

**Role of Trans-catheter Selective Arterial Embolization in The Management of Renal Angiomyolipomas**

**Abstract**

**Background:** Renal angiomyolipoma (AML) is the most common benign renal tumour with incidence from 0.2% to 0.6% of the general population, representing about 3% of all kidneys' tumours with a strong female predilection. The aim of this work was to assess trans-catheter selective arterial embolization (SAE) role in renal AML management (including control of symptoms and tumour size reduction).

**Methods:** This prospective minimally invasive trial was conducted on 30 cases with renal AMLs who were managed by SAE and diagnosed with renal AML by CT and/ or US. All patients were subjected to laboratory testing (complete blood count (CBC), coagulation profile, renal and liver function test and urine analysis) and radiological imaging (abdominal US, UECT scan, CECT scan and CTA for renal vessels, gadolinium enhanced MRA and diagnostic catheter angiography).

**Results:** Both lesions' volume and maximum diameter after SAE showed highly significant reduction ( $p < 0.001$ ). Serum creatinine and Haemoglobin levels before and after SAE showed no significant changes ( $P = 0.069$  and  $P = 0.055$ ) respectively.

**Conclusions:** SAE is a safe and effective technique in the management of renal AMLs either in emergency or preventively with preservation of renal functions and elimination of the potential risk of nephrectomy.

**Keywords:** Trans-catheter Selective Arterial Embolization, Renal Angiomyolipomas, Tumour size reduction

## **Introduction:**

Renal angiomyolipoma (AML) is the most common benign renal tumour with incidence from 0.2% to 0.6% of the general population, representing about 3% of all kidneys' tumours with a strong female predilection <sup>[1, 2]</sup>.

They are a heterogeneous neoplasms' group that have multiple types with different pathological, radiological features and clinical symptoms, even though they all have the same three elements with variable proportions which are: blood vessels, smooth muscle and fatty tissue <sup>[3]</sup>.

AMLs have tortuous blood vessels and susceptible to aneurysm formation and rupture <sup>[4]</sup>. Therefore, AMLs are more likely to rupture, retroperitoneal bleeding symptoms, hematuria and hemorrhagic shock <sup>[5]</sup>.

**Even** though some renal AMLs don't show symptoms, they can increase in size producing local symptoms including palpable mass, flank pain, gross hematuria, abdominal fullness and pain, abdominal visceral compression and anorexia <sup>[2]</sup>.

The tumours are visualized by the characteristic fat presence on ultrasonography (US), magnetic resonance imaging (MRI) or computed tomography (CT) of the kidneys <sup>[2]</sup>.

AMLs are usually classified into sporadic groups that have solitary lesions, more common in women and represents 80% of cases and non - sporadic groups that is related to the pulmonary lymphangioleiomyomatosis (LAM) or tuberous sclerosis complex (TSC) and represents 20% of cases. Around 75% of TSC cases develop renal AMLs and the tumours are often larger, bilateral, multiple and symptomatic <sup>[6, 7]</sup>.

Possible interventions include nephron-sparing surgery, selective arterial embolization (SAE), cryo- and radiofrequency ablation, treatment with mammalian target of rapamycin (mTOR) inhibitors and total nephrectomy <sup>[3]</sup>.

SAE has become the main renal AMLs treatment option as it is less invasive, allows targeting of the bleeding vessels with minimal severe complications' risk [8] [9, 10].

Management recommendations for SAE depends on tumour size and clinical signs. SAE can manage an acute renal AMLs bleeding with any size, as a prophylaxis of asymptomatic high-risk renal AMLs (>4cm), or as a pre-operative treatment to prevent intra-operative haemorrhage [10].

Asymptomatic lesions >4 cm carry high risk to become symptomatic and to present with acute tumour rupture with subsequent life-threatening haemorrhage and shock. Therefore, prophylactic treatment is crucial for these cases [10].

The aim of this work was to assess the role of trans-catheter SAE in the management of renal AML (including control of symptoms and tumour size reduction).

#### **Patients and Methods:**

This prospective minimally invasive trial was conducted on 30 cases (7 males, 23 females) aged from 23 to 60 years old, with renal AMLs who were managed by SAE and diagnosed with renal AML by CT and/ or US. All cases were admitted to the Interventional Radiology Unit, Radiology Department, Urology and Nephrology Center, Mansoura University, Mansoura, Egypt in the period from April 2021 to June 2022.

Exclusion criteria were chronic debilitating diseases, bleeding, coagulation disorders, anticoagulant users, severe hemodynamic instability, hemodynamically stable patients with high-risk conditions, acute sepsis and who underwent arteriography without embolization as another therapeutic strategy not due to technical failure.

All cases underwent full history taking, clinical examination, laboratory testing (complete blood count (CBC), coagulation profile, renal and liver function test and urine analysis) and

radiological imaging (abdominal US, UECT scan, CECT scan and CTA for renal vessels, gadolinium enhanced MRA and diagnostic catheter angiography).

**Embolization:**

The patients were appropriately placed on the angiography table, with adequate exposure of the groin area. The patient's skin in the groin area was then cleaned with Povidone iodine and a sterile gown was placed. Local anaesthesia [xylocaine 2% solution]. Femoral access: the case is placed in the supine position then using the modified Seldinger's technique, right common femoral artery puncture was done. The femoral pulse was felt, around 2-3 cm below the inguinal ligament. The operator's hand was used to fix the artery in position, with the fingers parallel to the course of the artery. The access needle was then introduced between the index and middle fingers, at 45-degrees to the skin. Once the arterial spurting was satisfactory, a 0.035-inch guidewire was then advanced coaxially in the access needle under fluoroscopic guidance to reach the proximal iliac artery, and then needle was withdrawn slowly over the wire which was held firmly in position. In all arteriographies, a 6-Fr vascular sheath was placed into the common femoral artery over the guidewire and the guidewire was then withdrawn. A Y-connector was connected to the tip of the vascular sheath, and continuous pressurized flush by saline was connected to the Y-connector under pressure of 300 mmHg.

**Diagnostic and therapeutic renal angiography:**

An Abdominal aortography was first performed in all arteriographies by a 5F pigtail catheter. The renal artery was then selectively catheterized via 5 French standard cobra catheters (C2) (Cordis, USA) in all arteriographies. The left renal artery was catheterized in 17 arteriographies and the right renal artery was catheterized in 18 arteriographies. All catheter advances were performed over 0.035-inch guidewire.

Using fluoroscopy-guided injection, the catheter's tip position was confirmed to be at a very proximal end of the catheterized renal artery with of test dose of contrast (2 cc of diluted

contrast with saline 1:1 ratio). Selective renal angiography was done by manual injection of 8-10 ml of contrast media in every injection. The runs were finished after visualizing the renal vein clearly followed by saline of the same amount of contrast media. Diagnostic images were evaluated carefully.

The catheter was further inserted super selectively into the segmental branch of the renal artery supplying the lesion (Dose of 4-5 ml of contrast media in each injection). Road mapping was performed in all patients. When vascular lesions were distal in location and not accessible by the standard cobra catheter, we reached it by 2.7F microcatheter (Renegade, HI-FLO Kit, Ireland). The microcatheter with the micro-guidewire inside were advanced coaxially in the guiding catheter. The microcatheter tip was placed as close as possible to the vascular lesion. Embolization technique: Once the standard/micro-catheter was ready in the feeding vessel, selective angiography was done to determine the pre-embolization tumor blush.

We used embolic materials in all arteriographies such as [microcoils (Pushable fibered platinum™, Boston Scientific, USA) ranges from 3 to 5 mm in diameter and 4 to 9 mm in Length, microspheres (Embosphere™, Guerbet, France) or absolute alcohol (Concentrated ethanol 95-99%)]. The embolic materials had been injected very cautiously under continuous fluoroscopic guidance to avoid reflux and non-target embolization.

After injecting satisfactory amount of embolic material till achieving near stagnation of flow in the feeding vessel, saline was injected in the same manner to clear the catheter 's dead space.

After inserting microcoils or injection of other embolic materials, post-embolization control angiography was performed while the catheter is in main renal artery to assess arterial feeders' occlusion by manual injection of contrast media (8-10 ml of contrast media in each injection) after about 2 minutes from the embolization.

The primary outcomes were the short-term outcomes in the form of technical and clinical procedure success as regard management of renal AMLs as an acute management of renal AMLs' haemorrhage, as a prophylaxis of asymptomatic high risk renal AMLs or as a pre-operative adjunct treatment to prevent intra-operative haemorrhage. Secondary outcomes were marked tumour size reduction, low rates of recurrence and acceptable complications.

### Statistical analysis

SPSS v26 was used to do statistical analysis (IBM Inc., Chicago, IL, USA). Using the Shapiro-Wilks test and histograms, the normality of the data distribution was determined. As mean and standard deviation, quantitative parametric data were given (SD). Non-parametric quantitative data were given as the median and interquartile range (IQR). The qualitative characteristics were provided in terms of frequency and percentage (%). A two-tailed P value < 0.05 was deemed statistically significant.

### Results:

**Table 1: Age, gender distribution and presenting symptoms and clinical signs at diagnosis of the studied patients**

<b>Age (years)</b>		<b>n=30</b>
23 - <35		9(30%)
35 - <45		12(40%)
45 - <55		6(20%)
55 - 60		3(10%)
<b>Mean ± SD</b>		40.633±9.800
<b>Gender</b>	<b>Male</b>	7(23.3%)
	<b>Female</b>	23(76.7%)
<b>Symptoms</b>		
<b>Flank pain</b>		27(90%)
<b>Palpable tender mass</b>		18(60%)
<b>Hematuria &amp; Hypovolemic shock</b>		15(50%)
<b>Pressure symptoms</b>		9(30%)
<b>Anemia</b>		6(20%)
<b>Fever</b>		3(10%)
<b>Blood pressure alteration</b>		2(6.7%)
<b>Urinary tract infection</b>		1(3.3%)
<b>Asymptomatic</b>		3(10%)

Data are presented as mean ± SD or frequency (%).

**Table 2: Tuberous sclerosis complex status and features, number of needed blood units, Pre-arteriography diagnostic imaging, and number and laterality of renal AMLs**

		<b>n=30</b>
<b>TSC status</b>		12(40%)
<b>Family history</b>		3(25%)
<b>Clinical features (Vogt triad)</b>	Seizures	12(100%)
	Intellectual disability	10(83.3%)
	adenoma sebaceum	9(75%)
<b>Imaging findings (Associated lesions)</b>	Cortical or subependymal brain tubers	12(100%)
	Pulmonary LAMs	4(33.3%)
	Hepatic AMLs	7(58.3%)
<b>Number of needed blood units</b>		
	1	1(4%)
	2	8(32%)
	3	6(24%)
	4	4(16%)
	5	2(8%)
	>10	4(16%)
<b>Median number of needed blood units</b>		3(1-13)
<b>Pre-arteriography diagnostic imaging</b>		
<b>Pelvi-abdominal US</b>		35(100%)
<b>UECT</b>		35(100%)
<b>Renal CECT &amp; CTA</b>		21(60%)
<b>Renal MRA</b>		2(5.7%)
<b>Both Renal CTA &amp; MRA</b>		2(5.7%)
<b>Number and laterality of renal AMLs</b>		
<b>Renal AML number</b>	Single	13(43%)
	Multiple	17(56.7%)
<b>Renal AML laterality</b>		
<b>Unilateral</b>	Right	10(33.3%)
	Left	6(20%)
<b>Bilateral</b>		14(46.7%)

Data are presented as frequency (%).

**Table 3: Renal AMLs' demographic data, intra-lesional vascular anomalies, indication of SAE, Renal vascular variants, arterial supply (feeders) of AMLs encountered and number of embolized renal AMLs per arteriography**

		<b>n=33</b>
<b>Type</b>	Sporadic	18(54.5%)
	TSC-associated	15(45.5%)
<b>Location</b>		
<b>Right</b>	Upper zone	8(24.2%)
	Mid-zone	4(12.1%)
	Lower zone	6(18.2%)
<b>Left</b>	Upper zone	6(18.2%)

	Mid-zone	4(12.1%)
	Lower zone	5(15.2%)
<b>Intra-lesional vascular anomalies</b>	Microaneurysms	6(18.2%)
	Aneurysms	26(78.8%)
	AVM	1(3%)
<b>Indication of SAE</b>		
<b>Urgent (Bleeding symptoms) (n = 28)</b>	Gross haematuria	15(45.5%)
	Intra-lesional bleeding	28(84.8%)
	Perinephric bleeding	25(75.8%)
	Retro-peritoneal bleeding	25(75.8%)
<b>Prophylactic (high risk) (n=3)</b>		
<b>Tumour size: ≥ 4cm.</b>		
<b>Tumour composition</b>	Abnormal tortuous vascularity	2(6.06%)
	Intralesional aneurysm ≥ 5mm	1(3.03%)
<b>Tumour type: TSC-associated</b>		
<b>Preoperative (n=2)</b>		
<b>Renal vascular variants</b>	Accessory renal arteries	3(9.1%)
<b>Supplying branch (feeder)</b>		
<b>Main renal artery</b>	Upper zonal segmental branch	15(45.5%)
	Middle zonal segmental branch	8(24.2%)
	Lower zonal segmental branch	13(39.4%)
<b>Accessory renal artery</b>	Upper zonal segmental branch	1(3.03%)
	Middle zonal segmental branch	2(6.06%)
	Lower zonal segmental branch	0(0.0%)
<b>Intra-lesional vascular anomalies</b>		
<b>Pathological vascularity</b>		
<b>Intralesional vascular anomalies</b>	Microaneurysms	6(18.2%)
	Aneurysms	26(78.8%)
	AVM	1(3%)
<b>Number of embolized renal AMLs per arteriography</b>	0	4(11.4%)
	1	30(85.7%)
	2	1(2.9%)

Data are presented as frequency (%), AVM: Arterio-venous malformation

**Table 4: Embolic agents used, residual tumor blush after embolization, overall success rate and technical success rate**

		<b>n=32</b>
<b>Embolic agents</b>		
<b>Microcoils</b>		18(56.25%)
<b>Microspheres</b>		3(9.4%)
<b>Microcoils + Microspheres</b>		6(18.75%)
<b>Microcoils + Absolute Alcohol</b>		3(9.4%)
<b>Absolute alcohol, gel foam and microcoils</b>		1(3.1%)
<b>Absolute alcohol, gel foam and lipidol</b>		1(3.1%)
<b>n=34</b>		
<b>Residual blush (%)</b>		3(8.8%)
<b>Degree of residual blush</b>	<b>0-9 %</b>	1(2.9%)
	<b>10-19 %</b>	2(5.9%)
	<b>20-29 %</b>	0(0%)
		<b>number of lesions=33</b>

<b>Overall success rate</b>		30(90.9%)
<b>Overall failure rate</b>	Technical failure & underwent total nephrectomy	1(3%)
	Recurrence on follow up & treated with total nephrectomy	2(6.1%)
		<b>number of arteriographies=35</b>
<b>Technical success of SAE</b>		31(88.6%)
<b>Technical failure of SAE</b>	Residual blush and need for re-embolization	3(8.6%)
	Need for renal surgery without re-embolization	1(2.8%)

Data are presented as frequency (%), SAE: Selective arterial embolization

**Table 5: Timing of surgery post embolization, need for renal surgery, complications related to arteriographies and embolizations**

		<b>n=32</b>
<b>Timing of surgery post embolization</b>	<b>36 hours</b>	1(50%)
	<b>48 hours</b>	1(50%)
<b>Need for renal surgery</b>		<b>n=6</b>
<b>Overall success rate</b>		30(90.9%)
<b>With no SAE</b>	Total nephrectomy	1(16.7%)
	Partial nephrectomy	1(16.7%)
<b>Post-SAE</b>	Total nephrectomy	4(66.6%)
	<b>Complications related to arteriographies and embolizations</b>	
<b>Minor complications</b>	Puncture site hematoma	1(2.9%)
	Post-embolization syndrome (PES)	8(22.8%)
	Persistent haematuria	1(2.9%)
<b>Major complications</b>	Puncture site pseudoaneurysm or AVF	0(0%)
	Iatrogenic retro-peritoneal hematoma	0(0%)
	Puncture site abscess	0(0%)
	Renal abscess	1(2.9%)
	Non-target embolization of normal parenchyma	0(0%)
	Cardio-vascular collapse by Ethanol	0(0%)
	Coil Migration	0(0%)
Death	0(0%)	

Data are presented as frequency (%),

**Table 6: Assessment of haematuria, intra-lesional bleeding, perinephric and retro-peritoneal bleeding and tumour size reduction post-embolization**

		<b>n=15</b>	<b>P value</b>
<b>Haematuria</b>	Stoppage of hematuria within 3 days post-embolization without recurrence	13(86.6%)	P= <0.001*
	Persistent haematuria for 10 days	1(6.7%)	

	(Partial nephrectomy was decided)		
	Recurrent haematuria 3 months after SAE (Total nephrectomy was decided)	1(6.7%)	
		<b>n=28</b>	
<b>Intra-lesional bleeding</b>	Complete disappearance or marked organization of intra-lesional hematomas	27(96.4%)	P= <0.001*
	Still present large hematoma (recurrence)	1(3.6%)	
		<b>n=25</b>	
<b>Perinephric &amp; retroperitoneal bleeding</b>	Complete disappearance or marked organization of perinephric & retroperitoneal hematomas	24(96%)	P= <0.001*
	Still present large hematomas (recurrence)	1(4%)	
		<b>n=32</b>	
	Tumour size reduction	29(90.6%)	P= <0.001*
	No size change	2(6.3%)	
	Increase in size	1(3.1%)	

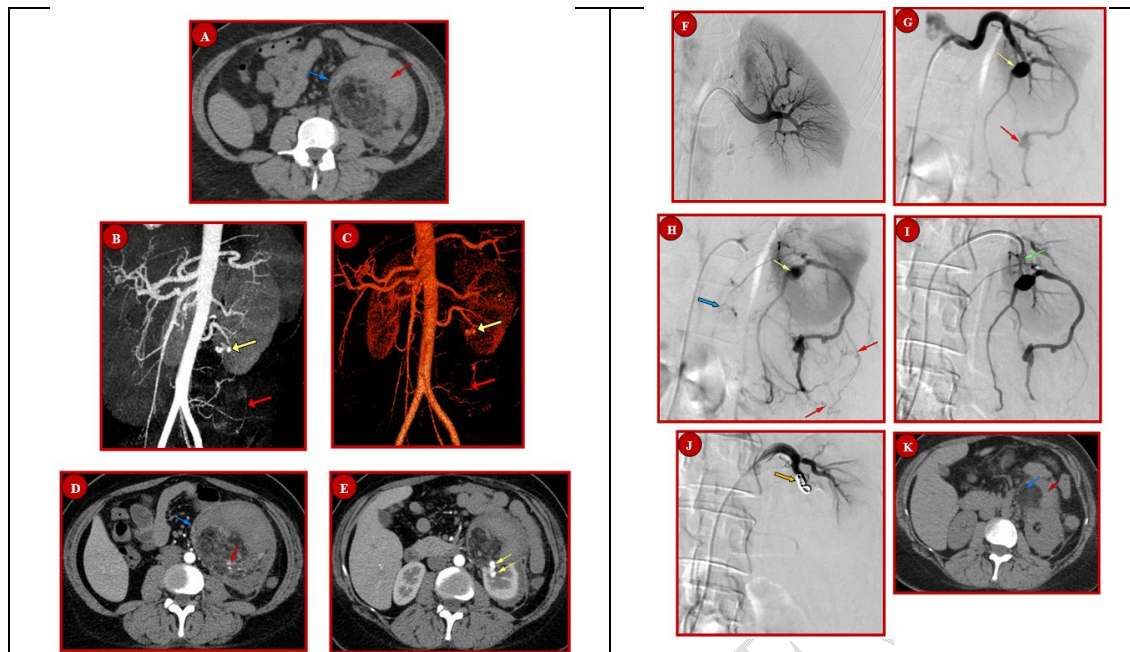
\* Statistically highly significant, Data are presented as frequency (%)

Both lesions' volume and maximum diameter after SAE showed highly significant reduction ( $p < 0.001$ ). Serum creatinine and Haemoglobin levels before and after SAE showed no significant changes ( $P = 0.069$  and  $P = 0.055$ ) respectively. Table 7

**Table 7: Tumour size reduction and laboratory investigations before and after SAE**

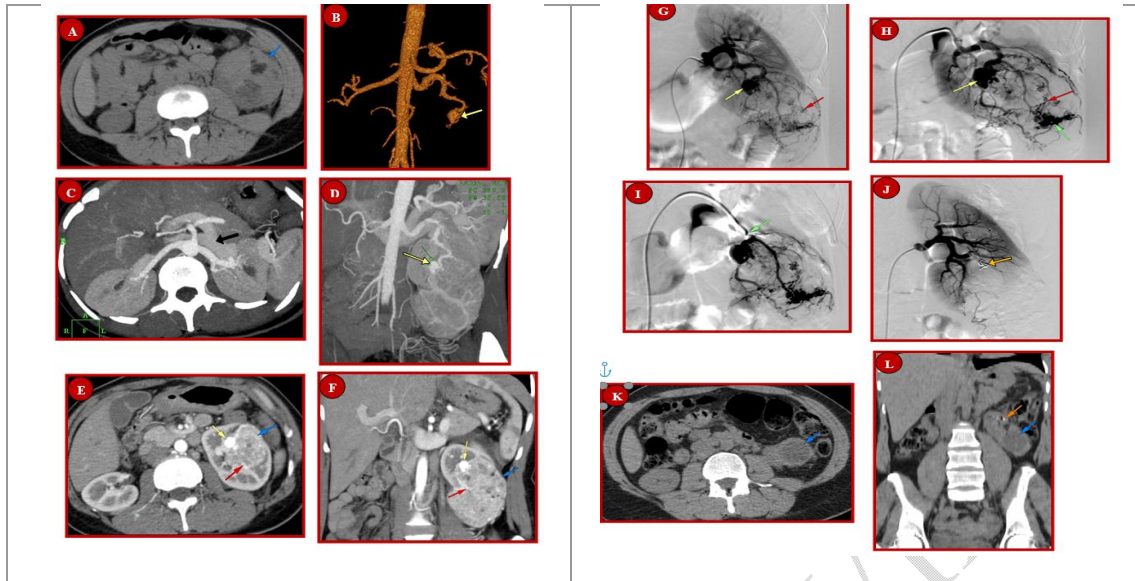
Maximum diameter (cm)	Pre- embolization	Post- embolization	P value
Median (range)	11.4 (9.28-14.1)	9.9 (8-11.9)	P<0.001*
Reduction% Median (range)	16.33 (13.16-20.34)		
<b>Volume (cc)</b>			
Median (range)	675 (220.75-1156)	379 (138-680)	P<0.001*
Reduction% Median (range)	42.66 (36.77-60.96)		
<b>Serum creatinine level (mg/dl)</b>			
Median (range)	0.9 (0.5-2.2)	0.85 (0.4-3.1)	P= 0.069*
<b>Haemoglobin level (g/dl)</b>			
Mean $\pm$ SD	9.684 $\pm$ 2.140	9.785 $\pm$ 2.216	P= 0.055*

Case 1: A 34-year-old female patient, presented with acute left loin pain and recurrent attacks of gross hematuria for 1 week. She was diagnosed as ruptured left renal AML. She was admitted with haemoglobin level of 6 g/dl. She underwent urgent SAE. Figure 1



**Figure 1: UECT scan before SAE axial image (A) revealed: solitary fat-containing left lower pole renal AML (blue arrow), measured about 10.6 x 9.5 x 12.6 cm at its maximum dimensions with intra-lesional hematoma seen (red arrow). CECT scan before SAE; coronal MIP image (B), coronal 3D image (C) and axial images (D & E) revealed: double left renal arteries. A large vascular left lower pole renal mass (blue arrow) with multiple abnormal pathological vascularities (red arrow) and intra-lesional 2 aneurysms from the accessory lower polar branch (yellow arrow). Main renal artery (F): no pathological vascularity or vascular malformations. Accessory lower polar renal artery (G & H): Pre-embolization angiography using Cobra catheter showed large vascular lower pole renal mass (blue arrow) with multiple abnormal pathological vascularities (red arrow) and lower polar small aneurysm (yellow arrow). Super selective segmental renal artery angiography (I): The cobra catheter was advanced further super selectively into the arterial feeder of the aneurysm (green arrow) then, embolization was done using microsphere particles and one micro-coil (orange arrow) under fluoroscopic control. Post-embolization control angiography (J) revealed: Successful embolization with no further opacification of both vascular mass and aneurysm. Then, the patient became haemodynamically stable, haematuria stopped after 48 hours, and her haemoglobin level started to build up and reached 9 g/dl on follow up. Follow up UECT scan 6 months after SAE; axial image (K) revealed: Significant tumour size reduction of about 90% (the mass –blue arrow- measured 5 x 4 x 6 cm) with marked organization of the previously described intra-lesional hematoma (red arrow).**

Case 2: A 32-year-old female patient, presented with incidentally discovered asymptomatic left renal mass by US. She was diagnosed as left lower polar exophytic renal AML. She underwent prophylactic SAE. Figure 2

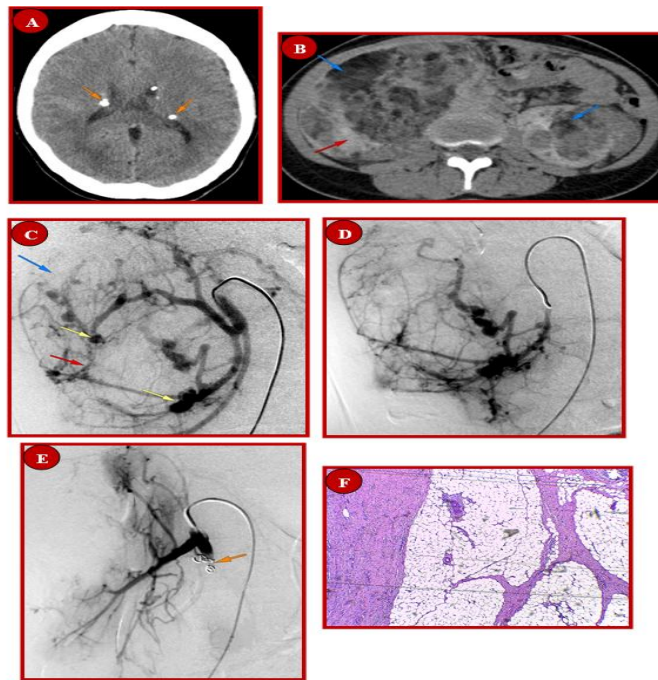


**Figure 2: UECT scan before SAE; axial image (A) revealed: Solitary hyperdense fat-containing exophytic left lower pole renal AML (blue arrow), measured about 8 x 6.3 x 10 cm at its maximum dimensions with no intra-lesional or perinephric hematomas.**

**CECT scan before SAE; coronal 3D image (B), axial MIP image (C), coronal MIP image (D), axial image (E) and coronal reformatted image (F) revealed: single left renal artery. A Large vascular left lower pole renal mass (blue arrow) that showed intense arterial enhancement with multiple abnormal pathological vascularities (red arrow). Intra-lesional one aneurysm 1x1 cm (yellow arrow). Early venous filling with enlarged ipsilateral renal vein (black arrow) denoting arterio-venous malformation. Diagnostic selective left renal angiography (G): Pre-embolization angiography using Cobra catheter showed large vascular exophytic lower pole renal mass with multiple abnormal pathological vascularities (red arrow) and multiple micro-aneurysms inside as well as larger aneurysm 1x1 cm (yellow arrow) and arterio-venous malformation (green arrow). The mass supplied by lower zonal segmental artery. Selective and Super selective segmental renal artery angiography (H & I): the cobra catheter was advanced further sub-selectively into the lower zonal segmental artery then, advanced distally and super selectively into the arterial feeder of the lesion, embolization was done using microsphere particles and two detachable micro-coils (orange arrow) under fluoroscopic control. Post-embolization control angiography revealed (J): Successful super selective embolization with no further opacification of the previously described vascular mass and aneurysmal dilatation. It also demonstrated the patency of rest of the vessels. Follow up UECT scan 3 months after SAE; axial image (K) and coronal reformatted image (L) revealed: left lower polar hypodense lesion 2x3x3 cm with fluid & fat density (blue arrow) indicating marked tumour size reduction of about 96%. Evidence of coil of previous angio-embolization (orange arrow).**

Case 3: A 25-year-old male with TSC, presented with bilateral loin pain for 1 year with newly developed gross haematuria for 5 days. He was diagnosed as multiple bilateral renal AMLs associated with ruptured right renal one. He underwent preoperative SAE followed by

right total nephrectomy with no intra-operative blood loss. Resected lesions were sent to pathologic analysis which revealed classic renal AMLs. Figure 3



**Figure 3: UECT scan of the brain; axial image (A) revealed: multiple hyperdense calcified subependymal hamartomas/tubers (orange arrow). UECT scan before SAE; axial image (B) revealed: multiple bilateral fat-containing AMLs (blue arrows). Most of the right renal tissue is seen replaced by huge AML, measured about 17 x 15 x 23 cm at its maximum dimensions with intra-lesional hematoma seen (red arrow). Diagnostic selective right renal angiography (C): Pre-embolization angiography using Cobra catheter showed huge vascular renal mass (blue arrow) with multiple abnormal pathological vascularities (red arrow) and multiple aneurysmal dilatations (yellow arrows). The mass supplied by lower zonal segmental artery. Super selective segmental renal artery angiography (D): the cobra catheter was advanced further super selectively into the lower zonal segmental artery, embolization was done using microsphere particles and two micro-coils (orange arrow) under fluoroscopic control. Post-embolization control angiography (E) revealed: Successful embolization with no further opacification of the previously described vascular mass and aneurysmal dilatations. Histopathologic image (F) revealed: Classic renal AML formed of a mixture of mature fat, thick walled poorly organized blood vessels and smooth muscles.**

## Discussion

Renal angiomyolipoma (AML) is the most common benign renal tumour with incidence from 0.2% to 0.6% of the general population, representing about 3% of all kidneys' tumours with a strong female predilection <sup>[1, 2]</sup>.

In the present study, all bleeding AMLs were diagnosed by recognition of intra-lesional fat tissue and perinephric hematoma by Ultrasonography and CT studies, perinephric hematoma was detected best on CT scan. This agreed with Maizlin et al. <sup>[11]</sup>, who stated that classic AML was easily diagnosed by fat tissue recognition within the lesion in the majority of cases. The diagnosis of ruptured or bleeding AMLs depended upon imaging. US scan was rapid, non-invasive and sensitive for hemorrhage detection, but it was less effective in defining the nature of the condition or hemorrhage source. CT scan was the imaging modality of choice because it could reveal the source of bleeding.

In the current trial, the majority of SAE were performed as an urgent bleeding renal AMLs (n=28, 84.8%) management, while the rest of embolizations were 'performed as a high-risk renal AMLs (n=3, 9.1%) prophylaxis or as a pre-operative treatment to avoid intra-operative haemorrhage (n=2, 6.1%). Bardin et al. <sup>[10]</sup> discussed urgent and prophylactic SAE of renal AMLs in 23 cases (26.1% versus 73.9%), while a few research discussed preoperative SAE of renal AMLs.

In the current trial, lesion size and loin pain were common indication in all embolizations. Bleeding symptoms as gross hematuria, intra-lesional, perinephric or retro-peritoneal haemorrhage (45.5%, 84.8%, 75.8 and 75.8% respectively) were the main indications for urgent SAE. This agreed with Kyo et al. <sup>[12]</sup> who stated that the indications for treatment of AML included intractable loin pain, gross hematuria, large tumor size, spontaneous ruptures and radiographic imaging that suggests malignant lesions.

Recent research have suggested that tumour type “sporadic or TSC-associated” and tumour composition “size of associated intra-lesional vascular anomalies” may be more significant regarding haemorrhage risk of renal AMLs, even though tumour size is also important <sup>[10]</sup>.

Yamakado et al. <sup>[13]</sup> found using the conventional cut-off of 4 cm has significantly lower specificity (38%) than 5 mm or larger aneurysm (86%) and size of aneurysm was the only factor significantly related to rupture in their multiple regression analysis (p=0.001).

In the present trial, TSC-associated lesions had significantly more frequent haemorrhage signs (15 of 28 bleeding lesions were TSC-associated, p=0.027,) and also more frequent with intra-lesional vascular anomalies (all 28 bleeding lesions showed intralesional vascular anomalies, p=0.016). In the current study, the target vessels of 20 (62.5%) lesions were accessed by Cobra catheter, while in 12 (37.5%) lesions, the target vessels were reached by microcatheter. In our study, different embolic agents were used in embolization of AMLs; Microcoils, microspheres, combined microcoils and microspheres in addition to combined microcoils and absolute alcohol were used in embolization of 18 (56.25%), 3 (9.4%), 6 (18.75%) and 3 (9.4%) lesions respectively. Microcoils are used systematically for aneurysms’ treatment. Absolute alcohol and microspheres enable the downstream vascular bed exclusion. Microspheres were used systematically to minimize the tumour flow as a first step, allowing minimum absolute alcohol infusion doses to prevent complications. When possible, proximal occlusion of supplying arteries with microcoils was favored to prevent reperfusion and recurrence <sup>[14]</sup>. This agreed with El-Assmy et al. <sup>[15]</sup> trial, who stated that microcoils with or without absolute alcohol or microspheres had been used successfully as embolization materials.

Each of Combined absolute alcohol, gel foam and microcoils, combined absolute alcohol, gel foam and lipidol were used in embolization of 1 (3.1%) lesion. This agreed with the study

done by Ramon et al. <sup>[16]</sup>, who stated that absolute alcohol with or without gel foam, microcoils, lipidol or PVA had been utilized as an embolization material successfully.

In the present study, an overall success rate of 90.9% was achieved as 30 of 33 renal AMLs were embolized successfully and no recurrence was found on follow-up visits. While 3 (9.1%) renal AMLs were not embolized successfully.

In the present study, there was no recurrences in sporadic AMLs' cases, while 13.3% of TSC-AMLs (2 of 15) showed recurrence on follow up (1 showed recurrent haemorrhage signs and the other showed size increase of 3 cm, both underwent total nephrectomy). These outcomes were better compared to those by El-Assmy et al. <sup>[15]</sup>, who found that no recurrences took place in sporadic AMLs' cases after SAE, whereas 42.9% of TSC-AMLs (9 of 21) showed recurrence. Of those 9 recurrent AMLs, all were re-embolized after a mean follow up time of 6.8 years (range, 3–11 years) due to an increase in size of 2 cm, recurrent signs, or hemorrhage.

In the current study, a technical (primary) success rate of 88.6% was achieved as 31 of 35 arteriographies showed successful embolization with complete devascularization on control angiogram in the first try. While 4 (11.4%) arteriographies showed failed or incomplete embolizations.

We reported 90.9% overall success rate, 88.6% technical success rate, 8.6% re-embolization and 6.1% recurrence. these outcomes were better compared to those by Bardin et al. <sup>[10]</sup> who reported 17.4% re-embolization and 13% recurrence rates.

In the present study, low complication rates were accomplished; major complications (n=1; 2.9%) -in the form of renal abscess after necrosis and liquefaction of tumour post SAE that was treated by percutaneous drainage and IV antibiotics – and had minor complications (n=10; 28.6%). This agreed with the study that was done by Chick et al. <sup>[17]</sup>, who reported

low major complication rates (n=1; 2.9%). In contrast we had favorable results compared to those by Bardin et al. <sup>[10]</sup>.

Regarding minor complications, post-embolization syndrome (PES) was the main minor complication (n=8; 22.8%). Other minor complications included persistent hematuria (n=1; 2.9%) and puncture site hematoma (n=1; 2.9%) that were subjected to conservative management.

The results of PES among our study patients were better compared to those reported by Jain et al. <sup>[18]</sup> who mentioned that no correlation could be established between the material used in embolization and this syndrome occurrence. These symptoms were self-limiting.

In the present trial, we did not report ischemia induced hypertension or renal failure during the follow up period in any of our cases, even those with area of initial parenchymal defect more than 20% after SAE due to super selective techniques. This agreed with studies that were done by Dorffner et al. <sup>[19]</sup> who stated that using super selective technique mandatory to reduce the risk of ischemia induced hypertension and related renal impairment.

In the current study, 86.6% of patients presented with gross hematuria (13 of 15) showed stoppage of hematuria within 3 days post-embolization (P= <0.001) and about 96% of bleeding AMLs showed complete disappearance or marked organization of intra-lesional, perinephric and retroperitoneal hematomas 3 months post-embolization (P= <0.001). This agreed with study that was done by Tso et al (262), who stated that particulate and liquefied materials had equal effect in achieving hemostasis for 77% to 100% of bleeding AMLs after a single session of SAE.

In the current study, we used tumour size reduction to predict successful embolization. 90.6% lesions (29 of 32) showed significant tumour size reduction (P= <0.001). Maximum diameter reduction rate of 16.33% and volume reduction rate of 42.66% (p<0.001) were achieved in our study that was considered a significant tumour size reduction after SAE.

In the present study, we didn't find any significant changes before and after SAE in serum creatinine levels and no acute deterioration of renal function occurred, median levels of serum creatinine before SAE were 0.9 (0.5-2.2) and after SAE was 0.85 (0.4-3.1) mg/dL. This agreed with Bardin et al. <sup>[10]</sup> and Hocquelet et al. <sup>[14]</sup> who also didn't report any significant changes before and after SAE in serum creatinine levels. In the present trial, no significant changes were found in haemoglobin levels before and after SAE on follow-up visits. These outcomes confirmed the efficacy and safety of SAE in renal AMLs regarding controlling the patients' haemodynamic status on follow-up visits. However, no previous studies discussed the changes in haemoglobin levels before and after SAE in renal AMLs.

In the present trial, we did not notice any retroperitoneal lymph nodes involvement in our cases (n=30). Boorjian et al. <sup>[20]</sup>, reported that retroperitoneal lymph nodes' presence in case of renal AML should be considered a benign multifocal disease rather than true metastasis.

Limitations: Difficulty of accurate measurement of large renal AMLs paired with intra-lesional, perinephric and/or retro-peritoneal haemorrhage, especially as multiple techniques were utilized (US, CT and MRI). some cases' pre-arteriography images were obtained from other hospitals that had different equipment's than ours. Our trial was prospective with short follow-up period. This should not affect our findings as most of tumour size reduction occurs within the first year following SAE (263).

### **Conclusions:**

SAE is a safe and effective procedure in renal AMLs management either in emergency or preventively with preservation of renal functions and elimination of the potential risk of nephrectomy.

### **Ethical Approval and consent :**

The trial was done after approval from the Ethical Committee Tanta and Mansoura University. Informed consent was obtained from all cases.

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## Abbreviation

<b>AML</b>	Angiomyolipoma.
<b>AVM</b>	Arterio-venous malformation.
<b>CT</b>	Computed tomography
<b>CBC</b>	Complete blood count
<b>ECG</b>	Electrocardiography
<b>GFR</b>	Glomerular filtration rate
<b>LAM</b>	Lymphangioliomyomatosis
<b>MRI</b>	Magnetic resonance imaging
<b>mTOR</b>	Mammalian target of rapamycin
<b>SAE</b>	Selective arterial embolization
<b>TSC</b>	Tuberous sclerosis complex
<b>US</b>	Ultrasonography

UNDER PEER REVIEW