Canadian Urological Association best practice report: Diagnosis and management of sporadic angiomyolipomas

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Introduction

Angiomyolipomas (AML) are benign neoplasms composed of varying amounts of blood vessels, smooth muscle, and adipose tissue. While being the most frequently occurring benign solid renal tumor, their incidence in the general population is still uncommon, occurring with a frequency of 13–30 per 100 000.[1] With the increased use of intra-abdominal sonography and cross-sectional imaging, more have been incidentally identified.[2]

Most of these tumors are asymptomatic, but some present with symptoms, including flank pain, hematuria, and rarely, life-threatening hemorrhage. The frequency of these presentations has been controversial and a point of contention in their management. In an influential case series and literature review of 253 patients, Oesterling et al reported that 64% were symptomatic, and 40% presented with hemorrhage. These numbers became more dramatic in tumors larger than 4 cm, with 82% being symptomatic and 51% presenting with hemorrhage.[3] This landmark review greatly influenced the 4 cm cutoff that has been ingrained into urologic literature and the historically high rate of intervention in lesions larger than 4 cm.[4]

In contrast, contemporary series have reported much more modest rates of 10% being symptomatic and only 2% risk of hemorrhage.[5] The lack of prospective, randomized studies in the management of AMLs and the significant heterogeneity in the available retrospective evidence presents a conundrum in clinical management.

While the majority of AMLs are sporadic, up to 20% are associated with hereditary conditions such as tuberous sclerosis complex (TSC) and lymphangioleiomyomatosis (LAM).[4] Management of these lesions tends to differ from sporadic AMLs, as they tend to present with multiple tumors and seem to respond well to mTOR inhibitors. In contrast, there is currently no indication nor data supporting the treatment of sporadic AML with mTOR inhibitor therapy. In patients with synchronous bilateral AMLs or clinical symptoms consistent with hereditary conditions, referral for further assessment and genetic testing should be discussed. The vast majority of AMLs in children are associated with syndromic conditions. Sporadic AMLs are extremely rare in children, with minimal published data available.[6] Given the paucity of data and experience for children diagnosed with AMLs on imaging, referral to a tertiary pediatric center should be strongly considered. This Best Practice Report (BPR) will focus on the sporadic form of AML in adults only.

Diagnosis and followup protocol, as well as indications for and type of management for sporadic AML vary widely. This BPR seeks to codify existing data to provide practicing urologists with the best evidence-based recommendations to inform decision-making in the management of sporadic AML. The following clinical questions will be discussed:

1. What imaging tests are necessary to confirm the diagnosis of AMLs?
2. What is the natural history of AMLs?
3. What is the optimum followup protocol for AMLs under observation?
4. What are the indications for intervention?
5. What interventions are available and preferred?
6. What is the management of acutely bleeding AMLs?

Methods

The search strategy registered on PROSPERO and was done electronically on OVID using MEDLINE and EMBASE. Given the limited amount of literature on the subject, articles regarding diagnosis and treatment were all grouped together in one search. Search terms included, "angiomyolipoma OR AML" and excluded "liver OR hepatic," "tuberous sclero-

sis OR TSC," "lymphangioleiomyomatosis OR LAM," "case report." The search was limited to peer-reviewed articles published in English since 1995 with adult (age >18) human subjects. A total of 468 studies were screened and 159 studies underwent full-text review. Disagreements between the two reviewers (YG & PC) were resolved by consensus. In general, there were no prospective comparative trials available. Reported patient, lesions, and outcomes varied significantly. There were no prospective comparative trials identified (Fig. 1).

Diagnosis

Recommendation #1: All cases of suspected renal AML should be confirmed with either unenhanced computed tomography (CT), contrast-enhanced CT, or magnetic resonance imaging (MRI). Percutaneous biopsy should be considered if neither CT nor MRI are diagnostic.

The radiological diagnosis of AMLs is dependent on the detection of intertumoral fat. On ultrasound (US), the fat content in these lesions results in a characteristic appearance of a hyperreflective lesion with acoustic shadowing.[7] However, up to 30% of small (<3 cm) renal cell carcinomas (RCC) can mimic this appearance, reducing the specificity of US.[8] There is also a small proportion of AMLs (5%) that have significantly lower fat content, traditionally referred to as minimal fat AMLs, and may not have this characteristic appearance on US.[9] To improve the accuracy of US, adjunct methods, such as Doppler or contrast-enhanced US have been investigated. However, even with the use of both adjuncts, Ascenti et al reported a diagnostic accuracy of 78% when compared to pathological diagnosis.[10]

Unenhanced CT (UECT) is sensitive to detecting macroscopic fat in renal lesions. Although attenuation values of <10 HU in region of interest (ROI) are most often used to confirm fat, some have advocated for a lower cutoff of -15 or -30 HU to increase specificity.[11] Thinner slices have also been demonstrated to detect intralesional fat in smaller AMLs, with 3–5 mm slices identifying the vast majority of lesions.[12,13]

While most AMLs can be diagnosed with UECT, the majority of the patients worked up for an undifferentiated renal mass will undergo a multiphasic contrast-enhanced CT (CECT). AMLs generally demonstrate homogenous enhancement, delayed washout, and high intrinsic attenuation. The addition of contrast does not add significantly to the sensitivity of CT for the diagnosis of AML. Woo et al published a meta-analysis of 15 studies with 2258 patients demonstrating multiple feature analysis of CECT finding similar sensitivity to UECT (78% vs. 81%).[14]

Similar to UECT, MRI is excellent at identifying intralesional fat and may be more sensitive. Classically, fat appears hyperintense on T1 sequences and hypointense on T2 images. However, hemorrhagic cysts can have a similar appearance and, in these cases, chemical shift fat suppression sequences may be useful.[15] This has also been shown to help identify minimal fat AMLs. Song et al reviewed 98 pathologically confirmed minimal fat AMLs and found that 23% of them were identifiable on MRI but not CT.[16] However, there remained another 23% of histologically confirmed AML that were not discernable on CT or MRI. Song also proposed radiologically based categories for AMLs. Those
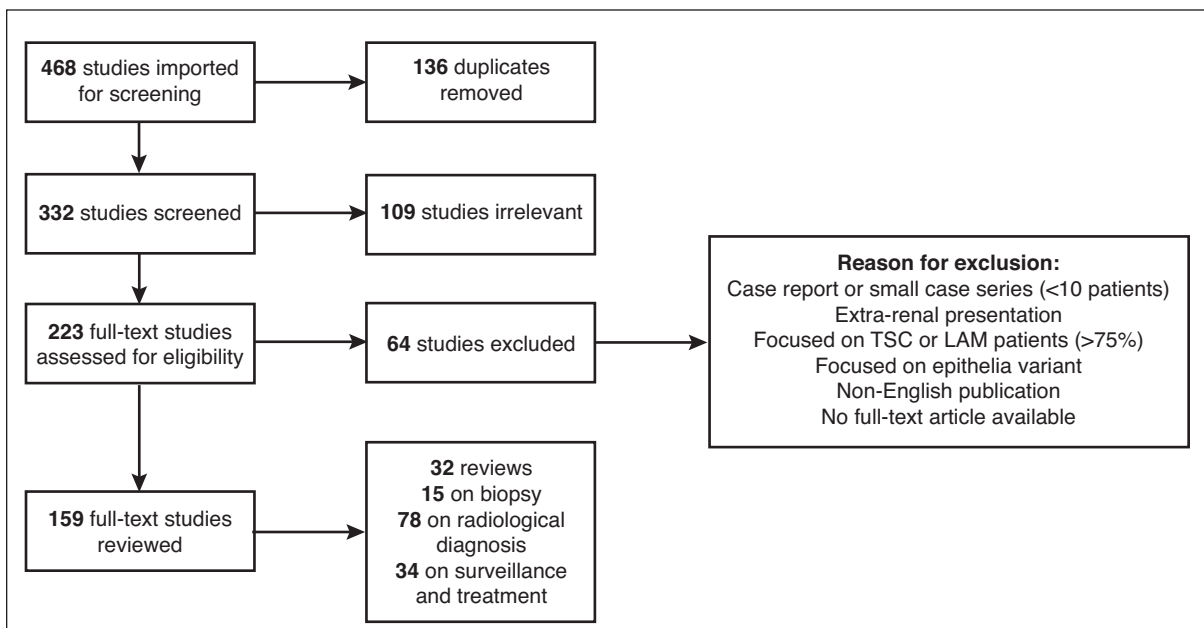

Fig. 1. PRISMA flow diagram of literature review. LAM: lymphangioleiomyomatosis; TSC: tuberous sclerosis complex.

with fat visible on CT were termed "fat-rich." The remainder, which would have been traditionally called minimal fat AMLs, further subdivided into "fat-poor" and "fat-invisible." Fat-poor AMLs were only identifiable with additional MRI imagining, while fat-invisible AMLs remain inconclusive.[16]

Although the diagnosis of AML depends on the identification of intra-tumoral fat, some rare fat-containing tumors may be malignant. Wilms tumors, extremely rare in adults, should be considered in pediatric populations. Liposarcomas are most often perirenal rather than developing from the kidney, and usually demonstrate renal displacement.[17] Rarely RCC may contain fat, especially large ones that entrap perirenal or sinus fat, or have calcifications representing osseous metaplasia.[18]

Epithelioid AMLs (EAMLs) are a rare variant of AMLs that are composed of epithelioid cells, with an absence of adipocytes and abnormal vessels.[19] While classified with classic AMLs, they can demonstrate malignant behavior. The majority of evidence we have regarding EAMLs is from case reports, and 18–49% of these have been estimated to be malignant.[20,21] Given the controversy over their malignant potential, some have further subdivided these lesions into pure EAMLs and AMLs with epithelioid components, with pure EAMLs more likely to be considered high-risk for metastatic spread. However, while EAMLs belong to the same pathological family as AMLs, they rarely resemble classic AMLs radiologically. The lack of adipose tissue in these lesions, particularly pure EAMLs, result in them being usually diagnosed as either RCCs or indeterminate/fat-invisible AMLs.[21,22] However, it must be noted that there remain rare case reports where these lesions were initially diagnosed as classic AMLs and only differentiated on pathology.[23] Unfortunately, given the lack of evidence, it is difficult to determine the incidence of such rare misclassifications. EAMLs must remain a consideration in the evaluation of fat-invisible lesions.

As there is no reliable way of imaging to differentiate fat-invisible AMLs from atypical-appearing RCCs or EAMLs, they may be managed as indeterminate solid renal masses and may require biopsy for diagnosis. A recent metanalysis on renal mass biopsies of 57 studies and 5228 patients from Marconi et al found an overall accuracy of 92% and only three significant (Clavian grade 2 or greater) complications.[24] They also found that core biopsies had a high sensitivity and specificity compared to fine needle aspiration (FNA), 99.1% and 99.7%, compared to 93.2% and 89.8%, respectively. There is also evidence that FNA may be particularly challenging in diagnosing AMLs. Zhou et al reviewed the FNA biopsies of 33 surgically diagnosed AMLs and found that only 49% of them were diagnosed correctly, with the remainder being non-diagnostic or described as RCCs.[25]

For lesions that are diagnosed as EAMLs or remain undifferentiated after biopsy, surgical resection is recommended, regardless of lesions size. After resection of pathologically confirmed EAMLs, there is no evidence for adjuvant therapy and observation is recommended. There is no data or evidence to suggest a followup schedule. However, applying the RCC followup guidelines may be reasonable.[26] In cases of metastatic EAMLs, again there is little evidence to guide local or systemic therapy but there are case reports of response to doxorubicin and everolimus.[27,28]

Natural history

The natural history of AMLs has been controversial and has played a significant role in treatment decision-making. Our review of contemporary reviews of AMLs on active surveillance (AS) identified nine articles with 1137 patients. It is important to note that these are all retrospective reviews of patients selected to be on AS and likely represent a favorable cohort. We found that over the average followup period of 37 months, 92% of AMLS observed were asymptomatic. The vast majority of AMLs remained stable in size, and only 9% of these lesions grew, with an average growth rate of 0.4 mm/year. The hemorrhage rate was also quite low, at 3%. No lesions were diagnosed to be malignant during followup.

Due to the influence of Oesterling's original paper, of the four articles that did differentiate outcomes by the size of the lesion, three used the 4 cm cutoff. When stratified by size, we found that lesions >4 cm appeared to be at a higher risk to be symptomatic (34% vs. 6%), grow (25% vs. 2%), and hemorrhage (16% vs. 1%). Examining individual articles that compared AMLs by size reveal significant heterogeneity of results. Maclean et al found that lesions >4 cm grew significantly faster than those <2 cm (odds ratio [OR] of 13.3 and p=0.02), while Bhatt et al found no difference (0.17 mm/year vs. 0.2 mm/year, p=0.86).[5,29] Ouzaid et al found that tumor size was significant as an independent predictor of discontinuation of AS for any reason (hazard ratio [HR] of 11.2, p=0.001), while Yamakato found that size was not a significant independent predictor of hemorrhage (p=0.07).[30,31] Based on our systematic review presented in Table 1, AMLs >4 cm did appear to be at a higher risk of hemorrhage compared to those <4 cm (1% vs. 16%) or those undergoing intervention (1% vs. 34%). The absolute risk, however, is much lower than originally described by Oesterling et al. We were also unable to find any high-level evidence demonstrating any statistically significant correlation between size and hemorrhage.

Followup

Recommendation #2: Once the diagnosis of AML is made, imaging and clinical evaluation should be carried out periodically. Traditionally, surveillance has been done on a biannual or annual basis, but consideration should be given to decreasing frequency once stability has been established.

Table 1. Baseline information and outcomes from active surveillance and observation groups

	n	Sporadic	Followup (months)	Size (cm)	Asymptomatic	Growth	Growth rate (mm/year)	Malignancy	Hemorrhage	Treatment
Sward, 2020[40]	45	100%	67	3.4	87%	47%	2.7	0%	2%	17%
Chan, 2018[41]	187	100%	24	0.9	100%	17%	0.13		0.5%	3%
Ruud Bosch, 2018[42]	53	100%	54					0%	17%	13%
Bhatt, 2016[29]	447	96%	43	NR 90% <4 cm	90%	9%	0.2	0%	2.5%	6%
Fittschen, 2014[43]	61	100%	25	NR	100%	3.3%				0%
Maclean, 201[45]	135	100%	22	NR 75% <2 cm 17% <4 cm 8% >4 cm		12%	0.7		2%	2%
Ouzaid, 2014[30]	130	92%	49	NR 71% <4 cm	78%	3%	0.9	0%	3%	13%
Mues, 2010[32]	45	100%	55	1.7			0.9		4%	6%
De Luca, 1999[44]	33	97%	60	NR	94%	8%	1	0%	0%	0%
All	1137	97%	37 22–67		92% 87–100%	9% 1–47%	0.4 0.1–1.3	0%	3.0% 0.5–17.0%	5% 0–13%
<4 cm	642				94%	2%	0.6 0.2–0.8		1% 0–4%	1% 0–4%
>4 cm	123				68%	25%	0.6 0.2–0.9		16% 6–31%	34% 23–38%

A decision for the cessation of monitoring should involve a discussion between provider and patient, weighing risks and benefits.

Oesterling's original paper recommended annual imaging for AMLs smaller than 4 cm and biannually for AMLs larger than 4 cm. Unfortunately, there have been no prospective studies to help guide our followup protocols since then. Our systematic review found that these lesions generally grow quite slowly, with average growth rates ranging from 0.1–1 mm/year, meaning it could take up to 10 years to grow 1 cm. However, there were outliers described in the case series, growing up to 1.5 cm per year.[32] Based on this, annual monitoring (or less frequently) would seem reasonable for the majority of lesions, and it may be reasonable to initially image more regularly and reduce frequency once stability is demonstrated. The majority of followup protocols we identified in our literature review used this strategy, with initially biannual imaging and then annual imaging after one year.

There is also limited evidence for identifying optimum imaging modality. While US alone is not sufficient for the diagnosis of AMLs, there is no evidence that CT or MRI improves followup care. An ideal followup protocol would minimize the risks of ionizing radiation and the costs of axial imaging. Another consideration is what duration of time routine imaging should continue for. The most prolonged followup protocol we found in our review was for approximately five years. However, given the lack of evidence, cessation of followup should be a shared decision between patient and provider,

taking into account the patient's general health status and competing risks of mortality, as well as their goals and concerns.

For indeterminate lesions, malignant lesions such as RCC or epithelioid AMLs cannot be ruled out. If proceeding with AS, these require more careful monitoring for progression.

Indications for intervention

Recommendation #3: The vast majority of AMLs are asymptomatic, have a low risk of hemorrhage, and can be monitored. There does appear to be an increased risk of symptoms and hemorrhage in lesions larger than 4 cm, but this is not based on high-level evidence. Symptomatic AML should be treated to ameliorate symptoms. Treatment for asymptomatic AML >4 cm should be discussed, with the understanding that the absolute risks of hemorrhage are lower than previously thought. Other factors that may influence the desire to treat include access to healthcare, women of childbearing age, and patient preferences.

Up to 92% of AMLs in contemporary series are asymptomatic; however, when symptoms are present, treatment should be considered to improve symptoms. Symptoms such as flank pain, palpable mass, or gross hematuria are more likely in larger lesions.[4] Based on natural history and the minimal risk of hemorrhage, small AMLs (<4 cm) rarely require intervention.

For AMLs larger than 4 cm, treatment should be discussed. While they do appear to be at a higher risk, the absolute risk of spontaneous hemorrhage seems lower than

previously estimated, and there is limited evidence for an absolute size threshold. In addition to size, several other factors may play a role in assessing the risk of hemorrhage of untreated AML. The presence of aneurysms and aneurysmal size has been linked to the risk of hemorrhage in several studies.[31] However, intratumoral aneurysms can only be reliably assessed through angiography and may not be clinically feasible for the majority of cases.[33,34]

Ongoing surveillance is a necessary pillar of AML management. For patients who have poor access to imaging or emergency care treatment, or who do not desire long-term monitoring, consideration (weighing risks/benefits) may be given to intervention.

Finally, hemorrhage of AML during pregnancy is an uncommon yet greatly feared complication. There may be a physiological basis to this increased risk, with estrogen receptor expression strongly associated with AMLs.[35] The only clinical evidence we have to rely upon are case reports. Cetin et al reviewed 26 case reports of AML during pregnancy in literature from 1994–2015 and found 81% presented with rupture (mean size 11 cm). Current evidence for rupture in this population is extremely weak and is based on case reports and a physiologic hypothesis.[36,37] However, given the high tradeoffs, the treatment of AMLs should be considered and discussed with reproductive-age women. These recommendations are consistent with the most recent European Association of Urology RCC guidelines.

Interventions

Recommendation #4: Both surgery and embolization are acceptable first-line management options for AML treatment. Surgery should be minimally invasive and nephron-sparing where possible. Re-treatment rates may be lower for surgery. Embolization is safe and may allow for a less invasive nephron-sparing approach in select cases; however, it appears to have a slightly higher recurrence rate.

In our systematic review, we identified: 12 articles on surgery, 10 articles on embolization, three articles on ablation, one article with surgery and embolization cohorts, and two articles with surgery, embolization, and active surveillance cohorts. Table 2 summarizes the reviewed studies by treatment intervention (See Supplementary Tables 1, 2, and 3 for more detail). Again, it is important to note the lack of prospective, randomized evidence in this space.

Our systematic review showed that surgical resection is an effective intervention in treating AMLs. In the 555 cases we identified in the literature, only four required a second treatment. In three, the retreatment was for a second AML on the contralateral kidney. The other was a patient who had a hematoma develop post-partial nephrectomy and then underwent a later radical nephrectomy. We found a 4% complication major complication rate (Clavian grade 2 or greater). The approach, whether laparoscopic or open, partial or radical, will depend on the individual tumor and surgeon preference. Given the benign nature of AML, a minimally invasive, nephron-sparing approach is preferred.

Transcatheter arterial embolization (TAE) is also an effective intervention in treating AMLs. TAE is advantageous in that it is minimally invasive, and it may be possible to offer a nephron-sparing approach in the face of large or technically challenging AMLs. Complication rates are similarly low; however, there is a significant re-treatment rate (41%) with either repeat TAE or surgery. In common practice, TAE is often considered to be the preferred intervention, especially in cases where a minimally invasive, nephron-sparing surgical approach is challenging, but there is a lack of evidence for its superiority over surgery.

There were no prospective, randomized trials comparing surgery and TAE. There appeared to be a difference in baseline characteristics between the treatment cohorts, with the TAE group having an average size of 10 cm compared to 5 cm in the surgery group. This likely represents selection bias in the trials, as TAE in larger tumors allowed a nephron-sparing approach. The quality of the studies makes it difficult to determine either treatment's superiority. Both will continue to have a role in the treatment of AMLs. Surgery does appear to be a more definitive approach, with minimal risk of re-operation. We found no evidence suggesting either is superior with regards to complications or changes in renal function. Surgery is the preferred approach in fat-invisible AMLs or indeterminate lesions where pathological diagnosis is needed

There is little evidence to support the use of ablation therapies in treating AMLs. This is compounded by the fact that AMLs small enough to be effectively treated by ablative techniques rarely require prophylactic treatment.

Table 2. Baseline information and outcomes from treatment groups

	# of studies	n	Sporadic	Followup (months)	Size (cm)	Asymptomatic	Minor adverse events	Major adverse events	Growth	Symptom resolution	2nd treatment
Surgery	12	555	90%	8–96	5.4	50%	16%	4%	0.50%	100%	0.75% (0–7%)
Embolization	10	267	85%	15–121	10.1	40%	37%	10%	19%	82%	41% (12–70%)
Ablation	3	45	91%	10–25	3.9	36%	52%	4%	0%	100%	0/NR
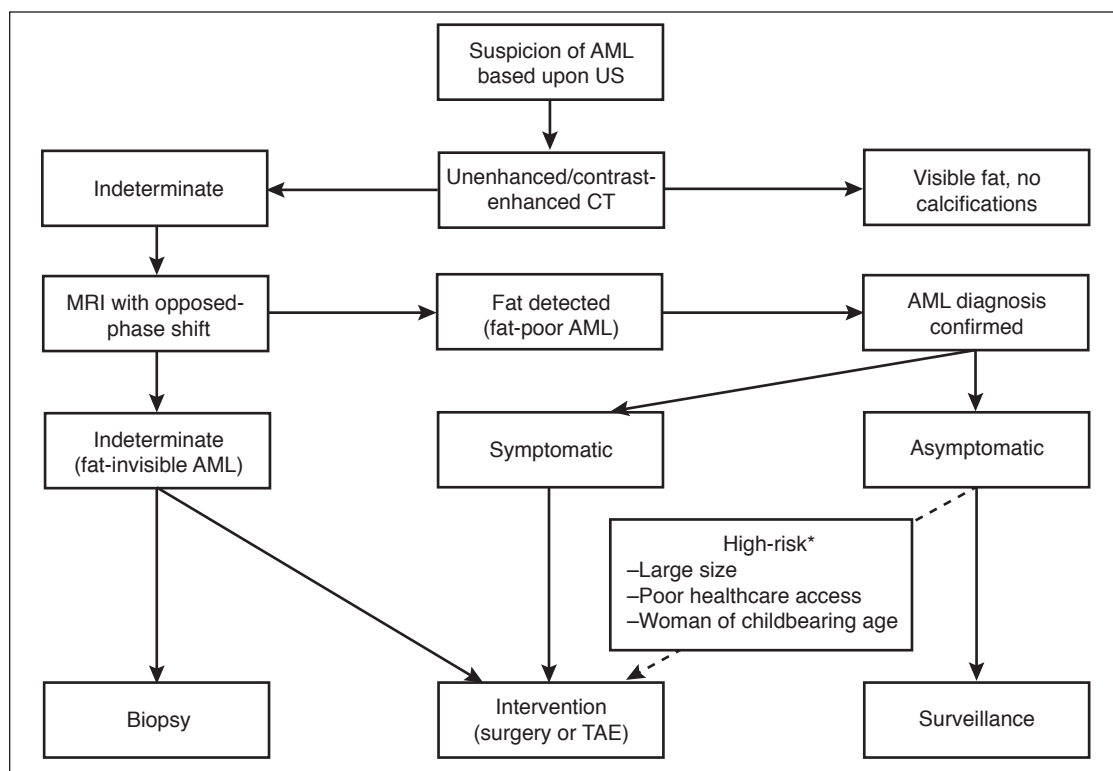
Fig. 2. Algorithm for the diagnosis and treatment of adult sporadic AMLs. *Intervention should be considered in those that are high-risk. AML: angiomyolipomas; CT: computed tomography; MRI: magnetic resonance imaging; TAE: transcatheter embolization; US: ultrasound.

Acutely bleeding AMLs

Recommendation #5: Transcatheter embolization should be the first-line treatment for acutely bleeding AML.

There have not been any prospective trials comparing interventions in acutely hemorrhaging AMLs. Traditionally, selective transcatheter embolization (TAE) has been the first-line treatment.[4] Compared to surgery, TAE is minimally invasive and preserves renal function, especially given the concern for the requirement of radical nephrectomy in this setting.

While there is minimal data in the acute setting, in general, embolization does appear to be associated with fewer complications but may have an increased risk of repeat intervention.[38] A surgical approach may be considered in patients that are hemodynamically unstable despite adequate supportive care.[39]

Acutely hemorrhaging AML in a pregnant woman is an extremely uncommon yet complex emergency that should be treated by a multidisciplinary team. In a hemodynamically stable patient with no sign of fetal distress, conservative management in a monitored setting can be attempted. Embolization and surgery are both options. In general, embolization offers a less invasive option, but factors such as fetal distress and maturity may make surgery the preferable option if an emergent C-section is mandated.[37]

Conclusions

Sporadic AMLs are seen and managed by most practicing urologists. The vast majority of these can be diagnosed radiologically with CT or MRI. While the risk of spontaneous retroperitoneal hemorrhage is present, this is much lower than originally described. Surveillance is a reasonable option in many of these cases. Despite the low level of evidence available, the previously prescribed strict 4 cm size cutoff for active intervention management is not supported by evidence in contemporary series. There is no evidence for the superiority of surgery or embolization for treatment. A proposed management algorithm is presented in Fig. 2.

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Supplementary Table 1. Literature review articles with multiple treatment arms

	n	Followup (months)	Size (cm)	Asymptomatic	Minor adverse events	Major adverse events	Growth	Symptom resolution	2nd treatment
Koo, 2010[45]	129	NR	4 (0.8–16)	75%					7 (5.5%)
Surgery arm	103						0%		1 (1%)
Embolization arm	26						23%		6 (23%) 2 partials, 4 embolizations
Mues, 2010[32]	91	55		80%					4
AS arm	45	55	1.7				0.8 mm/yr		3 (7%)
Surgery arm	38	54	3.8		2			100%	0 (0%)
Embolization arm	4	30	9.5					75%	1 (25%) partial
Seyam, 2008[46]	60	39	4	22%					
AS arm	31								
Surgery arm	23								
Embolization arm	6		11			0		83%	1 (17%)

It must be noted that these were all retrospective and did not have evidence of randomization. AS: active surveillance.

Supplementary Table 2. Literature review articles with surgical treatment of AMLs

	n	Followup (months)	Size (cm)	Asymptomatic	Treatment modality	Minor adverse events	Major adverse events	Growth	Symptom resolution	2nd treatment	Renal function
Fazeli-Matin, 1998[47]	27	39	7 (1.5–26)	48%	Partial and radical	6	1	0%	100%	0	Preop Cr 1.05, postop 1.43
Yip, 2000[48]	23	26 (1–80)	12.3 (1.5–30)	30%	Partial and radical	1	1	4%	100%	1 (RN)	NR
De Luca, 1999[44]	20	NR	8.1 (2.5–17)	55%	Partial and radical	NR	NR	NR	NR	NR	NR
Heidenreich, 2002[49]	28	58 (3–114)	5.5 (2.5–15)		Not specified	3	3	0%	100%	0	Preop Cr 0.9, postop 1.2
Boorjian, 2007[50]	58	96 (9–89)	3.9 (0.8–12.5)	41%	Partial	19	4	4%	100%	1 (embolization)	Preop Cr 1, postop 1.1
Minervini, 2007[51]	37	56 (10–120)	5.2 (1.5–15)	49%	Partial	4	1	0%		0	Preop Cr 0.95, postop 0.99
Lane, 2008[52]	209	41 (0–288)	4	50%	Not specified			0%	NR	0	NR
Msezane, 2010[53]	14	29	2		Partial	1	1	0%		1 (SAE after hemorrhage and NSS)	Preop GFR 99, postop 84
Lin, 2018[19]	23	40 (31–62)	5.2		Partial	5	0	0%		0	Preop GFR 102, postop 100
Liu, 2016[54]	40	23	6.2		Partial	2	1	0%		0	Preop GFR 43, postop 34
Golan, 2017[55]	40	8 (1–15)	7.2 (5–8.5)	75%	Partial	7	1	2.50%	100	1 (embolization)	Preop Cr 0.85, postop NR
Qin, 2017[56]	36		8.5		Partial ± embolization	4	0	0%	100%	0	NSS <33% GFR, NSS/SAE <15% GFR

AML: angiomyolipomas; Cr: creatinine; GFR: glomerular filtration rate; NSS: nephron-sparing surgery; RN: radical nephrectomy; SAE: selective arterial embolization.

Supplementary Table 3. Literature review articles with embolization of AMLs

	n	Followup (months)	Size (cm)	Asymptomatic	Treatment modality	Minor adverse events	Major adverse events	Growth	Symptom resolution	2nd treatment	Renal function
Tso, 2005[57]	12	48 (2–84)			Microsphere, coils	6	0	23%	41%		
Ramon, 2009[58]	41	58 (3–148)	10.3	51%	Polyvinyl alchohol	5	1	39%	97.50% (2 hemorrhage)		Preop Cr 0.89, postop Cr 0.87
Takebayashi, 2009[59]	10	26 (15–39)	7		Ethylene vinyl alchohol					3 (surgery)	4 pt 0.1–0.2mg/dl, 1 pt 1–2 mg/dl
Chick, 2010[60]	34	44 (12–116)	11.9 (2.9–24)	24%	Polyvinyl alchohol	12	6	17%	83%		
Chan, 2011[61]	27	85 (16–242)	10.9 (4–30)	48%	Polyvinyl alchohol, coils	11	6	6%	81% (2 hemorrhage, 1 SAE syndrome, 16 growth)	19 (2 embolization, 5 surgery)	
Chatziioannou, 2012[62]	10	15 (6–15)	8 (5–12)	30%	NR	4	0				
Duan, 2016[63]	25	50 (24–72)	12.7 (7.8–14)	0%	Polyvinyl alchohol, coils	15	2	4%	96%		Preop GFR 59 postop GFR 74
Sheth, 2016[64]	17	54 (2–266)	6.7 (3.3–14.6)	76%	Microspheres, coils, gelatin, alcohol	6	2			2 (embolization)	
Bardin, 2017[65]	23	21 (0–56)	8.9	74%	10 different agents	15	7	13%	91% (7 hemorrhage, 2 symptoms, 4 growth)	13 (8 embolization, 5 surgery)	Preop GFR 78 postop GFR 77
Anis, 2020[66]	68	121	9.8	46%	Ethanol and polyvinyl alcohol	NR	2		80%	32 (4 surgery, 28 embolization)	Postop GFR 82

AML: angiomyolipomas; Cr: creatinine; GFR: glomerular filtration rate; NSS: nephron-sparing surgery; SAE: selective arterial embolization.

Supplementary Table 4. Literature review articles with ablation of AMLs

	n	Sporadic	Followup (months)	Size (cm)	Asymptomatic	Treatment modality	Minor adverse events	Major adverse events	Growth	Symptom resolution	2nd treatment	Renal function
Castle, 2012[67]	15	100%	21 (1–72)	2.6 (1–3.7)		RFA (5 lap, 10 perc)	3	NR			NR	NR
Han, 2015[68]	14	100%	10 (6–36)	3.4 (0.8–6.1)	36%	Microwave	12	1	0%	100%	0	NR
Makki, 2017[69]	16	75%	25 (12–33)	4.7		Cryotherapy					NR	NR

AML: angiomyolipomas.