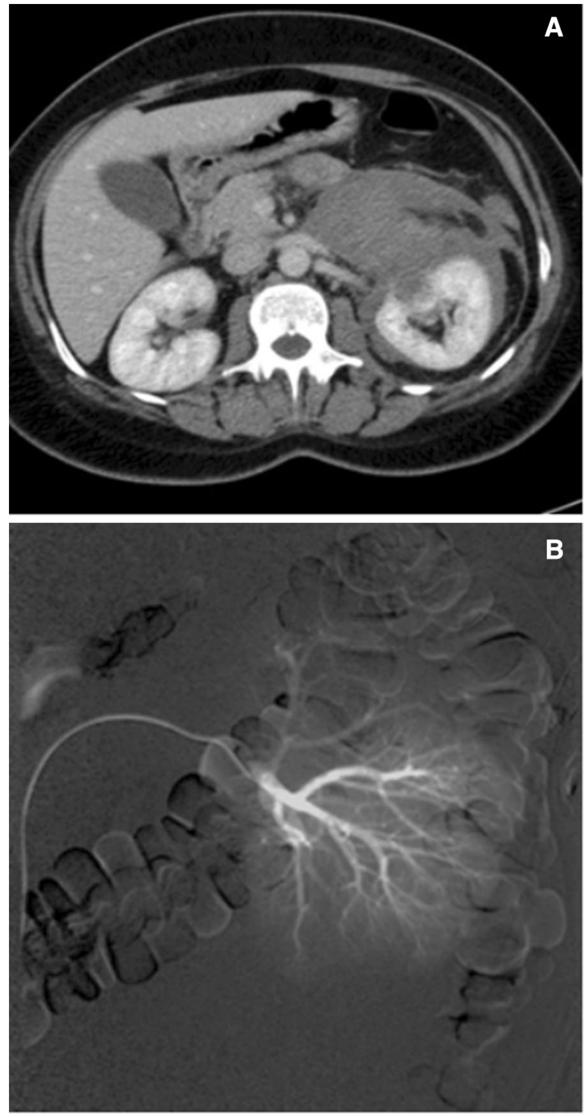

Fig. 4 Axial non-contrast computed tomography imaging of a 45-year-old male patient with a perinephric haematoma after percutaneous nephrolithotomy showing a large perinephric haematoma related to the left renal upper pole associated with parenchymal laceration (**A**). Selective left renal angiography using a cobra head catheter revealed normal intrarenal arteries with no vascular lesions (**B**)

in diameter and 4–9 mm in length (Pushable platinum coils; Boston Scientific, Marlborough, MA, USA), were frequently used. Other materials, such as alcohol and gel foam, were also used. Post-embolization, selective angiography was undertaken while the catheter was in the main renal artery to assess for arterial occlusion by manual injection of contrast media (8–10 ml of contrast media in each injection). All patients were treated by 3 intervention uroradiologists (TD, TM and HF), with 30, 25 and 10 years of experience, respectively.

Clinical outcome

For the purposes of statistical analyses, patients that were enrolled for RAE were classified into two groups; group (A) included patients that had positive findings on angiography regardless of whether the final outcome succeeded or failed; and group (B) included patients with negative renal catheter angiography findings that were subsequently denied RAE procedures.

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21 (IBM Corp., Armonk, NY, USA). For univariate analysis, frequency and percentage were used to express nominal and ordinal variables. Mean ± SD was used to express continuous variables with normally distributed data. Median and range were used for continuous data that were not normally distributed. For bivariate analysis, χ^2-test was used for nominal variables. Paired sample *t* test was used for normally distributed continuous data. A *P* value < 0.05 was considered statistically significant.

Results

This retrospective study enrolled 180 patients (126 males; 70%) with a mean ± SD age of 44 ± 14 years. The demographic and clinical characteristics are shown in Table 1. Iatrogenic causes (PCNL, PCN and post-open surgeries) were the most common indication for RAE (108 of 180 patients; 60%); followed by tumours (34 of 180 patients; 19%), trauma (blunt and penetrating; 21 of 180 patients; 12%) and unknown (17 of 180 patients; 9%).

Renal angiography showed abnormal findings with different types of lesions in 148 of 180 patients: pseudoaneurysm (80 of 148; 54%) (Fig. 1), tumours (28 of 148; 19%) (Fig. 2), arteriovenous (AV) fistulas (22 of 148; 15%) and both pseudoaneurysm and AV fistulas (18 of 148; 12%). Renal angiography was performed in all patients and clinical and radiological success were recorded in 136 of 148 patients (92%) after one or more trials. In the remaining 32 of 180 patients (18%) the renal angiography showed no lesions so no RAE embolization was performed. On bivariate analysis, neither sex, side of the lesions, haematuria prior to RAE, renal artery anatomy, or pre- and post-procedure haemoglobin levels were predictors for negative angiography (Table 2). However, the indication for RAE (spontaneous unknown reasons) of renal haemorrhage was the only predictor for negative angiography (9/17 (53%), $P = 0.001$).

With the exception of three patients (two post-traumatic with parenchymal laceration and one with AML), all of the patients with negative renal angiography findings had either unknown reasons or iatrogenic renal injury as indications for RAE. More than half of spontaneous patients (nine of 17 patients; 53%) were from the negative renal angiography group (Fig. 3). Twenty of 108 patients (19%) with an iatrogenic indication for RAE were from the negative renal angiography group (Fig. 4). The spontaneous subgroup ($n = 17$) had a lower mean ± SD age (28 ± 9 years) compared with the overall study population. Vascular lesions were identified in two patients: an AV malformation and heamangioma of the upper calyx.

All 32 patients with negative renal angiography findings were treated successfully with conservative management except in two patients that had large intrarenal and perirenal haematomas that were diagnosed with CT imaging. In view of persistent haematuria and unstable vital signs despite conservative management and blood transfusion, nephrectomy was performed for those two patients.

Discussion

Renal arterial embolization is considered to be a safe and effective method for treating a variety of renal lesions and pathology, as well as being regarded as an evolving treatment in the field of endoluminal therapy [9]. With the modern shift towards minimally-invasive techniques, the role of endovascular and interventional radiology in urological diseases has continued to evolve, especially in treating renal trauma for different reasons; blunt, penetrating or iatrogenic. Fortunately, most patients respond to conservative management that includes bed rest, correction of the underlying causes and bleeding disorders, i.v. fluids and blood transfusion (if required). However, if the conservative measures fail, or if the patient presents with shock due to severe haematuria or concealed renal haemorrhage, RAE is the optimal method not only to stop bleeding, but to preserve renal parenchyma and renal function [2].

In experienced surgical hands, RAE has been reported to be an effective modality with good overall success [1, 2]. In this current series of 180 patients, 148 had positive renal angiography findings with a variety of lesions. Of these, 136 cases (92%) had overall success after one or more trials, which was a similar success rate to those previously published series [1, 2, 7]. The majority of the published data recommend repeated trials with different indications in cases with the presence of definite lesions on angiography [1, 4, 7].

In this current series of 180 patients, 32 (18%) had no lesions despite being clinically symptomatic. This circumstance has not been frequently reported in the literature. For example, a previous study reported two of 21 patients (10%) of their series with negative angiography [7]; and another study reported six of 41 (15%) with no details regarding those patients [8]. Bivariate analysis in this current series identified the indication for RAE as the only predictor for negative angiography. More than half of the patients that were scheduled for RAE with no known reasons (spontaneous) were found to have no lesions on angiography.

As a minimally invasive procedure, RAE carries low morbidly with the advantages of a short hospital stay and early return to work [7]. More importantly, it saves the kidney with a minimal complication rate [10]. Despite all of the advantages of RAE, it is not free of complications that include radiation exposure and the side-effects of contrast media on the kidneys with increasing the odds of contrast-induced nephropathy [5]. If the procedure is successful and the patient avoids open surgery, the benefits outweigh the costs [6]. However, with an unsuccessful procedure, a negative angiography with no lesions or with the lesion that failed to be embolized and with denied procedure, the cost–benefit equation is different [5]. A few studies have ascertained the predictors of failed RAE trails especially after PCNL (the most common indication of RAE) [5, 6]. However, no previous studies have focused on patients that were scheduled for RAE and found to have no lesions on renal angiography.

Spontaneous cases of renal bleeding have been rarely reported. For example, a previous study reported three patients among 32 (9%) [11]. Other studies did not include patients with spontaneous haematuria [6, 7]. The pathogenesis of spontaneous renal bleeding is poorly understood and the literature draws from case reports. For example, it could be associated with warfarin use [12] or vasculitis and immune diseases [13]. The spontaneous subgroup in the current series had similar demographic characteristics to the overall study population with the exception of a lower mean ± SD age (28 ± 9 years versus 44 ± 14 years), which could suggest the predominance of these lesions in younger patients. Vascular lesions were identified by CT imaging in only two patients. No identifiable pathology was identified in the remaining patients.

The published data has increased our understanding for the natural history of renal trauma and encouraged conservative management as the first line of management. A large series using a national renal trauma data set of > 9000 patients found that 165 required RAE [1]. The procedures were executed in 77 (47%) and no identifiable lesions on angiography were noticed in the rest of the patients [1]. The authors referred to the unnecessary use RAE and recommended wise decision making in enrolling patients for RAE, especially for those with mild and minor parenchymal laceration [1].

The absence of lesions on renal angiography despite haematuria could be explained by the presence of only minor vascular lesions (pseudoaneurysm, AV fistula) or venous injury. This could explain the contribution of a relatively considerable number of iatrogenic cases post-PCNL in this current series. It might also explain the wide range of cases that enrolled for RAE post-PCNL (0.06–1.4%) in the literature [14, 15]. Those series included cases with minor renal injuries that would be treated conservatively without unnecessary embolization trials [14, 15].

Renal arterial embolization can be used in conjunction with laparoscopic or robotic partial nephrectomy in the treatment of renal tumours. For example, a previous study reported the initial experience in 23 patients in whom superselective embolization of the tumour blood vessels was performed before laparoscopic partial nephrectomy and zero ischaemia was achieved in all except in four patients [16]. Superselective renal arterial embolization allows surgeons to perform laparoscopic partial nephrectomy without clamping the hilum vessels, thus avoiding the time threshold associated with ischaemic damage. The successful long-term oncological and functional results of this technique have been reported in 210 consecutive patients [17]. Moreover, RAE can be used to facilitate robot-assisted partial nephrectomy. This novel technique was tried in 10 patients with delivery of an indocyanine green-lipiodol mixture with superselective RAE, which was used to enhance surgical margin control during purely off-clamp robotic partial nephrectomy with the use of near-infrared fluorescence imaging [18].

This current study had several limitations. First, it was a retrospective study. Unfortunately, the infrequency of patients scheduled for RAE would make it difficult to conduct a prospective study. Furthermore, the study reports on a topic that has not been addressed in previous research and was conducted in one of the largest tertiary institutes in the region by experienced interventional uroradiologists. Secondly, follow-up of renal function using a renal isotope scan was not available. Therefore, future studies are needed to address these limitations.

Conclusion

Patients scheduled for RAE may show negative findings with no lesions on renal angiography. Among the different indications for RAE, patients with spontaneous (unknown) have the highest probability (53%) of being associated with negative renal angiography findings, however, those with renal tumours and post-traumatic causes have a low probability. In those patients with spontaneous (unknown), conservative management should be the initial treatment of choice in order to avoid unnecessary RAE and its associated complications.

Abbreviations

RAE: Renal arterial embolization; SD: Standard deviation; AV: Arteriovenous; PCNL: Percutaneous nephrolithotomy; PCN: Percutaneous nephrostomy; AML: Angiomyolipoma; RCC: Renal cell carcinoma.

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None.

Authors' contributions
HMF: Data collection. MME: Project development/manuscript writing. KAS: Data analysis. MAB: Data collection. AE: Data collection. TM: Manuscript writing. TEI-D: Manuscript Editing. AA: Manuscript writing. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate
Was take for a retrospective study.

Consent for publication
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Competing interests
The authors declare that they have no competing interests.

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