Single-institution, retrospective review of elective and emergency embolization of renal angiomyolipoma

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Abstract

Introduction: We aimed to evaluate the size reduction and complications after transcatheter embolization of renal angiomyolipomas (AMLs).
Methods: Cases from a single tertiary center were analyzed retrospectively. A blinded radiologist provided measurements of AMLs using a combination of ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI). Electronic clinical notes, radiographic imaging, and laboratory data were reviewed.
Results: Twenty-one embolization procedures from 2002–2019 were analyzed. Four cases were emergency, the remainder elective. The average followup time after intervention was 42 months. Techniques included ethanol, polyvinyl alcohol (PVA), Gelfoam, Embospheres®, Histacryl®, and coils. The median diameter size of AMLs was 8.6 cm pre-procedure and 6.0 cm post-procedure. The median volume of AMLs was 200 cc pre-procedure and 67 cc post-procedure, with a median reduction in volume of 55%. One case (4.8%) had a re-embolization and three cases (14.3%) proceeded with surgical management of the AML. No cases re-presented with bleeding. Post-embolization syndrome is common. Renal arterial dissection and renal abscess are infrequent complications (9% and 4.5%, respectively). There was no treatment-based mortality.
Conclusions: Embolization for renal AMLs is an established, safe, and effective method of treatment and our series further supports that. Determining when to intervene and how long to follow up patients is an issue that has not been well-described; more research needs to be done in this area.

Introduction

Renal angiomyolipomas (AML) are the most common benign renal neoplasms. The majority are sporadic but are also found in association with tuberous sclerosis complex (TSC). AMLs are more common in females, with a 4:1 female to male predominance. The incidence is estimated at up to 0.4% of the population.[1,2]

AML composition is a mixture of fat, vascular tissue, and muscle.[2] The majority are mixed, however, a small proportion (less than 5%) are classified as minimal fat AMLs.[3]

Arteries within AMLs are frequently bizarre and tortuous and classically have disordered smooth muscle and absent internal elastic membranes on microscopy. For this reason, aneurysm formation and hemorrhage can occur. Large AMLs can recruit extra blood supply from surrounding vessels, including renal, adrenal, ureteral, gonadal, phrenic, and lumbar arteries.[4]

AMLs can present in several ways, including flank/loin pain, a palpable mass, and after hemorrhage. One-third of patients with hemorrhage present with shock,[5] and in this setting is one of the manifestations of Wunderlich syndrome.[5,6]

The natural history of renal AML has been described by Bhatt et al, who observed 471 AMLs. Of these, 91% did not grow or grew slowly (0.02 cm/year) over a median followup of 43 months. No difference in growth rate was observed for tumors less than or greater than 4 cm. TSC cases were more frequent among the 9% of AMLs found to grow more rapidly (>0.25 cm/year).[7] Longer-term active surveillance cohort studies of renal AMLs are scarce.[2]

The point at which AMLs should receive prophylactic intervention is not categorically stated. The previously recognized cutoff of 4 cm in diameter is open to debate. The latest European Association of Urology guidelines (2019) recommend treatment in cases where there is pain, bleeding, pregnancy, inadequate access for emergency care, or suspected malignancy. It is recommended large tumors be treated; however, a specific threshold does not exist. Active surveillance is appropriate for most AML, and factors associated with delayed intervention include tumor size >4 cm and symptoms at diagnosis. The evidence behind this recommendation is classified as weak.[8,9] Similarly, the Canadian Urological Association's recent guidelines (2020) note most AMLs are asymptomatic and are at low risk of rupture. They recommend discussion of elective treatment in AMLs >4 cm.[10] Other factors must be taken into account as well, including aneurysmal component, pregnancy, coagulopathy, trauma, hormone level, and comorbidity with TSC.[11] The duration, imagining modality, and which AMLs to follow up has no clear guidance.

Treatment options include percutaneous intervention via selective arterial embolization (SAE), nephron-sparing surgery, and nephrectomy. Patients with TSC can be offered mTOR inhibitors.

In this study, we retrospectively reviewed the acute and elective renal AML requiring embolization at a tertiary referral center over the last 20 years. We reviewed the size of AML for embolization and then the followup imaging of the AML and whether any patients required re-treatment or alternate treatment with surgery.

Methods

Cases from a single institution were analyzed retrospectively. Local ethical board approval was obtained. Cases were found using a systematic search of the hospital PACS system dating from January 2002 to June 2019 using the search terms "renal" or "kidney" and "embolization." From this list, cases relating to AML were reviewed. Only cases that involved SAE of an AML and had followup imaging were included in the statistical analysis.

Electronic clinical notes, radiographic imaging, and laboratory data were reviewed. Demographic data (age, gender, and ethnicity), AML type (sporadic or TSC-associated), intervention type (elective or emergency), re-admissions, complications, renal function, method of SAE, repeat SAE, and progress to surgery was tabled. Pre-procedure imaging modalities for providing AML measurement include computed tomography (CT) and magnetic resonance imaging (MRI), with the latest imaging prior to intervention used. Post-procedure imaging modalities included ultrasound (US), CT, and MRI. A blinded radiologist re-reviewed the imaging to provide the AML measurements over a one-week period. Volume was calculated using the ellipsoid formula (H × W × AP × ϖ/6). Statistical analysis was performed using SAS 9.4 software by the institution's statistics department.

The decision to treat a patient was based on multidisciplinary input involving urologists, interventional radiologists, and/or nephrologists/oncologists. Because the patients were gathered over 18 years, multiple clinicians were involved in the care of the patients. The procedure was performed under local anesthesia via a common femoral artery approach. Various embolic agents were used, including polyvinyl alcohol (PVA), histoacryl glue, coils, gelfoam, Embozene™, Embospheres®, and ethanol. Patients were admitted to the urology department for overnight admission and routine monitoring.

Results

A total of 25 individual patients were identified using the search technique, undergoing a total of 26 embolization procedures between them. Patients without followup or who underwent arteriography without embolization were excluded from the statistical analysis. The excluded procedures included three without followup imaging and two complicated by renal artery dissection, for which did not receive embolization (Fig. 1). One patient had three SAE procedures. The index procedure was a single AML SAE. The second procedure involved the aforementioned AML and a contralateral AML. The re-embolization results were not included in the analysis.

The final statistical analysis included 20 patients undergoing 21 SAE procedures.

Baseline demographics for all cases that received SAE and included in the analysis are outlined in Table 1

The primary embolization techniques included PVA (n=9, 42.9%), Histoacryl® (n=5, 23.8%), coils (n=2, 9.5%), ethanol (n=2, 9.5%), Embozene®/sphere (n=2, 95%), and Gelfoam® (n=1, 4.8%). Mean followup time was 42 months (range 1.9–172).

The image modality used for the final measurement for analysis was US in 23.8% (n=5), CT in 66.7% (n=13), and MRI in 14.2% (n=3). There was no fixed protocol.

Emergency procedures accounted for four SAE procedures (19%) and involved acute presentations with symptomatic and radiographically confirmed ruptured or bleeding AMLs. There were two additional cases with radiographic evidence of retroperitoneal hemorrhage that received SAE electively. In the elective cases, 4/17 (23.5%) had pain prompting their index scan diagnosing an AML. The remainder were on active surveillance because of TSC status or incidentally identified sporadic AMLs. All SAEs were on AMLs >4 cm. In emergency cases, the median diameter was 12.3 cm (range 4.7–22.2). In elective cases, the median diameter was 8.5 cm (range 4.1–17.9) (Table 2).

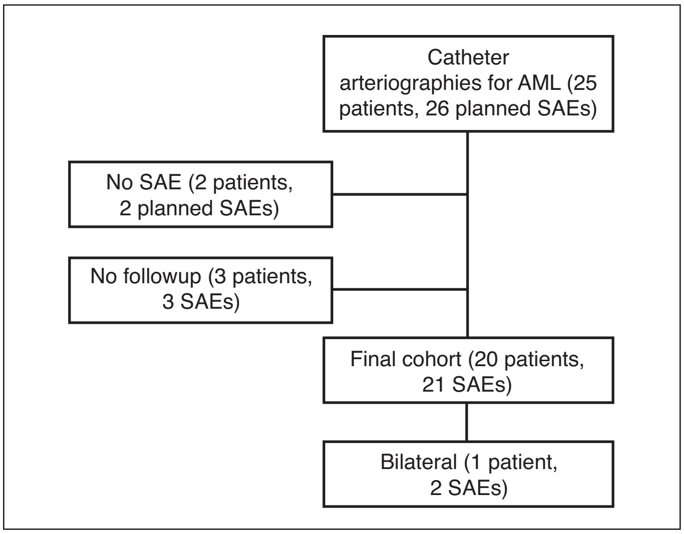

Fig. 1. Study cohort. AML: angiomyolipoma; SAE: selective arterial embolization.

Table 1. Patient baseline demographics	
Variable	
Gender, n (%)	
Female	15 (75%)
Male	5 (25%)
Age (years)	
Mean	54
Range	23–87
TSC, n (%)	
Yes	2 (10%)
No	18 (90%)
Bilateral AML on imaging, n (%)	
Yes	4 (80%)
No	16 (20%)
Side of treated AML, n (%)	
Left	12 (57%)
Right	9 (43%)

AML: angiomyolipoma; TSC: tuberous sclerosis complex.

Table 2. Tumor size before SAE	
Variable	
Size of all AMLs before SAE, cm	**n=21**
Mean ± SD	9.1±4.4
Median (range)	8.6 (4.1–22.2)
Size of electively treated AMLs before SAE, cm	**n=17**
Mean ± SD	8.4±3.3
Median (range)	8.5 (4.1–17.9)
Size of emergency treated AMLs before SAE, cm	**n=4**
Mean ± SD	12.3±6.4
Median (range)	11.1 (4.7–22.2)
Size of ruptured AMLs before SAE, cm	**n=6**
Mean ± SD	12.7±5.8
Median (range)	11.1 (4.7–22.2)

AML: angiomyolipoma; SD: standard deviation; SAE: selective arterial embolization.

Mean creatinine (Cr) pre-embolization was 76 umol/L compared to 83 umol/L on day 1 post-embolization, with no statistical difference between the two groups. Maximum Cr was 148 umol/L pre- and 178 umol/L post-embolization. The renal function of the patient who had bilateral and repeat embolization was unchanged pre- and post-embolization.

All SAEs included in the analysis were deemed technically successful by the performing radiologist. In six cases (28.5%), the performing radiologist reported insignificant residual flow within the tumor; the remaining reported complete cessation of flow within the tumor (Table 3).

There was a statistically significant decrease in volume post-embolization ($p=0.002$), with a median of 200 ml pre-compared to 67 ml post-embolization. There was a statistically significant decrease in diameter post-embolization ($p<0.001$), with a median of 8.6 cm pre-compared to 6.0 cm post-embolization. The median percentage volume decrease post-embolization was 54.5%. Median values have been reported, as the results showed a skewed distribution (Table 4).

No patients were re-admitted to the major hospitals in the region with bleeding AML or flank pain during the study period.

Re-embolizations

One patient had a re-embolization of the same AML, representing 4.8% of AMLs and 4.5% of patients. The indication for this was a persistent arterial feeder and a small increase in size was evident on imaging during workup for an enlarging contralateral AML. The time to re-embolization was 15 years, 11 months.

Surgical intervention

Three patients proceeded to surgical management of same AML that had received SAE. This represents 14.3% of AMLs and 13.6% patients.

Factors leading to surgical intervention included young age, future pregnancies, and minimal size change or increasing size. One had an increase in size, going from 8.5 cm to 9.1 cm, and given future planned pregnancies, proceeded with surgery. The second had minimal size change, decreasing from 12.5 cm to 12.3 cm and ongoing flank pain, prompting surgical treatment. The third had an initial decrease of 1.9 cm from 12.4 cm, with subsequent growth to 11.7 cm. All were female under 45 years old.

The absolute post-procedure volume was the only statistically significant association to subsequent surgical management, with a median post-volume size of 241 ml in those going on to surgery vs. 55 ml in those who did not. The

Table 3. Various outcomes post-SAE	
Variables	
Renal function (Cr, mmol)	
Before	76
After	83
Technical success, n (%)	
Complete	16 (76.2%)
Trivial feeders	6 (28.6%)
Unsuccessful	0
Need for re-embolization (indication), n (%)	
Symptoms	0
Imaging	1 (4.8%)
Need for surgery post SAE, n (%)	3 (14.3%)
Re-bleed, n (%)	0
Minor complications, n (%)	5 (23.8%)
Major complications, n (%)	3 (14.3%)
Abscess	1 (4.8%)
Dissection	2 (9.5%)

Cr: creatinine; SAE: selective arterial embolization.

Table 4. Key embolization results of all SAE cases (n=21)

Variable	Minimum	Median	Maximum	Lower 95% mean	Upper 95% mean	p
Volume pre-embolization (ml)	23.6	200.3	2276.6	127.5	549.9	
Volume post-embolization (ml)	3.48	67.1	753.0	79.9	273.4	
Maximum diameter pre-embolization (cm)	4.1	8.6	22.2	7.2	11.0	
Maximum diameter post-embolization (cm)	2.4	6.0	13.9	5.5	8.5	
Diameter change (cm)	-2.3	1.8	8.3	0.91	3.3	0.002
Volume decrease (%)	-177.8	54.5	98.6	3.5	62.2	0.07

SAE: selective arterial embolization.

pre-procedure volume, relative volume change, and change in diameter were not associated with proceeding to surgery .

Complications

Overall, the complication rate was low. There were three grade 3 Clavien-Dindo complications. Two cases resulted in dissection of an intrarenal artery; these two cases were included in the complication rate but not in any other analysis of SAE outcomes, as the intention was to review results of those successfully treated by embolization. One was the embolization of a 5.9 cm AML in a patient with TSC that involved dissection of the superior segmental branch arising from right renal artery resulting in a functional occlusion. Secondary intraluminal thrombus was evident and cleared with a coaxial aspiration thrombectomy catheter. No other treatment was required, and followup imaging showed stable size. The second was the embolization of 3.6 cm AML that bled after thrombolysis and resulted in dissection of a medial vessel branch that supplied the AML, stopping blood flow to the AML. No other treatment during the procedure was required. One patient developed a perirenal abscess requiring percutaneous drainage and resulting in prolonged admission.

Five grade 1 Clavien-Dindo complications occurred. These were all post-embolization syndrome, defined as fever, abdominal pain, nausea, or vomiting. These were all managed conservatively with analgesia, anti-pyretics, and anti-emetics.

No treatment-based mortality was identified.

Discussion

Embolization for renal AMLs is an established, safe, and effective method of treatment.[12-14] Our study showed a significant decrease in volume and maximal diameter post-embolization, with a median decrease in size of 55%. There were no episodes of re-bleeding during the study followup time, and only a small proportion required surgical management or re-embolization.

Overall complication rate was low, consistent with other recent series.[13,15,16] Minor complications included post-embolization syndrome in 24% of patients. Three major complications occurred. Two cases resulted in catheter- or wire-related dissection of an intrarenal artery, which provided a functional occlusion to the tumor in both cases, and were managed conservatively. One patient developed a perirenal abscess requiring percutaneous drainage, an infrequent complication noted in other series.[13,17] No treatment-based mortality was detected during the study period.

The lack of prospective, randomized studies in the management of AMLs and the significant heterogeneity in the available retrospective evidence presents a challenge in many aspects of their clinical management.[10] Current evidence shows that the chance of becoming symptomatic from an AML increases significantly with size greater than 4 cm or growth rate greater than 0.25 cm/year. The traditional cutoff has been 4 cm before intervention, however, some now recommend not intervening until size is greater than 6 cm.[18]

Using size as the only parameter for intervention is an overly simplified approach and other factors that should be included in decision-making include size of aneurysmal component and multifocal tumors, TSC status, pregnancy status, patient preference, coagulopathy, trauma, access to emergency services, availability of surveillance imaging, and renal function.[11,18]

Using maximal diameter as a predictor of rupture, one study showed that using a cutoff of 4 cm resulted in a sensitivity of 100% and specificity of 38%. If a cutoff of 6 cm is used, the sensitivity is 100% and specificity is 67%. Using an aneurysmal component of greater than 5 mm as a predictor of rupture is more accurate, again with sensitivity of 100% and specificity of 86%.[19] We did not measure the largest aneurysmal component in our series.

Kuusk et al have shown that 74% of hemorrhagic AMLs are greater than 6 cm.[20] AMLs less than 6 cm are still at risk of rupture, however, to prophylactically treat all AMLs greater than 4 cm would overtreat up to 65% of patients.[18] Ouzaid et al showed that of 130 patients on active surveillance, 13% (n=17) proceeded to intervention. In tumors >4 cm, 34% (n=13) failed active surveillance, with only a small proportion due to hemorrhage.[18] Other studies have shown 9.4% of <4 cm AMLs rupture[21] and AMLs >10 cm can safely receive active surveillance,[22] indicating both ends of the spectrum can behave unexpectedly from previous thinking. Neither the most recent Canadian nor European guidelines recommend a specific size threshold for treatment.[8,10]

In our series, emergency cases receiving SAE had a mean diameter of 12.3 cm and the smallest tumor by diameter was 4.7 cm, with the remainder greater than 9 cm. This was similar for patients with pre-intervention evidence of retroperitoneal hemorrhage. Our study is not designed or powered to make statements on thresholds for elective treatment. However, our data suggests if 6 cm was the threshold, 75% of emergency AMLs would have been electively treated.

There was variation in followup imaging. MRI has been proposed as the superior imaging modality, especially in the case of fat-poor AML and cumulative radiation exposure.[23] However, time and resource constraints around the use of MRI often mean this is not practical. There are no firm guidelines regarding appropriate followup of treated AMLs.

Limitations of this study include the retrospective design with no randomization or control groups. A major limitation is the variation of embolization materials, which limits generalizability and given the numbers, no statistical analysis between these groups could be undertaken. There was a limited number of interventions and no standardized followup. A significant proportion (24%) of post-treatment imaging was based on US rather than cross-sectional modalities. This may have affected the reliability of the results, as a comparison was being made across imaging modalities. Of note, none of the patients proceeding with surgical management had US as their most recent imaging modality prior to surgery. Despite blinding of the radiologist, evidence of treatment (e.g., coils) would have been apparent and may have introduced bias. Furthermore, the radiologist is limited in the interpretation of US images to those that have been saved.

Further research is needed to clarify when intervention is required, particularly for AMLs within the 4—6 cm size range. The length of followup and imaging modality also need further study.

Conclusions

Embolization for renal AMLs is an established, safe, and effective method of treatment and our series further supports this. Our series showed no re-bleeds, low complication rates, and only a small proportion proceeding with surgical management. Determining when to intervene and how long to follow up patients is an issue that has not been well-described, with more research required in this area.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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