

#### NARRATIVE REVIEW

# New Trends and Evidence for the Management of Renal Angiomyolipoma: A Comprehensive Narrative Review of the Literature

Juan Camilo Álvarez Restrepo<sup>1,2</sup>, David Andres Castañeda Millan<sup>1,2</sup>, Carlos Andres Riveros Sabogal<sup>3</sup>, Andres Felipe Puentes Bernal<sup>1,2,4</sup>, Wilfredo Donoso Donoso<sup>1,2,4</sup>

<sup>1</sup>Department of Urology, School of Medicine, Universidad Nacional de Colombia, Bogotá, Colombia; <sup>2</sup>Urology Research and Innovation Group, Universidad Nacional de Colombia, Bogotá, Colombia; <sup>3</sup>School of Medicine, Universidad Nacional de Colombia, Bogotá, Colombia; <sup>4</sup>Department of Urology, Hospital Universitario Nacional de Colombia, Bogotá, Colombia

#### Abstract

Treatment of renal angiomyolipoma (AML) seeks to reduce related complications and preserve kidney function. The purpose of this article was to perform an updated literature review on the diagnosis, therapeutic options, and criteria for invasive intervention in patients with renal AML. Computerized tomography is the standard diagnostic method for renal AML, while definitive diagnosis is made by histopathology. The management of choice in most cases is active surveillance (AS), with a clinical and imaging follow-up protocol. In high-risk cases, therapeutic management should be considered, with alternatives such as selective arterial embolization (SAE), nephron-sparing surgery (NSS), and mTOR inhibitors in selected patients. Renal AML in women of childbearing age, those with growth >0.25 cm/year, intralesional aneurysms >5 mm, and clinically significant symptoms may qualify for active treatment. Despite the limitations derived from the available evidence, it is possible to consider SAE, NSS, and the use of mTOR inhibitors as management alternatives for selected patients.

Keywords: angiomyolipoma; diagnosis; kidney neoplasms; review; therapeutics

Received: 3 March 2021; Accepted after revision: 4 September 2021; Published: 21 January 2022

Author for correspondence: Juan Camilo Álvarez Restrepo, MD, Resident (PGY2), Department of Urology, Universidad Nacional de Colombia, School of Medicine, Carrera 30 No. 45-03, Edificio 471, Bogotá, Colombia, Email: juancalvarezr92@hotmail.com

How to cite: Álvarez-Restrepo JC, et al. New Trends and Evidence for the Management of Renal Angiomyolipoma: A Comprehensive Narrative Review of the Literature. J Kidney Cancer VHL. 2022; 9(1): 33–41.

Doi: https://doi.org/10.15586/jkcvhl.v9i1.177

Copyright: Álvarez-Restrepo JC, et al.

License: This open access article is licensed under Creative Commons Attribution 4.0 International (CC BY 4.0). http://creativecommons.org/licenses/by/4.0

# Introduction

Renal angiomyolipoma (AML) is a rare benign renal tumor that is part of the group of perivascular epithelioid cell neoplasms (PEComas) (1, 2). It is derived from mesenchyme, and

is thus composed of mature adipose tissue, smooth muscle, and dysmorphic blood vessels (3). Immunohistochemistry tends to be positive for the expression of HMB-45, melan-A, actin, desmin, and calponin (4).

It is responsible for 1-3% of kidney tumors with an incidence of 0.3-3% in the general population; it has a femaleto-male ratio of 2:1 (2). Fifty to seventy percent of cases correspond to sporadic renal AML, characterized by a smaller size (average 1–4 cm), slow growth (0.19 cm/year), unilateral presentation, and an average age between 43 and 53 years at diagnosis (3, 5–7). The remaining 30–50% is associated with genetic syndromes such as sporadic lymphangioleiomyomatosis (LAM) and tuberous sclerosis complex (TSC) (3, 4). The latter is due to an autosomal dominant mutation of the TSC1 (9q34) or TSC2 (16q13.3) genes, with activation of the mTOR intracellular signaling pathway, associated with a multisystemic disease, a greater number of lesions, a higher growth rate (1.25 cm/year), lower mean age at diagnosis (18 years), and considerable complications during follow-up (4, 8–10).

With regard to its histological classification, there are two subtypes of renal AML, classic and epithelioid. The classic subtype has been characterized in the active surveillance (AS) series, documenting slow growth and a low rate of complications in sporadic cases (2, 11). The epithelioid subtype encompasses 3.9% of renal AML, classified in 2004 by the World Health Organization as a potentially malignant neoplasm with aggressive behavior, and one-third of cases showing local invasion and metastasis at the time of diagnosis (3, 4, 12).

The clinical presentation of renal AML is generally asymptomatic; in 80% of the cases, it is found incidentally in diagnostic images (1, 13–15). Despite this, a classic triad of abdominal pain, palpable mass, and hematuria is described in 40% of the cases (4, 16). The diagnosis is made by the presence of macroscopic fat on images, mainly noncontrast computed tomography (CT) (1, 9).

The main complications of renal AML are chronic kidney disease (CKD), with a rate five times higher than the general population, and spontaneous retroperitoneal hemorrhage, present in 10–15% of patients, which may cause hypovolemic shock in up to 30% of these patients (1, 6, 17). The risk of bleeding is associated with the size of the lesion, aneurysms >5 mm, gravidity, TSC, anticoagulation, and trauma (1). Aggressive behavior and concomitant malignancy are also important but less prevalent complications (6).

Currently, the main therapeutic objective is to avoid complications, while preserving renal function. Indications for active treatment include growth during follow-up, associated symptoms, suspicion of malignancy, bleeding (hematuria or retroperitoneal hemorrhage), and size. This last indication has generated considerable controversy in the most recent scientific publications, which suggest that it is not an isolated predictor of complications, and that the symptoms and other imaging parameters should be given more importance. Recent studies in AS have modeled the natural history of AML, documenting a slow growth rate, low risk of surgical

complications, and overtreatment for lesions >4 cm in diameter (4, 11, 18).

Current therapeutic options for preventive and active treatment are AS, selective arterial embolization (SAE), ablation therapies, surgical management, and mTOR inhibitors in patients with TSC-associated AML (3, 8, 19).

The purpose of this article is to perform an updated literature review on the diagnosis, therapeutic options, and criteria for invasive intervention in patients with renal AML.

### Methods

The primary search protocol was performed using the PubMed, Embase, and LILACS databases using the MeSH terms "angiomyolipoma," "kidney," "kidney neoplasm," "diagnosis," and "therapeutics." The search was limited to studies in adults aged 18 years or older published within the last 20 years, written in English or Spanish. Articles were included if they reported on the diagnosis and treatment options for sporadic, TSC-associated, or epithelioid AML. All titles and abstracts were assessed by two of the authors and included according to their contribution to the objective of the article. Some additional references were incorporated given their clinical and historical relevance. We excluded from the primary protocol all duplicated registries, editorial letters, and articles concerning pediatric population.

#### Results

A total of 415 articles were found after the primary search protocol. According to the inclusion criteria, we included 36 articles for the final analysis, while another 15 articles were included by consensus based on their historical and clinical relevance (Figure 1).

#### Discussion

#### Diagnosis

The diagnostic approximation of classical AML by non-contrast CT is based on the presence of fat in a renal mass, defined in Hounsfield units (HU) as -10 (-15 to -30 HU) (4). Likewise, renal AML can be classified as fatrich, fat-poor, and fat-invisible using CT or MRI (20). It should be kept in mind that this finding can also be seen in renal cell carcinoma (RCC), lipoma, liposarcoma, oncocytoma, Wilms tumor, and teratoma; therefore, other characteristics such as the contrast enhancement pattern and the presence of calcifications must also be considered (3, 4, 21). Some research centers have reported cases of AML concomitant with renal cancer in 1% of the patients (6).

In search of a more accurate imaging diagnosis, tomographic techniques such as pixel mapping have emerged,

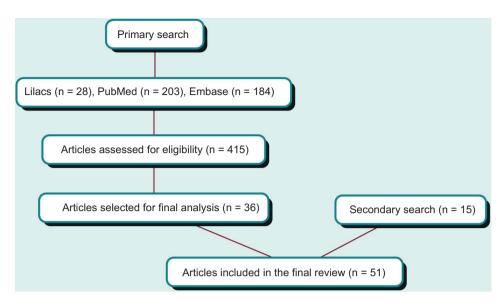


Figure 1: Literature review algorithm.

improving the specificity for fat detection by up to 100%, along with advanced magnetic resonance techniques, such as chemical shift, FLASH, India Ink, gradient echo, and fat suppression (9). Within a retrospective study, it was documented that 81.4% of sporadic AML cases, 47.1% of those associated with TSC, and 78% of epithelioid AMLs were diagnosed with ultrasound (US) and tomography. Less than 8% of the cases (1% for sporadic AML and 7.8% for TSC-associated AML) were diagnosed using MRI, with the exception of the epithelioid subtype (21.7%) (7).

After the suspicion of AML in imaging, a definitive diagnosis must be made by histopathology, highlighting the importance of the pathologist and the utility of preoperative diagnostic percutaneous biopsy in inconclusive or complex cases (14, 19, 22). Percutaneous biopsy histology is concordant with final pathology in 93% of the cases with a series reporting a complication rate of only 1.5% (23).

#### Sporadic AML

For the management of AML, the following have to be considered: symptoms (intractable pain, hematuria), suspicion of malignancy, the risk of retroperitoneal hemorrhage (women of childbearing age, size), growth during follow-up (>0.25 cm/year), inadequate access to an emergency department, and episodes of spontaneous rupture (1, 5, 14, 24, 25).

The most widespread cutoff point for treatment has been a diameter of >4 cm. This imaging finding is present in 82–94% of symptomatic patients, without being a sine qua non, with other series reporting symptoms in only 30% of the cases (9, 14). Using 4 cm as a cutoff value to predict

retroperitoneal bleeding is very sensitive (100%) but not very specific (38%) and yields many false positives (4). Ouzaid's study in AS concluded that treatment based on a cutoff size of  $\geq$ 4 cm caused overtreatment in 65% of the patients, and identified an increased risk of bleeding in lesions of >6 cm in diameter (11). In concordance with these findings, Kuusk et al. found an association with bleeding in 74%, 17%, and 9%, related to sizes of >6 cm, 4-6 cm, and <4 cm, respectively (1).

In a review of statistically significant publications, it was identified that the risk of bleeding is greater for lesions with a mean diameter of 8 cm versus 4 cm (P < 0.001) (7). This review included the study by Yamakado et al. where hemorrhage occurred in lesions with an average size of 11.4 cm versus 5 cm in nonhemorrhagic lesions. Finally, the authors identified a cutoff size of  $\geq 7.35$  cm as the best predictor of bleeding, with this finding present in 36% of the bleeding patients analyzed (26).

Gandhi et al. published their experience with CT angiography in AML, where they evaluated predictors of rupture. Using a cutoff size of >4 cm had a sensitivity of 20%, specificity of 89%, positive predictive value (PPV) of 83.3%, and a negative predictive value (NPV) of 28.5%, while the presence of an aneurysm of >5 mm had a sensitivity of 75%, specificity of 90%, PPV of 50%, and NPV of 96.4% (27). Other studies have shown an association between the presence of aneurysmal vessels with a diameter of >5 mm and an increased risk of retroperitoneal bleeding, with a sensitivity of 100% and a specificity of 86% (26, 28). Likewise, other studies including a review by Murray et al. identified that high vascularity and the presence of tortuous vessels were potential risk factors for retroperitoneal bleeding (9, 29, 30).

Other risk factors for bleeding are accelerated growth, association with TSC, and pregnancy status (6, 11, 17). Concerning AML during pregnancy, no clinical studies or large case series are available; case reports suggest a hormonal effect that conditions an increased growth rate (31). An elevated risk of rupture and obstetric complications have been related to vaginal delivery with a possible benefit in scheduling cesarean delivery (6, 18). Raft et al. reported 72 cases of AML in pregnancy, 58 of which experienced rupture at an average gestational age of 27 weeks, 30% presented hemorrhagic shock, and 13% were associated with fetal death (32). Likewise, there have been case reports where active management was necessary in pregnant women (nephrectomy, embolization) (6).

#### TSC-Associated AML

Angiomyolipoma associated with TSC usually has systemic manifestations (central nervous system, heart, lungs, and skin). The mutation in the TSC1 and TSC2 genes conditions the activation of the mTOR-PI3K/AKT pathway, with renal compromise as the most common cause of death in adults (14, 17, 33). Renal AML is present in up to 80% of the patients with TSC. Patients are predominantly young (mean age of 18 years), with a tendency for rapid growth (0.55-1.25 cm/year), more symptoms, larger lesions (mean 3.5–19.3 cm), 90.2% bilateral and 94.1% multiple in their presentation, without a sex difference in incidence (7, 17). In addition to the increased risk for retroperitoneal hemorrhage, complications of TSC-associated renal AML are chronic arterial hypertension and CKD, the latter with a fivefold higher rate and a 30-year earlier onset (CKD stage 3) compared to the general population (3, 8, 17).

Management with mTOR inhibitors currently has evidence in TSC-associated AML and LAM, without being able to document its usefulness in sporadic cases. Everolimus has more robust evidence and is currently the only FDA-approved drug for TSC-associated renal and LAM. This is indicated by the Tuberous Sclerosis Renal Guidelines with an effectiveness against placebo demonstrated by the EXIST-1 and EXIST-2 trials, indicating a reduction of 50% in size in lesions of >3 cm in 42–54% of the patients. Likewise, a sustained volume reduction of up to 192 weeks, no bleeding, and a statistically significant lower rate of progression was observed in the high-risk population. Its main adverse effects include stomatitis, nasopharyngitis, acne, proteinuria, headache, cough, and hypercholesterolemia (3, 17, 34, 35).

# Epithelioid AML

According to the current literature, it represents approximately 3.9% of the renal AML cases and ≤1% of the renal tumors (6, 7, 12). It appears predominantly in women (3:1

ratio); up to 79% are symptomatic, with a mean age at diagnosis of 46 years, a mean size of 10.5 cm, and a more aggressive behavior, with an overall survival rate of 50% at 3 years, and one-third of the patients with local extension or metastasis at diagnosis (6, 9). Its imaging diagnosis is more complex because these are tumors with a lower fat content, in many cases with aggressive characteristics (venous extension, distant metastases), making it harder to differentiate from RCC, with a requirement for MRI or histopathology in 21.7% and 7.7% of cases, respectively, to clarify the diagnosis (6, 7).

The prognostic factors identified for aggressive behavior include lesion size of >7 cm, extrarenal extension, young age, tumor necrosis, and an epithelioid histological pattern (3, 36). This subtype is treated as RCC, given its risk of aggressive behavior and high recurrence rate (9).

# Choosing a treatment option

Understanding the natural history of renal AML has changed the therapeutic paradigm, with a current trend toward a more conservative approach. Active surveillance is the first-line intervention in most cases. It seeks to identify low-risk renal AML cases, qualified for close follow-up, and supervise early indicators of complications, mainly rupture or retroperitoneal bleeding, to offer timely treatment.

In the Ouzaid et al. series, 130 patients underwent AS, 17 (13%) required active treatment at the mean follow-up of 49 months, three patients (2.3%) due to retroperitoneal hemorrhage. In a univariate analysis, predictors of late intervention included a larger tumor size (>4 cm), a higher body mass index, contralateral lesions, and symptomatic disease (11). Despite associating a 4 cm cutoff size as a predictor for intervention, it was evident that it led to overtreatment. It was found that 67% of the symptomatic patients managed with AS did not require subsequent intervention, making necessary an assessment of symptomatic severity and the possibility of conservative management (1, 11).

Bhatt's retrospective series evaluated growth in cases of sporadic AML without treatment, finding that >92% of the asymptomatic or oligosymptomatic cases do not grow or grow very slowly regardless of their initial size (> or < 4 cm) in a follow-up at 43 months (37). Therefore, they recommend AS in sporadic AML regardless of size in asymptomatic patients, evaluating treatment if a rapid growth rate (>0.25 cm/year) is present during follow-up (24, 37). In a systematic review from 2015, 44 studies with 2,580 patients were included, 281 presented spontaneous rupture with only five deaths (1.9%); all deaths in this series were related to TSC (18, 29). A different series of AS documented only 2.2% of patients with hematuria or retroperitoneal bleeding during follow-up, with 5.7% requiring active treatment (19).

Currently, there is no guideline that standardizes the frequency of follow-up. The existing protocols are based on AS

studies that suggest physical examination, renal function, and CT or US at 6 and 12 months, and then annually, with closer follow-up intervals in high-risk populations (2, 9, 14, 19). With regard to TSC-associated AML, the 2012 Tuberous Sclerosis Renal Guidelines consensus suggests MRI follow-up every 1–3 years (17).

Selective arterial embolization has become the first line of management, being a safe, minimally invasive alternative, with a success rate of 90-100%, and emergency control in 96-100% of the patients (6, 9). It is useful in symptomatic patients, in prophylactic and presurgical management, and acute retroperitoneal hemorrhage (38). The embolic agents used are ethanol, polyvinyl alcohol, gelfoam, coils, and triacyl gelatin microspheres, without studies documenting superiority of any over the others (39). In the study by Kothary et al., the use of an ethanol-based agent over polyvinyl alcohol was suggested, without recommending the use of coils due to the risk of collateral formation (40, 41). It has a grade C indication in prophylactic management of hemorrhage in growing AML of > 0.25cm/year, and/or the presence of aneurysms of >5 mm. There are no studies comparing prophylactic embolization versus mTOR inhibitors in the TSC-associated AML population (24). The recurrence rate in the results of 16 series is 25%, with a reintervention requirement in up to 37% of the patients managed with this technique (11, 14, 17). The role of SAE prior to partial nephrectomy reduces, according to Tan et al. blood loss, hospital stay, and residual tumor in renal AML cases of >7 cm (42). In addition, 93.3% of the patients who received preoperative SAE preserved their kidneys versus 33.3% who did not receive prior SAE and later required radical nephrectomy intraoperatively (8).

In prophylactic and symptomatic management, SAE offers a 43% reduction in the volume of renal AML, with other studies reporting a 26-99% decrease in the volume of lesions (11, 42). Among its advantages, it conditions fewer major complications compared to surgery, less bleeding, and a shorter hospital stay (5). Its most prevalent complication is post-embolization syndrome (PES), present in up to 89% of the cases, characterized by fever, flank pain, and leukocytosis; it improves with symptomatic management (3). The study by Bissler et al. evidenced a 30% decrease in PES with the use of corticosteroids and a prophylactic antibiotic, with the need for more studies to be recommended in clinical practice (9, 43). Other described complications are vascular injury, abscess formation, pleural effusion, renal infarction, and impact in glomerular filtration rate (GFR) (2). A series of 45 AML cases taken to SAE did not manifest any bleeding, nor did they require renal replacement therapy; there were also no deaths in the following 14 months (42). Another series of 71 patients over 10 years reported a complete loss of renal unit function in 2.9% of the patients (44). Arguments against this technique include a study in which AML cases of ≥8 cm had a hazard ratio of 2.36 (P < 0.05) for reintervention (1).

Ablation arises as an alternative for the management of small and asymptomatic renal AML (<4 cm), with few studies, and without high-level evidence, but with promising results. Ablation has been considered superior to Nephronsparing surgery (NSS) in comparative studies with regard to renal function preservation (45). The most studied technique has been radiofrequency ablation with two series that have documented good effectiveness, low reintervention rates, and minor complications during follow-up (19). Prevoo et al. reported the successful case of a sporadic 4.5 cm renal AML managed with radiofrequency ablation in a solitary kidney without recurrence as evidenced in imaging, and with preservation of renal function at 12 months (46). Evidence on the clinical utility of this technique, along with cryoablation and microwave ablation, is still lacking (2, 3).

Surgical management has been displaced to a second plane with the advent of SAE, with the advantage of NSS over radical nephrectomy (RN), due to the already well-understood relationship with CKD and increased associated morbidity and mortality (3). Radical nephrectomy conditions twice the GFR compromise compared to NSS in the immediate postoperative period; it is only indicated in AML rupture with retroperitoneal bleeding and uncontrolled hypovolemic shock after failed embolization (4, 47).

Boorjian et al. described in the largest series of sporadic AML and open NSS, at 8 years of follow-up, a recurrence rate of 3.4%, and 12% de novo CKD, respectively (48). Berglund et al. reported a 14% loss of renal function due to a requirement for conversion to RN (49). In addition, Minervini et al. revealed less blood loss, shorter ischemic time, and hospital stay with NSS when compared with RN. Nephron-sparing surgery presents surgical complications of 21.4% with a very low reintervention requirement (<1%) (6, 19). Additional series report an 86.9% preservation of the GFR, without complications or recurrence (6). Despite new trends, a systematic review of the European Association of Urology in 2019 concluded that NSS had similar morbidity to SAE but seemed to be the most effective option to prevent recurrence and the need for secondary treatments (19).

Table 1 summarizes some of the most important series in terms of different treatment modalities, their success rate, and main points to consider.

# Considerations on available evidence and management proposal

Research in renal AML has led us to understand this renal tumor as a heterogeneous pathology, with a variable natural history needing different therapeutic strategies. The mainstay in management is symptomatic control and prevention of morbidity and mortality, with a specific focus on retroperitoneal bleeding and secondary hemorrhagic shock.

Table 1: Case series in renal AML management.

| Study                | Treatment modality                      | Success rate/Response | Effects/Adverse events   |
|----------------------|---|-----------------------|--|
| EXIST 1 (17)         | Everolimus in TSC-AML                   | 53.3%                 | Stomatitis, nasopharyngitis, headache, acne, hyperlipidemia, hematologic disorders |
| EXIST 2 (17)         | Everolimus in TSC-AML                   | 58%                   | Stomatitis, nasopharyngitis, headache, acne, hyperlipidemia, hematologic disorders |
| Ouzaid et al. (11)   | Active surveillance                     | 87%*                  | Active treatment in 13% of the patients during follow-up                           |
| Bardin et al. (50)   | SAE                                     | 96%                   | Recurrence in 13%, repeat embolization in 17%, PES in 80%                          |
| Murray et al. (29)   | SAE                                     | 93.3%                 | PES in 35.9%, repeat embolization in 20.9%   |
| Lin et al. (51)      | Robotic-assisted NSS                    | 100%                  | CKD in 10%, perioperative complications Clavien $\leq$ II in 26%                   |
| Castle et al. (45)   | Radiofrequency ablation in sporadic AML | 100%                  | Perioperative complications in 13.3%   |
| Kuusk et al. (1)     | Radical nephrectomy                     | 100%                  | Bleeding in 10.8%, no reinterventions  |
| Boorjian et al. (48) | NSS                                     | 96.6%                 | Complications in 12%, no CKD   |

TSC-AML – TSC-associated angiomyolipoma; SAE – selective arterial embolization; PES – post-embolization syndrome; NSS – nephron-sparing surgery; CKD – chronic kidney disease.

Active surveillance as expectant therapy has permitted the study of the natural history of AML, managing to identify early indicators of treatment. The conservative management approach is based on a slow growth rate, the risks of overtreatment, the low risk of rupture, and the related mortality.

As for symptomatic patients, TSC-associated AML, pregnant women or those of childbearing age, aneurysms of >5 mm, and those with rapid growth rates, represent a highrisk population qualifying for early interventions. Likewise, among the interventions, minimally invasive techniques predominate as the first line of treatment, with the emergence of new thermal ablation therapies with promising results.

Undoubtedly, studies and guidelines that standardize the management of renal AML are lacking in order to facilitate a focused approach in the urological community. Figure 2 outlines a proposed management algorithm based on current evidence.

# Future perspective

Due to the low incidence of renal AML, there is a scarcity of high-level evidence comparing the various treatment options for this pathology. In terms of future research, there is a necessity for updated clinical guidelines that assist the physician toward suggesting a treatment that minimizes morbidity and mortality. Furthermore, translational research in immunotherapy or gene therapy might be the key to reaching a potential cure in the future.

## Conclusion

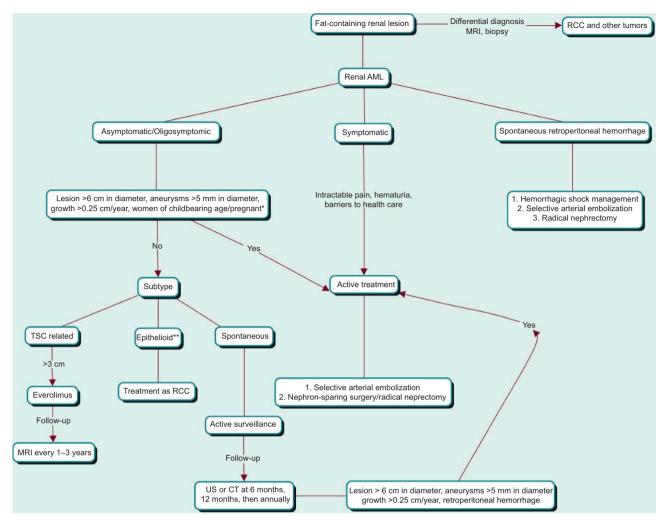
Renal AML is a pathology of urological management with low prevalence but with a significant risk of morbidity and mortality. Recent data have allowed us to define CT as the ideal diagnostic method and postulate that patients with growth >0.25 cm/year, intralesional aneurysms of >5 mm, uncomfortable symptoms, pregnancy status, and women of child-bearing age are the ideal candidates for active management.

Despite the limitations of the available evidence, it is possible to consider AS, NSS, and the use of mTOR inhibitors as management alternatives for selected patients.

### Conflict of interest

None of the authors of this manuscript have any conflict of interest to disclose.

<sup>\*</sup>Patients did not require active treatment during follow-up.



**Figure 2:** Proposed updated management algorithm. RCC – renal cell carcinoma; AML – angiomyolipoma; TSC – tuberous sclerosis complex; MRI – magnetic resonance imaging; US – ultrasound; CT – computerized tomography.

\*Associated with other risk factors, according to medical criteria. \*\*See characteristics and risk factors in "epithelioid AML."

#### References

- Kuusk T, Biancari F, Lane B, Tobert C, Campbell S, Rimon U, et al. Treatment of renal angiomyolipoma: Pooled analysis of individual patient data. BMC Urol. 2015;15:123. http://dx.doi. org/10.1186/s12894-015-0118-2
- Wang SF, Lo WO. Benign neoplasm of kidney: Angiomyolipoma. J Med Ultrasound. 2018;26(3):119–22. http://dx.doi.org/10.4103/JMU.JMU\_48\_18
- Flum AS, Hamoui N, Said MA, Yang XJ, Casalino DD, McGuire BB, et al. Update on the diagnosis and management of renal angiomyolipoma. J Urol. 2016;195(4 Pt 1):834–46. http:// dx.doi.org/10.1016/j.juro.2015.07.126
- Murad Gutiérrez V, Aponte Barrios WO, Romero Enciso JA. Angiomiolipoma renal: nuevas perspectivas [Renal angiomyolipoma: New perspectives]. Rev Colomb Urol. 2016;25(1):16–24. [Article in Spanish]. http://dx.doi.org/10.1016/j.uroco.2015.12.009

- Urciuoli P, D'Orazi V, Livadoti G, Foresi E, Panunzi A, Anichini S, et al. Treatment of renal angiomyolipoma: Surgery versus angioembolization. G Chir. 2013;34(11–12):326–31.
- Seyam RM, Alkhudair WK, Kattan SA, Alotaibi MF, Alzahrani HM, Altaweel WM. The risks of renal angiomyolipoma: Reviewing the evidence. J Kidney Cancer VHL. 2017;4(4):13–25. http://dx.doi.org/10.15586/jkcvhl.2017.97
- Lee KH, Tsai HY, Kao YT, Lin HC, Chou YC, Su SH, et al. Clinical behavior and management of three types of renal angiomyolipomas. J Formos Med Assoc. 2019;118(1 Pt 1):162–9. http://dx.doi.org/10.1016/j.jfma.2018.02.012
- Samuels JA. Treatment of renal angiomyolipoma and other hamartomas in patients with tuberous sclerosis complex. Clin J Am Soc Nephrol. 2017;12(7):1196–202. http://dx.doi. org/10.2215/CJN.08150816
- Halpenny D, Snow A, McNeill G, Torreggiani WC. The radiological diagnosis and treatment of renal angiomyolipoma-current

- status. Clin Radiol. 2010;65(2):99–108. http://dx.doi.org/10.1016/j.crad.2009.09.014
- Courtney M, Mulholland D, O'Neill D, Redmond C, Ryan J, Geoghegan T, et al. Natural growth pattern of sporadic renal angiomyolipoma. Acta Radiol. 2020;62(2):284185120918372. http://dx.doi.org/10.1177/0284185120918372
- Ouzaid I, Autorino R, Fatica R, Herts BR, McLennan G, Remer EM, et al. Active surveillance for renal angiomyolipoma: Outcomes and factors predictive of delayed intervention. BJU Int. 2014;114(3):412–17. http://dx.doi.org/10.1016/ S1569-9056(14)60089-0
- Troncoso P, Sarras MA, Calvo CI, Barra L, Méndez GP, Bustamante C. Angiomiolipoma renal: ¿Es siempre un tumor benigno? [Renal angiomyolipoma: Is it always a benign tumor?]. Rev Chil Urol. 2014;79(4):71–4. [Article in Spanish]
- Idilman IS, Vesnic S, Cil B, Peynircioglu B. Giant renal artery pseudoaneurysm caused by rupture of renal angiomyolipoma following pregnancy: Endovascular treatment and review of the literature. Saudi J Kidney Dis Transpl. 2014;25(2):385–9. http:// dx.doi.org/10.4103/1319-2442.128570
- Vos N, Oyen R. Renal angiomyolipoma: The good, the bad, and the ugly. J Belg Soc Radiol. 2018;102(1):41. http://dx.doi. org/10.5334/jbsr.1536
- Koo KC, Kim WT, Ham WS, Lee JS, Ju HJ, Choi YD. Trends of presentation and clinical outcome of treated renal angiomyolipoma. Yonsei Med J. 2010;51(5):728–34. http://dx.doi. org/10.3349/ymj.2010.51.5.728
- Ellis RJ, Edey DP, Del Vecchio SJ, McStea M, Campbell SB, Hawley CM, et al. End-stage kidney disease following surgical management of kidney cancer. Clin J Am Soc Nephrol. 2018;13(11):1641–8. http://dx.doi.org/10.2215/CJN.06560518
- Kingswood JC, Bissler JJ, Budde K, Hulbert J, Guay-Woodford L, Sampson JR, et al. Review of the tuberous sclerosis renal guidelines from the 2012 consensus conference: Current data and future study. Nephron. 2016;134(2):51–8. http://dx.doi.org/10.1159/000448293
- Murray TE, Lee MJ. Are we overtreating renal angiomyolipoma: A review of the literature and assessment of contemporary management and follow-up strategies. Cardiovasc Intervent Radiol. 2018;41(4):525–36. http://dx.doi.org/10.1007/s00270-017-1862-3
- Fernández-Pello S, Hora M, Kuusk T, Tahbaz R, Dabestani S, Abu-Ghanem Y, et al. Management of sporadic renal angiomyolipomas: A systematic review of available evidence to guide recommendations from the European Association of Urology Renal Cell Carcinoma Guidelines Panel. Eur Urol Oncol. 2020;3(1):57–72. http://dx.doi.org/10.1016/j.euo.2019.04.005
- Park BK. Renal angiomyolipoma based on new classification: How to differentiate it from renal cell carcinoma. AJR Am J Roentgenol. 2019;212(3):582–8. http://dx.doi.org/10.2214/ AJR.18.20408
- 21. Ortega Hrescak MC, Ezquer AJ, Pérez Renfiges A, López Galíndez AJ, Cenice FF, López RE. Angiomiolipoma renal atípico versus carcinoma de células renales: dilema diagnóstico. Hallazgos útiles por tomografía computada para la discriminación de estos tumores [Atypical renal angiomyolipoma versus carcinoma renal cell: Diagnosis dilemma. Findings by computed tomography for the discrimination of these tumors]. Rev Argent Radiol. 2016;80(2):99–111. [Article in Spanish]. http://dx.doi.org/10.1016/j.rard.2016.04.010
- Sutherland EL, Choromanska A, Al-Katib S, Coffey M. Outcomes of ultrasound guided renal mass biopsies. J

- Ultrasound. 2018;21(2):99–104. http://dx.doi.org/10.1007/s40477-018-0299-0
- Lobo JM, Clements MB, Bitner DP, Mikula MD, Noona SW, Sultan MI, et al. Does renal mass biopsy influence multidisciplinary treatment recommendations? Scand J Urol. 2020;54(1):27–32. http://dx.doi.org/10.1080/21681805.2019.170 3805
- Ryan JW, Farrelly C, Geoghegan T. What are the indications for prophylactic embolization of renal angiomyolipomas? A review of the current evidence in the literature. Can Assoc Radiol J. 2018;69(3):236–9. http://dx.doi.org/10.1016/j.carj.2018.01.002
- Nelson CP, Sanda MG. Contemporary diagnosis and management of renal angiomyolipoma. J Urol. 2002;168(4 Pt 1):1315–25. http://dx.doi.org/10.1016/S0022-5347(05)64440-0
- Yamakado K, Tanaka N, Nakagawa T, Kobayashi S, Yanagawa M, Takeda K. Renal angiomyolipoma: Relationships between tumor size, aneurysm formation, and rupture. Radiology. 2002;225(1):78–82. http://dx.doi.org/10.1148/ radiol.2251011477
- 27. Gandhi SP, Pal BC, Patel KN, Sutariya H, Trivedi HL. Role of 64 slice multidetector computed tomography and angiography to establish relationship between tumor size, aneurysm formation and spontaneous rupture of renal angiomyolipomas: Single center experience. Urol Ann. 2016;8(2):173–7. http://dx.doi. org/10.4103/0974-7796.172213
- Champagnac J, Melodelima C, Martinelli T, Pagnoux G, Badet L, Juillard L, et al. Microaneurysms in renal angiomyolipomas: Can clinical and computed tomography features predict their presence and size? Diagn Interv Imaging. 2016;97(3):321– 6. http://dx.doi.org/10.1016/j.diii.2015.12.004
- Murray TE, Doyle F, Lee M. Transarterial embolization of angiomyolipoma: A systematic review. J Urol. 2015;194(3):635– 9. http://dx.doi.org/10.1016/j.juro.2015.04.081
- Swärd J, Henrikson O, Lyrdal D, Peeker R, Lundstam S. Renal angiomyolipoma-patient characteristics and treatment with focus on active surveillance. Scand J Urol. 2020;54(2):141–6. http://dx.doi.org/10.1080/21681805.2020.1716066
- Hatano T, Egawa S. Renal angiomyolipoma with tuberous sclerosis complex: How it differs from sporadic angiomyolipoma in both management and care. Asian J Surg. 2020;43(10):967–72. http://dx.doi.org/10.1016/j.asjsur.2019.12.008
- Raft J, Lalot JM, Meistelman C, Longrois D. Rôle de la grossesse dans la rupture d'un angiomyolipome rénal [Influence of pregnancy on renal angiomyolipoma]. Gynecol Obstet Fertil. 2005;33(11):898–906. [Article in French]. http://dx.doi.org/10.1016/j.gyobfe.2005.09.015
- Brakemeier S, Bachmann F, Budde K. Treatment of renal angiomyolipoma in tuberous sclerosis complex (TSC) patients. Pediatr Nephrol. 2017;32(7):1137–44. http://dx.doi.org/10.1007/ s00467-016-3474-6
- 34. Zonnenberg BA, Neary MP, Duh MS, Ionescu-Ittu R, Fortier J, Vekeman F. Observational study of characteristics and clinical outcomes of Dutch patients with tuberous sclerosis complex and renal angiomyolipoma treated with everolimus. PLoS One. 2018;13(11):e0204646. http://dx.doi.org/10.1371/journal.pone.0204646
- Bissler JJ, Budde K, Sauter M, Franz DN, Zonnenberg BA, Frost MD, et al. Effect of everolimus on renal function in patients with tuberous sclerosis complex: Evidence from EXIST-1 and EXIST-2. Nephrol Dial Transplant. 2019;34(6):1000–8. http:// dx.doi.org/10.1093/ndt/gfy132

- Nese N, Martignoni G, Fletcher CD, Gupta R, Pan CC, Kim H, et al. Pure epithelioid PEComas (so-called epithelioid angiomyolipoma) of the kidney: A clinicopathologic study of 41 cases: Detailed assessment of morphology and risk stratification. Am J Surg Pathol. 2011;35(2):161–76. http://dx.doi.org/10.1097/PAS.0b013e318206f2a9
- Bhatt JR, Richard PO, Kim NS, Finelli A, Manickavachagam K, Legere L, et al. Natural history of renal angiomyolipoma (AML): Most patients with large AMLs >4cm can be offered active surveillance as an initial management strategy. Eur Urol. 2016;70(1):85–90. http://dx.doi.org/10.1016/j.eururo.2016.01.048
- Muller A, Rouvière O. Renal artery embolization-indications, technical approaches and outcomes. Nat Rev Nephrol. 2015;11(5):288–301. http://dx.doi.org/10.1038/nrneph.2014.231
- Rosenov A, Schindewolf M, Baumgartner I, Saely C. Selective arterial embolizations of renal angiomyolipomas using 96% ethanol: A case series of 5 patients. Clin Med Insights Case Rep. 2020;13:1179547620906863. http://dx.doi.org/10.1177/1179547620906863
- Rimon U, Duvdevani M, Garniek A, Golan G, Bensaid P, Ramon J, et al. Ethanol and polyvinyl alcohol mixture for transcatheter embolization of renal angiomyolipoma. AJR Am J Roentgenol. 2006;187(3):762–8. http://dx.doi.org/10.2214/ AJR.05.0629
- Kothary N, Soulen MC, Clark TW, Wein AJ, Shlansky-Goldberg RD, Crino PB, et al. Renal angiomyolipoma: Long-term results after arterial embolization. J Vasc Interv Radiol. 2005;16(1):45–50. http://dx.doi.org/10.1097/01. RVI.0000143769.79774.70
- Lin L, Wang C, Pei R, Guan H, Wang J, Yang M, et al. Prophylactic selective arterial embolization for renal angiomyolipomas: Efficacy and evaluation of predictive factors of significant shrinkage. Int Urol Nephrol. 2018;50(10):1765–70. http://dx.doi.org/10.1007/s11255-018-1953-3
- Bissler JJ, Racadio J, Donnelly LF, Johnson ND. Reduction of postembolization syndrome after ablation of renal angiomyolipoma. Am J Kidney Dis. 2002;39(5):966–71. http://dx.doi. org/10.1053/ajkd.2002.32770

- Anis O, Rimon U, Ramon J, Khaitovich B, Zilberman DE, Portnoy O, et al. Selective arterial embolization for large or symptomatic renal angiomyolipoma: 10 years of follow-up. Urology. 2020;135:82–7. http://dx.doi.org/10.1016/j.urology. 2019.09.035
- 45. Castle SM, Gorbatiy V, Ekwenna O, Young E, Leveillee RJ. Radiofrequency ablation (RFA) therapy for renal angiomyolipoma (AML): An alternative to angio-embolization and nephron-sparing surgery. BJU Int. 2012;109(3):384–7. http://dx.doi.org/10.1111/j.1464-410X.2011.10376.x
- Prevoo W, van den Bosch MA, Horenblas S. Radiofrequency ablation for treatment of sporadic angiomyolipoma. Urology. 2008;72(1):188–91. http://dx.doi.org/10.1016/j.urology. 2008.02.059
- Streja E, Kalantar-Zadeh K, Molnar MZ, Landman J, Arah OA, Kovesdy CP. Radical versus partial nephrectomy, chronic kidney disease progression and mortality in US veterans. Nephrol Dial Transplant. 2018;33(1):95–101.
- Boorjian SA, Frank I, Inman B, Lohse CM, Cheville JC, Leibovich BC, et al. The role of partial nephrectomy for the management of sporadic renal angiomyolipoma. Urology. 2007;70(6):1064–8. http://dx.doi.org/10.1016/j.urology. 2007.07.045
- Berglund RK, Bernstein M, Manion MT, Touijer KA, Russo P. Incidental angiomyolipoma resected during renal surgery for an enhancing renal mass. BJU Int. 2009;104(11):1650–4. http://dx. doi.org/10.1111/j.1464-410X.2009.08677.x
- Bardin F, Chevallier O, Bertaut A, Delorme E, Moulin M, Pottecher P, et al. Selective arterial embolization of symptomatic and asymptomatic renal angiomyolipomas: A retrospective study of safety, outcomes and tumor size reduction. Quant Imaging Med Surg. 2017;7(1):8–23. http://dx.doi.org/10.21037/ qims.2017.01.02
- Lin CY, Yang CK, Ou YC, Chiu KY, Cheng CL, Ho HC, et al. Long-term outcome of robotic partial nephrectomy for renal angiomyolipoma. Asian J Surg. 2018;41(2):187–91. http://dx. doi.org/10.1016/j.asjsur.2016.11.003