Selective Arterial Embolization of Renal Angiomyolipoma: Efficacy, Tumor Volume Reduction, and Complications

Walailak Chaiyasoot, M.D., Jirawadee Yodying, M.D., Thanita Limsiri, M.D.

Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: To evaluate the efficacy and complications of selective arterial embolization in renal angiomyolipoma and to identify predictive factors for tumor rupture.

Materials and Methods: Twenty-one patients with 25 renal angiomyolipoma (AML) underwent selective arterial embolization (SAE) between January 2008 and June 2019, 15 lesions involving prophylaxis embolization of a tumor >4 cm diameter and 10 involving embolization for a ruptured tumor. Multidetector computed tomography (MDCT) was performed pre- and post-SAE, using the 2D tumor diameter measurement in the ruptured AMLs. Three-dimensional volumetry and density histogram were performed for determining the total tumor volume, fat, and angiomyogenic component reduction in the unruptured AMLs. The predictive factors for tumor rupture, the treatment outcome and complications were analyzed.

Results: The clinical success rate was 84% (21/25 lesions) and the technical success rate was 96% (24/25 lesions). The 3D volume post-SAE within 1-3 months showed a greater decrement of the enhanced angiomyogenic component than the fat component, with median percentages of -62.2% and -18.4%, respectively (p-value = 0.333). Minor complications were post-embolization syndrome (5 lesions, 20%) and minimal renal infarction (4 lesions, 16%). Renal abscesses were the major complications (3 lesions, 12%). A factor associated with tumor rupture was the presence of an intra-tumoral aneurysm (p-value < 0.05).

Conclusion: SAE is an effective treatment for renal AML with a high technical and clinical success rate and limited complications. Three-dimensional volumetry and density histogram analysis might be better tools than two-dimensional CT to evaluate post-SAE response. The presence of an intra-tumoral aneurysm is a significant predictive factor associated with tumor rupture.

Keywords: Renal angiomyolipoma; selective arterial embolization (Siriraj Med J 2021; 73: 337-343)

INTRODUCTION

Renal angiomyolipoma (AML), a benign neoplasm accounting for 0.3-3% of all renal tumors[1], composed of dysmorphic blood vessels, fat, and smooth muscle.[2] Eighty percent of renal AML is a sporadic group, found among women in their 4th - 5th decade, usually presented as a solitary AML. The remainder has a female predilection, usually symptomatic with multiple bilateral AMLs associated with tuberous sclerosis complex (TSC).[3-5] Renal AMLs can potentially grow substantially and cause many complications[5,6] which the major fatal complication is a retroperitoneal bleeding.[3,4,7] Previous studies have

Corresponding author: Jirawadee Yodying
E-mail: jirawadee.yod@gmail.com
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ORCID ID: http://orcid.org/0000-0002-2369-9008
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proposed predictive factors for tumor rupture, including tumor size, aneurysm formation, associated TSC[3,8,9], the size of an intra-tumoral aneurysm and a proportion of angiogenic component.[10,11] The bleeding tendency of the tumor might be come from an irregular shape appearance of the intra-tumoral aneurysm.[12]

Computed tomography (CT) and magnetic resonance imaging (MRI) are important tools to diagnose renal AML based on the tumors' fat component to be differentiated from a renal cell carcinoma.[13,14] The treatment modalities for asymptomatic renal AML are surgery, selective arterial embolization (SAE), tumor ablation, and the use of Mamalian Target of Rapamycin (mTOR^{R}) inhibitors.[5] Recently, SAE has been accepted as the first-line treatment of renal AML, either for prophylaxis in tumor >4 cm or treatment in acute hemorrhage patients with hemodynamic instability.[15,16] However, from the literature review, there is no research concerning the efficacy of SAE in renal angiomyolipoma in Thailand.

Objectives

The primary objective of our study aimed to evaluate the efficacy of transarterial embolization using multidetector CT (MDCT) measurement of total tumor volume, quantification of the fat and angiomyogenic component reduction post-SAE. The secondary objectives were to analyze the post-procedural complications and to identify the predictive factors for tumor rupture.

MATERIALS AND METHODS

Population

The study protocol was approved by the Institutional Review Board (IRB) of Siriraj Hospital, Mahidol University (Si 051/2020). Totally 161 patients with renal AML, we retrospectively analyzed 54 patients (56 lesions) who had CT diagnosis as renal AML (Fig 1) and undergone SAE during January 2008 to June 2019. Thirty-three patients were excluded due to unavailable CT studies, lost on follow-up or expired. This left 21 patients enrolled in the study.

Embolization procedure

Of the 21 patients with renal AMLs, 12 patients were embolized electively and 9 patients had emergency embolization. Most procedures were performed under local anesthesia, only 3 cases needed general anesthesia due to unstable vital signs. Selective renal angiogram was performed using a 5 Fr catheter, followed by superselective catheterization using a microcatheter to spare the normal renal parenchyma. A coaxial system comprised of a microcatheter; a 2.7 Fr Progreat® (Terumo, Tokyo, Japan) were performed in 14 lesions, a 1.98 Fr tip Masters Parkway® (Asahi Intecc USA, Inc.) in 7 lesions, and a 2.8 Fr Renegade HI-FLO® (Boston Scientific, Natick, MA, USA) in 1 lesion. Three lesions used only 5 Fr selective catheters because of large arterial feeders. Several embolic materials were selected depend on each operator, including polyvinyl alcohol, PVA (Contour®, Boston Scientific, Ireland), absolute ethyl alcohol (Siriraj Hospital), N-butyl cyanoacrylate (NBCA) or glue (Histoacryl®, Braun, Spain), interlocking coil (Interlock® Boston Scientific, Ireland), and thrombin (Thrombin-JMI®, Pfizer, United States). Technical success was defined as stasis of tumoral blood flow and lack of contrast opacified renal AMLs on post-embolization angiogram.[17]

Imaging studies

A diagnostic CT scan (120 kVp; 115-500 mA; section thickness, 1.25-3 mm; pitch, 0.992:1 and 1.375:1) was conducted on a 64-slice and a 256-slice MDCT. Contrast-enhanced CT was performed using non-ionic iodinate contrast medium (320-370 mg I/ml) at a dose of 1.5-2 ml/kg.

All the patients had pre- and post-procedural MDCT. The most recent pre-procedural CT (median, 29 days; range, 0-219 days) and all post-procedural follow-up CT (median, 2 months; range, 1–76 months) were reviewed by a radiology resident and an interventional radiology (IR) staff including maximal 2D diameter of the ruptured tumor, the presence of an intra-tumoral aneurysm, the aneurysm size and post-procedural complications. In unruptured cases, we analyzed changes in the tumor volume, enhanced angiomyogenic and fat component of renal AMLs. The data analysis was performed using an Advantage Workstation from Diagnostic Imaging (ADW 4.6, GE Healthcare). The tumor volume was calculated by drawing a region of interest (ROI) covering the tumor on axial pre- and post-contrast (80-100 sec) images and converting to 3D volumetry. The ROI of the AML was then converted to a density histogram. The enhanced angiomyogenic component volume was calculated using the difference between the area under the curve of the density histogram with a density >100 HU on pre- and post-contrast MDCT.[18] The fat component volume was defined as the area under the curve of the density histogram with a density <-20 HU on pre-contrast phase (Fig 2). The percentage reduction was compared between the pre- and post-procedural CT.

Clinical success was defined as no recurrence, no new bleeding episode or complication related to SAE within 30 days, and no further surgery or re-embolization.[19] Complications were categorized as major and minor

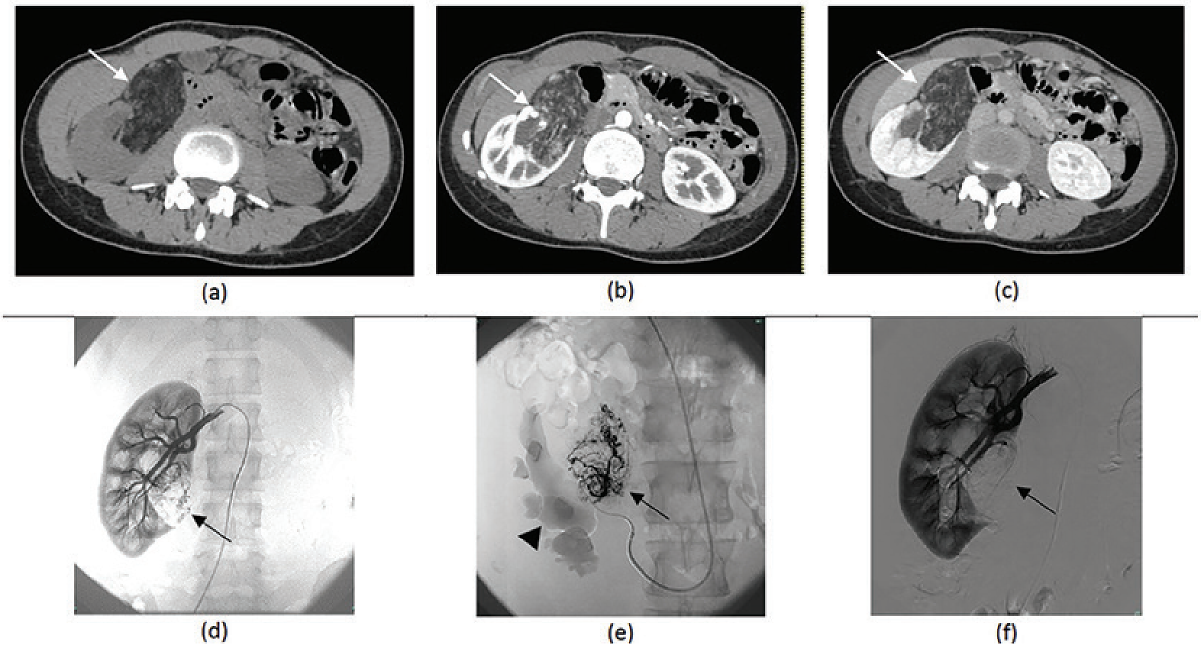

Fig 1. Typical CT and angiographic features of renal angiomyolipoma in the same patient (lesion no. 21)

(a) Pre-contrast axial phase CT showed a well-defined macroscopic fat-containing lesion at right kidney *(arrow)*

(b) Arterial phase CT demonstrated tortuous blood vessels *(arrow)* in the lesion

(d) Post-contrast phase CT revealed a heterogeneously enhanced fat-containing lesion *(arrow)*

(a) Right renal angiogram revealed a renal mass at interpolar region *(arrow)*

(b) Superselection into inferior segmental branch of right renal artery revealed a neovascularized and hypervascularized tumor *(arrow)*.

Note contrast excretion into dilated right renal pelvis, indicating hydronephrosis *(arrowhead)*

(c) Post-embolization angiogram showed arterial occlusion supplying the tumor *(arrow)* with preservation of normal renal parenchymal blood supply

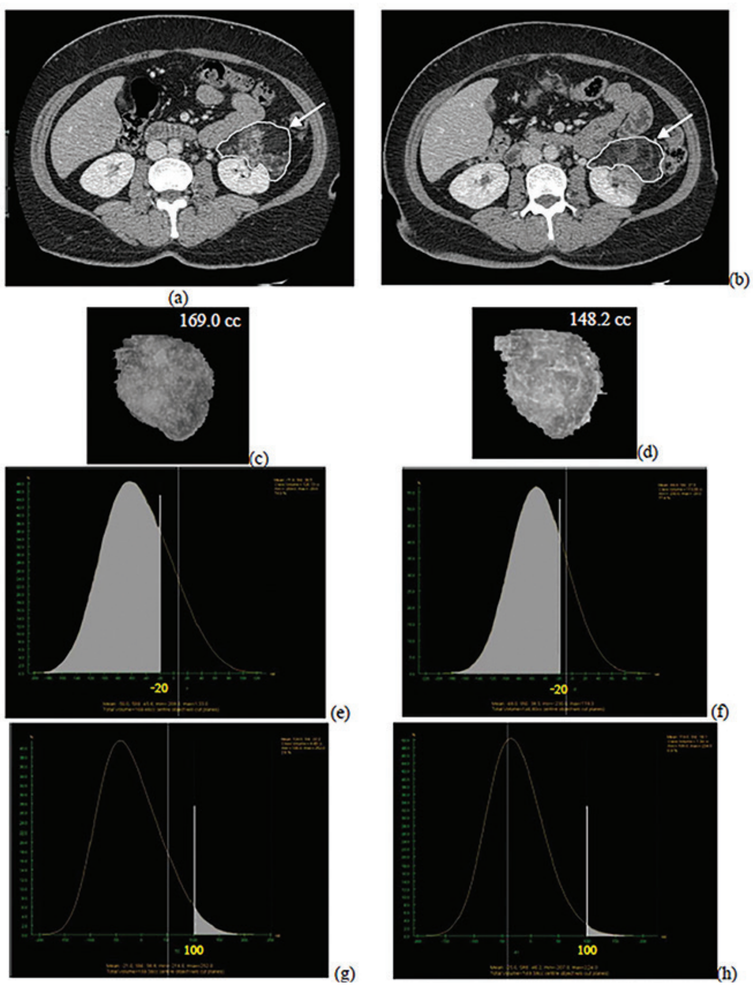

Fig 2. Three-dimensional (3D) volumetry and density histogram comparing between pre- (a, c, d, g) and 1-month post-procedural CT (b, d, f, h)

(a-b) Axial post-contrast CT showed a right renal AML *(arrows)* containing macroscopic fat. The region of interest (ROI) was drawn encircling the mass

(c-d) 3D volumetry of a total tumor volume measured 169.0 and 148.2 cc, respectively (12.3% reduction)

(e-f) Density histogram of the fat component volume (attenuation <- 20 HU) measured 126.1 cc and 113.7 cc, respectively (9.8% reduction)

(g-h) Density histogram of the enhanced angiomyogenic component volume (attenuation >100 HU) measured 4.48 cc and 1.34 cc, respectively (69.8% reduction) complications according to the Society of Interventional Radiology Clinical Practice Guidelines.[20] The patients' medical records and MDCT findings were reviewed for the predictive factors associated with tumor rupture.

Statistical analysis

Data were analyzed using PASW Statistics 21.0 (SPSS Inc., Chicago IL USA). Patients' demographic data and the lesions' characteristics were recorded as the mean±SD (range) and median (P_{25}, P_{75}) for the quantitative variables, while numbers and percentages were summarized for the qualitative variables. Comparisons between the percentage reduction of fat and enhanced angiomyogenic component were calculated using the Wilcoxon Signed Rank test. Fisher's exact test, 2-sample T-test, and Mann-Whitney test were used to identify predictive factors associated with tumor rupture. A p-value of <0.05 was considered as a statistically significant difference.

RESULTS

Patients' demographic data

A total of 21 patients (16 female, 5 male) and 25 lesions were analyzed. The mean patient's age at the diagnosis was 47 years old (range, 9-68 years) and during the treatment was 50 years old (range, 22-68 years). Four patients (19%) had underlying tuberous sclerosis complex. Nine asymptomatic lesions were incidentally found renal AMLs from prior check-up ultrasound. Fourteen lesions presented with abdominal pain, 5 with anemia, and 1 with hematuria. Single renal AML was found in 12 patients (57.1%), and multiple AMLs in 9 patients (42.9%). Bilateral and unilateral lesions were found in 13 cases (61.9%) and 8 cases (38.1%), respectively. The mean renal AML diameter before SAE was 8.93.3 cm (range, 3.8-18.4 cm). Among 25 lesions, 10 were ruptured AMLs (40%) and 15 were unruptured AMLs (60%).

Embolization and outcome

The embolic materials and outcomes of SAE are shown in Table 1. The most common embolic material was PVA particles (13 lesions, 54%) and the second common was combined materials (4 lesions, 17%).

The technical success rate of SAE was 96% (24/25) and a clinical success rate of 84% (21/25) including 9 lesions in asymptomatic patients, who had no complication within 30 days post SAE and no re-intervention. Four lesions had clinical failure and one lesion had technical failure. Fifteen unruptured AML patients had imaging follow-up intervals. Almost 19/21 patients had long-term clinical follow-up period (range 14-128 months, mean 63 months) and all were well without requiring re-intervention. Two patients died from the other non-related diseases.

Post-embolization syndrome found in 5 lesions characterized by fever, nausea, and abdominal pain. Four lesions had a minimal renal infarction which did not contribute to renal impairment during the follow-up period (mean, 41.3 months; range, 16-70 months). Two lesions with renal abscesses post-SAE required percutaneous drainage and conservative treatment. Another lesion with infected hematoma underwent percutaneous drainage.

Imaging comparison between pre- and post-SAE

Three-dimensional (3D) volumetry and the density histogram showed the total tumor volume, fat, and angiomyogenic component reduction after SAE during the follow-up period (1 to >12 months) (Table 2). The median percentage of fat reduction was -18.4% while the median percentage of enhanced angiomyogenic reduction was -62.2% at 1-3 months follow-up, with a p-value of 0.333.

The analysis of predictive factors for tumor rupture showed that the presence of an intra-tumoral aneurysm was statistically significantly associated with tumor rupture (p-value = 0.015). The tumor size and aneurysm size were also associated with tumor rupture but did not show a significant difference (p-value = 0.071 and 0.154, respectively) (Table 3).

DISCUSSION

Recently, SAE has become widely accepted as a first-line treatment for symptomatic renal AMLs or an AML sized >4 cm.[15,16] Planché et al[18] also suggested that SAE is effective, especially on the angiomyogenic component. Our study showed a high technical success (96%) and clinical success rate (84%) of SAE, agreed with Bardin et al[10] who reported a 95.6% technical success rate of SAE in 34 cases of symptomatic and asymptomatic renal AMLs over a mean follow-up period of 20.5 months. Ramon et al[8] found a clinical success rate of 91% in 48 symptomatic renal AMLs or renal AML >4 cm. over a mean follow-up period of 58 months.

The total tumor size reduction in our study measured by 3D volumetry at 1-3 months, 6-12 months, and >12 months follow-up were -7.1%, -48.9%, and -65.3%, respectively, corresponding with the study by Planché et al[18], which showed a mean total volume reduction of -54% and -81% during 1-12 months and >12 months follow-up period, respectively.

Previous studies reported that the size of the intra-tumoral aneurysm and a proportion of the angiogenic

TABLE 1. Embolic materials and outcomes.

Embolic material used (n=24 lesions*)	
Particles (PVA†)	13 (54%)
Alcohol	3 (13%)
Glue	2 (8%)
Coil	1 (4%)
Thrombin	1 (4%)
Combined	4‡ (17%)
Treatment success (n=25 lesions)	
Technical success	24/25 (96%)
Clinical Success	21/25 (84%)
Complication§ (n=25 lesions)	
Minor complications	
Post-embolization syndrome	5/25 (20%)
Non-target Embolization	4/25 (16%)
Major complications	3/25 (12%)
Renal abscess	Conservative
Renal abscess	Percutaneous drainage
Infected hematoma	Percutaneous drainage

* Twenty-four lesions were embolized and one lesion was not embolized due to failure selection into arterial pedicle
† PVA = Polyvinyl alcohol
‡ Combined particles and glue (3 lesions) and combined coil and glue (1 lesion)
§ Categorized followed Society of Interventional Radiology Guidelines

TABLE 2. Total tumor volume, fat component volume and angiomyogenic component volume in pre-treatment, post-treatment and %reduction during follow-up.

	Follow-up period		
	1-3 months	**6-12 months**	**>12 months**
Total tumor volume (ml): median (P_{25}, P_{75})			
Lesion (n)*	10	4	6
Pre-treatment	146.9 (52.3, 177.2)	140.2 (76.7, 315.7)	65.2 (61.5, 76.7)
Post-treatment	142.2 (40.5, 154.8)	67.2 (37.5, 298.3)	27.8 (9.3, 64.3)
% Reduction	-7.1 (-26.6, +0.6)	-48.9 (-58.9, -8.1)	-65.3 (-85.7, -11.4)
Fat component volume (ml): median (P_{25}, P_{75})			
Lesion (n)*	10	4	6
Pre-treatment	127.1 (46.0, 164.0)	115.0 (73.5, 274.0)	63.4 (53.3, 73.5)
Post-treatment	107.0 (34.8, 129.5)	59.0 (34.5, 274.6)	24.8 (8.8, 58.0)
% Reduction	-18.4 (-32.3, -3.8)	-48.2 (-56.7, -5.6)	-66.2 (-86.0, -10.0)
Angiomyogenic component volume (ml): median (P_{25}, P_{75})			
Lesion (n)*	10	3†	3†
Pre-treatment	1.4 (0.4, 4.0)	1.5 (0.4, 3.9)	0.5 (0.4, 1.8)
Post-treatment	0.7 (0.2, 1.4)	0.4 (0.2, -)	1.5 (0.3, -)
% Reduction	-62.2 (-72.8, +13.5)	-82.8 (-85.5, -)	-13.1 (-49.0, -)

*Number of lesions are depended on post-treatment MDCT availability during follow-up period
†Only 3/4 lesions and 3/6 lesions had post-contrast MDCT for angiomyogenic component volume analysis in 6-12 months and >12 months follow-up period, respectively

TABLE 3. Predictive factors associated with tumor rupture.

Factors	Unruptured (n=15)	Ruptured (n=10)	p-value
TSC			
Related	3 (60%)	2 (40%)	1.000*
Not related	12 (60%)	8 (40%)	
Lesion size (cm)			
Mean±SD	7.9±2.7	10.3±3.7	0.071†
Aneurysm			
Present	4 (33.3%)	8 (66.7%)	0.015*
Not present	11 (84.6%)	2 (15.4%)	
Aneurysm size (mm)			
Median (P_{25}, P_{75})	5.3 (3.2, 8.0)	15.7 (4.8, 29.0)	0.154‡

*Fisher's Exact Test
†2-Sample T-Test
‡Mann-Whitney Test

component were the main causes of tumor rupture.[9,10-12,21] Therefore, a reduction of the total tumor size might not represent the treatment endpoint of SAE. Planché et al[18] and Han et al[21] suggested that the angiomyogenic component disappeared faster with a higher percentage of decrement than the fat component. Correspond to our study that a median percentage of fat reduction was -18.4% while the median percentage of enhanced angiomyogenic reduction was - 62.2% within 1-3 months follow-up post-SAE.

There were 4/25 lesions (16%) of clinical failure. The first lesion was a ruptured AML with an increased tumoral size containing hemolyzed blood on 2 months follow-up CT. This patient underwent surgical nephrectomy 9 months later. The second was also a ruptured AML with 30% decreased tumoral size plus resolving hematoma on CT 3 months follow-up post-SAE. Six-month later, this patient received surgical tumor removal. In these two lesions, the associated perirenal hematoma might limit the accuracy of the tumor measurement, resulting in an unnecessary surgery. The third lesion was an unruptured AML locating at renal collecting system (lesion no. 21) (Fig 1) which showed decreased total tumor size, fat, and enhanced angiomyogenic components on follow-up CT at 1 and 29 months. However, the tumor gradually increased causing obstructive left hydronephrosis on follow-up CT at 75 months, then it was surgically removed 6 years later.

The last clinical failure lesion was the same as a technical failure lesion (1/25, 4%). This was a 7.5 cm unruptured AML receiving a 2nd SAE due to an inadequate decreased size (38.7%) on follow-up CT at 6 months after the 1st SAE. The 2nd SAE was unsuccessful due to the inability to catheterize into the arterial feeder, this patient subsequently received surgery. However, our retrospectively 3D-volumetry and density histogram showed a significant reduction of the total tumor volume (41%), fat component (44%), and enhanced angiomyogenic component (53%) on follow-up CT at 6 months after the 1st SAE. This could imply that 3D measurement and density histogram might be more precise than 2D measurement to evaluate post-treatment response, thus avoiding further unnecessary treatment.

Post-embolization syndrome, a common minor complication of SAE[10] found in 5/25 lesions (20%), all were improved after conservative treatment. Four lesions (16 %) had limited renal infarction without impact on renal function. There were only 3 lesions (12%) of major complications, consisting of renal abscesses. These results suggested that SAE had low rate of major complication, in agreement with other studies.[10,15,18]

We used several embolic materials depend on the operator and the lesions. For devascularization distally, we usually used particles. But for an intra-tumoral aneurysm, we preferred glue injection or microcoil placing at the proximal arteries feeding the aneurysm.

Many prior studies have reported predictive factors associated with ruptured renal AMLs, including the tumor size, aneurysm formation, and the presence of TSC.[3,8,9] Similar to our study that found statistically significantly of an intra-tumoral aneurysm associated with tumor rupture. The tumor size and aneurysm size were also associated with tumor rupture but TSC failed to show the association.

Our study had some limitations. First, only symptomatic or large renal AMLs are indicated for SAE, leading to a small sample size. Second, the retrospective study design could make the selection bias. Third, we did not have a standard protocol of MDCT after SAE, resulting in different interval and imaging follow-up.

CONCLUSION

SAE is an effective treatment for renal AML with a high technical and clinical success rate and limited major complications. Three-dimensional volumetry and density histogram analysis might be better tools than 2D CT measurement for evaluation of post-SAE response. The presence of an intra-tumoral aneurysm is a significant predictive factor associated with tumor rupture.

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