Journal of Surgery
[Jurnalul de Chirurgie]

Review Open Access

# Angiomyolipomas, A Shift in Perspective: from Benign to Malignant – Revisiting Diagnosis and Management Approaches

**Năstase Grigorie-Alexandru [1,8], Manole Maria[8,¥], Briceanu Oana-Georgiana[8] , Iftimie Nicolae-Florin[8], Harter-Radu Miruna[8], Cadar Ramona[1,8] , Trofin Ana-Maria[1,8] , Năstase Anda-Lucia[3] , Zabara Mihai[1,8] , Buescu Ovidiu-David[1,8], Buzincu Iulian[2,8], Duvac Rares-Cristian[4], Tailup Roxana[6], Akad Fawzy[7], Lupașcu Ursulescu Corina[6,8] , Vasilescu Alin-Mihai[5,8], Vlad Nuțu[5,8],Lupașcu Cristian Dumitru[1,8]**

1. Saint Spiridon Emergency County Hospital Iași, 2nd Surgery and Liver Transplant Clinic
2. Saint Spiridon Emergency County Hospital Iași, Anesthesia and Intensive Care Unit
3. Regional Institute of Oncology Iași. Anesthesia and Intensive Care Unit
4. Saint Spiridon Emergency County Hospital Iași, Clinical Pharmacology Department
5. Saint Spiridon Emergeny County Hospital Iași, 1st Surgery Clinic
6. Saint Spiridon Emergency County Hospital Iași, Radiology department
7. University of Medicine and Pharmacy "Grigore T. Popa" Iași, Morpho-Functional Sciences I, Anatomy
8. University of Medicine and Pharmacy "Grigore T. Popa" Iași, Faculty of Medicine, Romania

**Abstract.** Angiomyolipomas (AMLs) are mesenchymal tumors predominantly affecting the kidneys, with hepatic involvement being rare. Once considered uniformly benign, emerging evidence suggests a malignant potential in specific subtypes, particularly epithelioid AML (EAML). The classification of AMLs within the perivascular epithelioid cell tumor (PEComa) family has further expanded the complexity of diagnosis and management. Given their variable fat content, distinguishing AMLs from renal cell carcinoma (RCC) or hepatocellular carcinoma (HCC) through imaging alone remains challenging, often necessitating histopathological and immunohistochemical confirmation. **Aim.** This review aims to provide a comprehensive analysis of renal and hepatic AMLs, focusing on their classification, epidemiology, imaging characteristics, genetic alterations, and treatment strategies. We explore the challenges in differentiating AMLs from malignant tumors, highlighting the role of imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI). Additionally, we assess the evolving therapeutic landscape, including surgical intervention, transarterial embolization, and targeted therapies such as mammalian target of rapamycin (mTOR) inhibitors. Special attention is given to the management of high-risk cases, particularly those associated with tuberous sclerosis complex (TSC) and aggressive EAML variants. **Conclusion.** The recognition of AMLs' malignant potential has necessitated a shift in diagnostic and therapeutic approaches. While conservative management remains appropriate for smaller, asymptomatic tumors, surgical resection is recommended for larger or symptomatic lesions. The introduction of mTOR inhibitors has provided a non-surgical alternative in selected cases, particularly in TSC-associated AMLs. Further research is needed to refine risk stratification criteria and develop standardized treatment protocols for these complex tumors.

**Key words**: angiomyolipomas, mesenchymal tumors

**Corresponding author:** : Maria Manole mariamanole35@yahoo.com **Received**: January 31, 2025; Accepted March 20, 2025; Published March 31, 2025 Citation: Năstase G.-Al., Manole Maria, Briceanu Oana-Georgiana, Iftimie N-Fl., Harter-Radu Miruna, Cadar Ramona,Trofin Ana-Maria, Năstase Anda-Lucia , Zabara M., Buescu O.-D., Buzincu I., Duvac R.Cr., Tailup Roxana, Akad Fawzy, Lupașcu Ursulescu Corina, Vasilescu Al.-M., Vlad N., Lupașcu Cr.D. **Angiomyolipomas, A Shift in Perspective: from Benign to Malignant – Revisiting Diagnosis and Management Approaches.** Journal of Surgery [Jurnalul de chirurgie]. 2025; 21(4): 32 - 46, DOI: 10.22551/JSURG.2025.01.04 

**INTRODUCTION.** Angiomyolipoma (AML) is a benign mesenchymal tumor primarily localized in the kidneys, with hepatic involvement being a rare occurrence first described in 1911 (1). The hepatic variant, first described by Ishak in 1976, remains sparsely documented in literature (2).

AMLs are characterized by a triphasic composition of blood vessels, smooth muscle, and adipose tissue. While the presence of abundant lipid tissue typically facilitates

diagnosis, atypical cases lacking this feature pose diagnostic challenges, necessitating advanced investigative modalities. According to the World Health Organization (WHO) classification, AMLs originate from perivascular epithelioid cells (PECs), classifying them within the perivascular epithelioid cell tumor (PEComa) family. This broader category encompasses various tumor types, including angioleiomyomas, lymphangioleiomyomatosis, and non-specific PEComas of soft tissue and viscera (PEComa-NOS) (3). Historically, AMLs were uniformly considered benign, leading to predominantly conservative management strategies (1). However, the recognition of malignant potential and recurrence, particularly since the 2000s, has prompted a reevaluation of diagnostic and therapeutic paradigms. Dalle's report (4) of a renal AML (RAML) exhibiting vascular invasion, recurrence, and subsequent hepatic metastases challenged the conventional understanding of these tumors. Notably, differentiating epithelioid AML (EAML) from renal cell carcinoma (RCC) remains a persistent challenge in radiological imaging (5).

Renal AMLs are the most common presentation, occurring sporadically in approximately 80% of cases or in association with tuberous sclerosis complex (TSC) and lymphangioleiomyomatosis (LAM), both genetically linked conditions. TSC is the second most common etiological factor for RAML, with a female predilection. RAMLs represent the most prevalent benign renal neoplasm, accounting for 0.3-3% of all renal tumors, and were initially described by Grawitz in 1900. Fischer further defined this pathological entity in 1911, noting its disproportionate prevalence in females [1, 5].

Hepatic AMLs (HAMLs) are predominantly sporadic, with 5-10% occurring in the context of TSC, a significantly lower association compared to RAML's 20% [6]. Both renal and hepatic AMLs are frequently incidental findings, detected during routine investigations or evaluations for unrelated pathologies, as patients are often asymptomatic [7, 8].

Although the typical radiological presentation of AML is a fat-containing mass, HAMLs can exhibit minimal or absent fat, complicating differentiation from hepatocellular carcinoma (HCC), cholangiocarcinoma, or hepatocellular adenoma (HCA). Conversely, tumors with abundant fat may mimic lipomas. Given that HAMLs typically arise in non-cirrhotic livers, distinguishing them from HCC in the absence of viral hepatitis or cirrhosis history can be particularly challenging [7, 9, 10]. Furthermore, standardized management guidelines for HAML are currently lacking.

**EPIDEMIOLOGY.** The prevalence of AML is 0.28% in males and 0.6% in females. Approximately 80% of RAMLs occur sporadically, with 20% associated with TSC. RAMLs develop in 50-75% of individuals with TSC. These tumors exhibit a female predominance, with a mean age of presentation around 60 years, and typically present with larger tumor sizes in women. Estrogen therapy and pregnancy are associated with increased tumor growth and hemorrhage risk. While sporadic AMLs usually manifest between 50-60 years of age, TSC-associated AMLs tend to occur earlier, around 30-40 years [5, 11, 12,].

Hepatic AMLs also predominantly affect middle-aged women, although hormonal influence on tumor development is not established [13]. HAMLs most commonly present as solitary tumors in non-cirrhotic livers, predominantly in the right lobe (60% of cases), with a median size ranging from 2 cm to 12.7 cm [8]. A 2022 study of 113 patients with hepatic epithelioid AML (HEAML) reported a mean age of 36-60 years and a female-to-male ratio of 3.35:1 [14].

**DIAGNOSTIC. Clinical features:**

***A) RENAL ANGIOMYOLIPOMA:***

The majority of RAML patients are asymptomatic. Symptomatic presentations may include flank pain, gross hematuria, and hypertension, with severe retroperitoneal hemorrhage as a potential complication. The classic symptomatic triad consists of flank pain, palpable flank mass, and hematuria. Lenk's triad, indicating rupture and hemorrhage, involves abdominal tenderness and acute flank pain. Wunderlich syndrome, characterized by non-traumatic spontaneous perinephric hemorrhage, is a medical-surgical emergency, with one-third

of cases progressing to hemorrhagic shock. Hypovolemic shock or retroperitoneal hematoma, occurring in 10% of symptomatic patients, may also be the initial presentation [15, 16, 17]. Epithelioid AML (EAML) is a rare variant with malignant potential, occurring in various locations, including the kidney. Renal EAML (REAML) can manifest with non-specific symptoms such as fever, fatigue, and abdominal pain, as well as hematuria, dysuria, and renal dysfunction. Anemia and urinary tract infections may also be present [18, 19, 20, 21, 22].

**B) HEPATIC ANGIOMYOLIPOMA:**

Most HAML patients are asymptomatic, with symptoms generally arising from mass effect, including a palpable mass, abdominal discomfort, upper abdominal pain, and bloating. Non-specific symptoms such as fatigue, fever, and weight loss can also occur. Symptom onset is more common with tumors exceeding 5 cm, a size threshold considered a surgical indication due to increased risk of complications such as rupture and hemorrhage. These complications are also associated with pregnancy. Additional non-specific symptoms include weight loss, malaise, and fever. Symptom incidence reaches 89% in tumors exceeding 10 cm, supporting the recommendation for resection of tumors larger than 5 cm [6,8]. Liver function tests and serum tumor markers (alpha-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9) are typically normal [8,23]. However, large tumors may result in biochemical evidence of altered liver function [24].

## GENETICS:

Tuberous sclerosis complex (TSC) is a significant etiological factor for AML, an autosomal dominant condition caused by mutations in the TSC1 (9q34) and TSC2 (16p13) genes. These genes encode tuberin and hamartin, respectively, which form a complex inhibiting the mTOR pathway. Mutations result in increased mTOR activation, leading to uncontrolled cell growth and differentiation [25, 26]. Cohort analyses have identified TSC2 as the most common pathogenic factor in EAML, with ATRX, TP53, and RB1 mutations frequently observed in malignant cases [28]. TFE3 gene rearrangements have been reported in malignant PEComas, activating the mTOR pathway and potentially driving tumorigenesis. Recent studies suggest that TFE3-rearranged tumors represent a distinct clinical and pathological entity [28, 29].

In genetic cases, the situation differs significantly, as when TSC is associated with kidney disease, it becomes the leading cause of death in adults with TSC. The renal lesions found are often multiple, bilateral, and progress in time, with a tendency to recur after embolization. Additionally, new formations may develop over time, ultimately leading to end-stage renal disease (ESRD). This represents a major morbidity for patients, necessitating dialysis or renal transplantation [30].

Sporadic RAMLs are typically solitary and smaller than 4 cm, while TSC-associated RAMLs are often multifocal, larger, and bilateral [25, 32, 33]. Renal PEComas with Xp11 translocation can mimic Xp11 translocation renal cell carcinoma; however, the two can be differentiated by the epithelial marker expression. Furthermore, renal PEComas with this translocation exhibit a more aggressive phenotype and poorer prognosis [34].

## IMAGING:

***A) RENAL ANGIOMYOLIPOMA:***

Imaging studies are essential for the detection of renal AML, particularly EAML due to its malignant potential. Ultrasonography (US) is limited in its ability to differentiate AML from other renal tumors but can be useful for follow-up. Typical RAML appears as a homogeneous hyperechoic mass with acoustic shadowing, whereas EAML, due to its low-fat content, lacks specific US features. Contrast-enhanced computed tomography (CT) is the preferred imaging modality, demonstrating high sensitivity and specificity. RAML characteristically presents as a hypodense lesion with a CT value less than 10 HU. EAML exhibits abnormal hypervascularization, increased cellular density, and heterogeneous enhancement. Larger tumors (over 7 cm) may display mixed-density mass shadows (greater than 45 HU), necrosis, and hemorrhage. Magnetic resonance imaging (MRI)

is useful for differentiating fat-rich tumors, with AML typically being T1 and T2 hyperintense. Fat-poor or epithelioid tumors with rich vascularization raise suspicion for malignancy and may exhibit hyperintensity on T1 and hyposignal on T2. CT scan classify fat-rich versus fat-poor RAML using a threshold of −10 HU, with MRI further differentiating fat-poor from fat-invisible RAML [17, 35, 36, 37].

***B) HEPATIC ANGIOMYOLIPOMA**:*

A review analyzing data up to 2016, of 292 patients, reported, of 195 patients with image conclusions, 28,2% where diagnosed with HAML, 16,3% with another benign tumor, and 39,2% with malignat formations, and 2,2% were not able to produce a diagnosis. Biopsies of 32 patients determined that 78.1% of those were HAMLs [13]. US reveals a heterogeneous hyperechoic mass with hypoechoic areas, but is limited in low-fat content tumors. CT and MRI are essential for evaluating hepatic tumors [37].In most hepatic epithelioid AMLs (HEAMLs), imaging reveals a hypervascular mass with intratumoral fat and tortuous vessels [15]. On unenhanced CT, HAML appears as a heterogeneous, low-density mass with attenuation values less than -50 HU. Vascularized HAMLs exhibit washout, while less vascular tumors demonstrate persistent portal and late-phase enhancement. MRI shows hyperintensity on both T1- and T2-weighted sequences. Angiography can highlight hypervascularity and tumor blush [38].

Maebayashi et al. described a blotchy vascular pattern in some cases, potentially reflecting abnormal leiomyomatous vessels, which may aid in the imaging diagnosis of PEComa [39]. Preoperative imaging often misinterprets HEAML as hepatocellular carcinoma, angiosarcoma, hemangioma, or metastatic lesions. The CT and MRI characteristics of HEAML are similar to other hypervascular liver tumors, such as HCC, focal nodular hyperplasia (FNH), and hepatic hepatocellular adenoma (HCA). HEAML is hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Differentiation from HCC relies on HCC's "rapid filling and rapid excretion" pattern and a well-defined border in the delayed phase. FNH, the second most common benign liver lesion, exhibits homogeneous arterial enhancement except for the central scar, which is a key distinguishing feature, along with delayed enhancement. Tumors with poor vascularity, such as fat-rich lipomas and HCA, demonstrate minimal enhancement [14]. For the differential diagnosis, it has been suggested that in tumors smaller than 7 cm, the presence of hemorrhage should be assessed, while for tumors of any size, a blotchy vascular pattern should be investigated. In the absence of a history of viral hepatitis and in the presence of imaging findings that do not suggest PEComa or are atypical for hepatocellular carcinoma (HCC), PEComa should still be considered a presumptive diagnosis [38].

**HISTOLOGY:**

Histological examination remains the gold standard for diagnosing both renal and hepatic AML. PEC omas are classified into three histological patterns: Pattern A (carcinomatous growth), resembling RCC, characterized by large, polygonal cells with eosinophilic cytoplasm arranged in cohesive clusters, with atypical mitoses, nuclear pleomorphism, and prominent nucleoli, indicating high malignant potential; Pattern B (diffuse growth), less aggressive, with uniform epithelioid cells arranged in compact cords and sheets, exhibiting lighter cytoplasm and fewer mitoses; and mixed pattern tumors with transitional areas between the two. The PEC oma family also includes lymphangioleiomyomatosis (LAM), clear cell "sugar" tumor of the lung, and other rare tumors [40, 41, 42, 43]. The modern classification of RAML, based on fat content, includes fat-rich (classic), fat-poor, and epithelioid (fat-invisible) variants. Traditional renal classification distinguishes typical (triphasic) AML from atypical (monophasic or epithelioid) AML. AML classification based on predominant cell type categorizes tumors as epithelioid, spindle, or intermediate. Macroscopically, RAMLs vary in color depending on the predominant tissue component. In addition to AMLs, patients with TSC may develop renal cysts, which can lead to

end-stage renal disease (ESRD). The overall risk of ESRD in TSC patients is estimated to be up to 7% [30, 41, 42, 43, 44, 45].

Epithelioid PEComa of the kidney is a malignant tumor with a high risk of metastatic disease and mortality. Renal epithelioid AML (REAML) has malignant potential, with the ability to invade the renal vein, metastasize, and cause significant morbidity, with unfavorable prognostic factors, such as necrosis, frequent mitoses, carcinoma-like growth pattern, and extrarenal extension [46, 47, 48]. Carcinoma-like growth pattern and extrarenal extension were found as independent prognostic factors [35]. Some authors consider cellular atypia, multicentricity, mitotic activity, and distant metastasis as pathological criteria for malignancy [41, 49].

Hepatic AMLs are classified according to the relative proportions of tissue types: mixed (conventional), lipomatous, myomatous, and angiomatous. The mixed and myomatous types are most common. The angiomatous variant can mimic an intrahepatic aneurysm. Inflammatory AML (IAML) and pelioid types have also been described, complicating diagnosis due to their similarity to other mesenchymal tumors [50, 51]. IAML requires more than 50% inflammatory infiltration for diagnosis, has a good prognosis, and is treated surgically. Hypotheses regarding association of IAML with IgG4-pseudotumor have been raised [51, 52]. Inflammatory cells include lymphocytes, plasma cells, and histiocytes [53]. Metastatic breast cancers can present as IAML in the liver [54, 55, 56].

HAML dimensions vary widely. It is well-circumscribed but unencapsulated, although partial encapsulation has been reported [6, 57, 58, 59, 60]. It is typically slow-growing. Most HEAMLs are solitary lesions [6]. Macroscopically, they are well-circumscribed and vary in color [8]. HEAML can be misdiagnosed as HCC due to similar appearances, but HEAML lacks a true capsule [58]. PEComas are more common in the right lobe of the liver [39].

**IMMUNOHISTOCHEMISTRY:**

As we have seen, imaging is not sufficent for a certain diagnosis. Biochemical tests are also inconclusive, as for HEAML liver function tests and serum tumor markers (alpha-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9) are typically normal [23]. However, large tumors may result in biochemical evidence

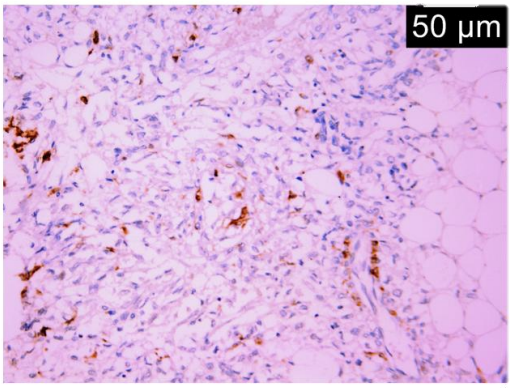


Figure 2. Renal Angiomyolipoma (IHC) from Saint Spiridon Emergency County Hospital Iaşi archive: HMB-45 focal

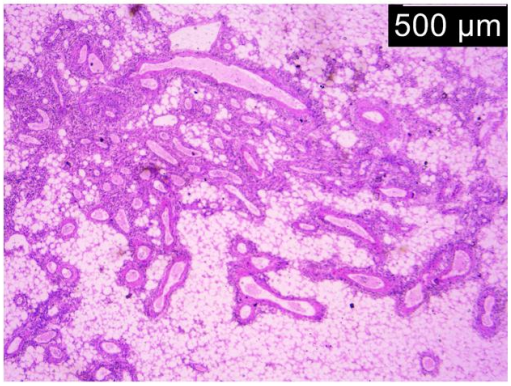


Figure 1. Renal Angiomyolipoma (HE) from Saint Spiridon Emergency County Hospital Iaşi archive: Triphasic tumor, well-defined, with a pseudocapsule; the tumor consists of three components: spindle cells (moderate nuclear pleomorphism, perivascular distribution), mature adipose tissue, blood vessels of varying calibers.

of altered liver function [24]. The “gold standard”for diagnosing EAML is through immunohistochemistry techniques. There is no standard threshold for epithelioid cells to diagnose EAML. WHO recommends greater than 80%. Core needle biopsy (CNB) has better sensitivity and specificity than fine needle aspiration (FNA), but EAML's large size can affect CNB accuracy [61]. Surgical exploration is recommended for tumors not evaluable by FNA. Macroscopically, EAML is nodular, soft, and partially cystic. Microscopically, epithelioid cells are arranged around hyalinized vessels, with abundant cytoplasm, clear or eosinophilic

staining, and potential for abnormal mitoses and necrosis [62, 63].

Immunohistochemistry confirms the diagnosis by demonstrating melanocytic factors (SOX10, HMB-45, Melan A, MITF, NKI-3) and muscle factors (SMA- fig. 3). HMB-45 (fig. 2, fig. 6) and Melan-A are the most sensitive markers [64, 65]. Epithelial markers are absent, aiding in differentiation from HCC and RCC [64, 65, 66]. S100 (fig. 4) can differentiate EAML from melanoma. PNL2 is sensitive and specific for malignant PEComa. Pervalbumin is also present in EAML [67]. Cathepsin K and muscle markers are explored for PEComa, with cathepsin L as a potential therapeutic target [68]. Spindled tumors express muscle markers, while epithelioid tumors express melanocytic markers [69].

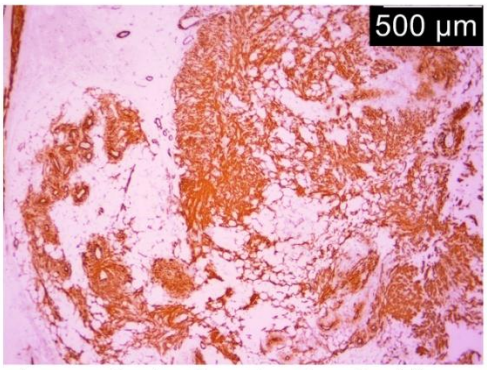


Figure 3. Renal Angiomyolipoma (IHC) from Saint Spiridon Emergency County Hospital Iași archive: SMA difuse positive

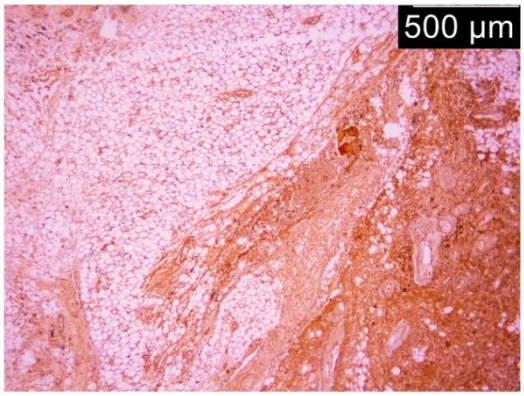


Figure 4. Renal Angiomyolipoma (IHC) from Saint Spiridon Emergency County Hospital Iași archive: S100 difuse positive

Gastrointestinal stromal tumors (GISTs) can be considered due to fusiform cells and KIT (CD117) expression, but adipocytic tissue and low mitotic rate differentiate HAML. HEAML must be distinguished from HCC and leiomyoma [10, 40]. HCC shows atypical trabecular cells, increased nucleus-to-cytoplasm ratio, and infiltrative growth [70]. Leiomyoma expresses myogenic markers but lacks chromatophore markers [65, 71].

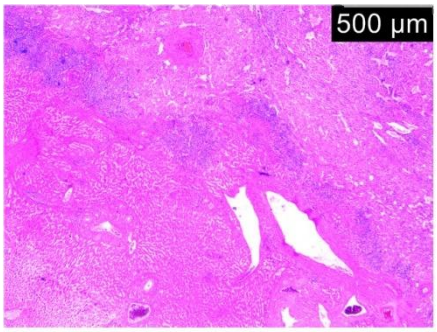


Figure 5. Hepatic Angiomyolipoma (HE) from Saint Spiridon Emergency County Hospital Iași archive with Subcapsular nodular mesenchymal proliferation, circumscribed but non-encapsulated; the tumor consists of spindle cells (myoid/myofibroblastic, eosinophilic cytoplasm), myxoid stroma with xanthomatous, lipoid, and lipoblast-like cells.

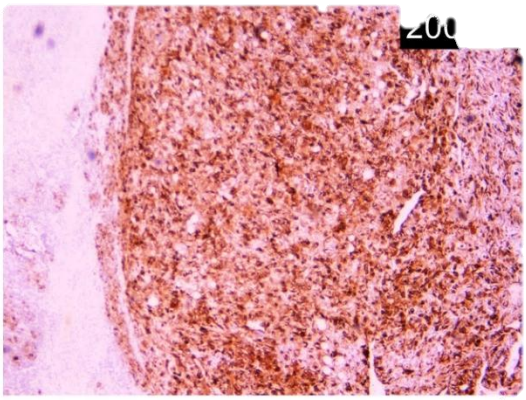

Figure 6. Hepatic Angiomyolipoma (IHC) from Saint Spiridon Emergency County Hospital Iași archive: HMB-45

## TREATMENT:

### *A) RENAL ANGIOMYOLIPOMA:*

Risk factors such as tuberous sclerosis complex (TSC), childbearing age, and large tumor size significantly influence treatment decisions. For patients diagnosed with sporadic renal angiomyolipoma (RAML), treatment is guided by the risk of hemorrhage and the

potential for malignant transformation [16, 38, 72, 73, 74]. **Biopsy in guiding the treatment.**

A definitive diagnosis of angiomyolipoma (AML) typically requires a biopsy; however, its use is limited by the risk of rupture. Biopsy is generally avoided in fat-rich AML but may be considered for fat-invisible AML when MRI findings are [16, 38, 72, 73, 74]. Histopathological findings associated with a high risk of malignant transformation include:

- Presence of >70% epithelioid cells
- Lymphovascular invasion
- ≥2 mitotic figures per 10 high-power fields
- Atypical mitotic figures
- Necrosis [16, 17]

### *I. Conservative Management*

Patients with benign-appearing lesions, tumor size below 6 cm, or low hemorrhagic risk may be managed conservatively. There is no standardized surveillance protocol; however, clinical examination and CT scans at 6 and 12 months, followed by annual imaging, are recommended to assess tumor growth [16, 38, 72, 73, 74].

Monitoring tumor progression is crucial, as a rapid increase in size correlates with a higher risk of hemorrhage. Specifically, tumor growth exceeding 0.25 cm per year has been associated with a significant increase in hemorrhagic risk. Conversely, tumors with poor vascularization demonstrate minimal risk of hemorrhage [75].

Most sporadic RAMLs exhibit a slow growth rate of 0.015–0.1 cm per year, warranting less frequent imaging follow-ups [76]. However, TSC-associated RAMLs (TSC-RAMLs) exhibit a markedly higher growth rate of approximately 1.25 cm per year. For these patients, the **International Tuberous Sclerosis Complex Consensus Conference** recommends abdominal MRI screening every 1–3 years to ensure timely intervention [77].

### *II. Active management*

Approximately 11% of monitored tumors grow, and 5.7% require active treatment [73,74]. Laparoscopic or robotic partial nephrectomy is used for symptomatic, large, or suspicious tumors [73]. The indication for **active treatment** is based on **tumor size, malignant potential, and increased hemorrhagic risk**. Available treatment options include **mammalian target of rapamycin (mTOR) inhibitors, embolization, and surgery [4]**.

**Surgical intervention** is recommended for **symptomatic tumors or those with a high risk of malignancy** [72, 73, 74]. **Tumors larger than 6 cm** are associated with a **higher risk of bleeding**, as well as the **presence of aneurysms exceeding 5 mm in diameter**, which further increases the hemorrhagic risk [78]. A study conducted by Zhang Y et al. identified independent factors influencing the risk of RAML rupture, including symptoms at presentation (e.g., flank pain on the affected side), tumor size, tumor vascular supply, and tumor growth rate. The authors developed a scoring system based on four independent risk factors, demonstrating that patients with sporadic RAML and a score ≥7 were at a higher risk of tumor rupture and required early intervention. The most critical risk factor for RAML rupture was flank pain, which was highly associated with tumor rupture and subsequent hemorrhage [79].

*a) Embolization*

Embolization is the preferred approach in cases of rupture or hemorrhage. **Selective arterial embolization (SAE)** has additional advantages in specific situations, such as tumors located in difficult-to-access areas (e.g., hilar tumors). It can also be utilized for patients with high surgical risk. For large RAMLs, SAE provides the added benefit of tumor size reduction when performed prior to surgery. This preoperative embolization facilitates the surgical procedure by reducing operative time, minimizing hemorrhagic risk, and preserving renal function. Otherwise, it has a considerable risk of reccurence [4, 36, 80, 81].

*b) Ablative procedures*

Cryoablation and radiofrequency ablation (RFA) also have a low risk of reccurence and are preferred for small tumors, while nephrectomy is suitable for tumors larger than 7 cm [16, 72, 73, 74].

Cryotherapy has shown success in some angiomyolipoma cases, but data is insufficient for routine recommendation. Clinical trial

participation is recommended, and combining embolization with cryotherapy may improve outcomes for larger tumors, though no data currently supports this approach [4,82]. RFA is a minimally invasive and effective treatment for angiomyolipomas, with minimal complications. It is ideal for small asymptomatic tumors but can also target larger masses. RFA selectively ablates tumor tissue while preserving normal renal function. Studies on small renal angiomyolipomas show promising results, with successful treatment leading to tumor shrinkage and low complication rates. In larger tumors, RFA has demonstrated safety and effectiveness without hemorrhagic events. The procedure is typically guided by CT, though ultrasonography is an alternative. Combining RFA with superselective renal artery embolization has shown high success rates, but further research is needed to confirm long-term benefits [4, 83].

*c) Surgical treatment*

Surgical treatment, particularly nephron-sparing surgery (NSS), has the lowest risk of recurrence [16, 72, 73, 74]. **NSS** offers significant advantages over nephrectomy, including **better renal function preservation and improved survival outcomes**. However, when **RAMLs displace the majority of the renal parenchyma** or present a **high risk of malignancy**, nephrectomy may be the preferred approach [16, 36, 72, 73, 74, 84].

***d) Treatment for TSC-Associated RAMLs***

In TSC-associated renal angiomyolipomas (TSC-AML), surgery is generally not first-line due to the multifocal and bilateral nature of lesions, which can lead to significant renal tissue loss. Up to 80% of individuals with TSC develop AMLs, often at a young age (median 8.6 years), in contrast to sporadic AMLs, which typically appear around 45–50 years. Lesions larger than 3 cm and aneurysms over 5 mm carry a significant risk of life-threatening hemorrhage. These tumors are linked to loss of heterozygosity in TSC1 or TSC2 genes, affecting the mTOR signaling pathway. The development of mTOR inhibitors, especially everolimus, has transformed treatment paradigms. While embolization was previously recommended for all lesions >3 cm, it is now largely reserved for acute bleeding. For most patients without contraindications, everolimus is considered first-line therapy. As an mTORC1 inhibitor, it not only reduces tumor volume but also helps preserve renal function and may positively influence life expectancy. In patients with TSC2/PKD1 contiguous gene syndrome, everolimus decreases tumor volume but has limited impact on renal function. Clinical trials have demonstrated that over 50% of patients achieve at least a 50% reduction in AML volume after 24 weeks of treatment. Although generally well tolerated, common side effects include stomatitis, nasopharyngitis, and acneiform rash. Given the potential for tumor regrowth after discontinuation, long-term mTOR inhibitor therapy is often necessary, with growing evidence supporting its safety and efficacy in adults [30, 85, 86].

A 2019 study demonstrated that everolimus reduces the size of angiomyolipomas in more than half of cases, particularly when the lesions are smaller than 4 cm. It is primarily used as a second-line treatment for TSC-AML following embolization. No significant difference was observed in the mean reduction rate of angiomyolipoma volume between second-line everolimus therapy for regrown TSC-AML after transarterial embolization (TAE) and first-line everolimus treatment [87].

*e) Oncological treatment for malignant PEComa*

The treatment of malignant PEComa remains a significant challenge, as the tumor exhibits poor responsiveness to both chemotherapy and radiotherapy [88]. Current therapeutic approaches for malignant PEComas include surgical intervention, chemotherapy, targeted therapy, endocrinological therapy, and immunotherapy. For localized disease, surgical resection remains the optimal course of action [89].

Nab-sirolimus, an mTOR inhibitor formulated as a sirolimus albumin-bound nanoparticle, received FDA approval in 2021 for the treatment of PEComa. A phase II clinical trial assessed the efficacy of nab-sirolimus in malignant PEComas, demonstrating a clinically meaningful overall response rate, with a median

duration of response exceeding three years. Additionally, the treatment was associated with durable disease control and prolonged survival. The most pronounced responses were observed in patients with tumors harboring **TSC2** mutations; however, responses and sustained disease control were also noted in patients with other tumor genotypes. These findings suggest that mTOR inhibition may be effective in a broader patient population with malignant PEComa. Further studies are required to validate these results and fully establish the therapeutic potential of nab-sirolimus [90].

***B) HEPATIC ANGIOMYOLIPOMA:***

Surgical resection remains the only curative treatment for hepatic epithelioid angiomyolipoma (HEAML). However, overtreatment should be avoided to minimize the risk of surgical complications. Currently, there is no standardized protocol for the management of HEAML patients [8, 13, 23, 40, 91]. ***Biopsy in guiding the treatment***

If the tumor is in an accessible location, biopsy is recommended [34]. However, biopsy is not advised in patients with a documented diagnosis of tuberous sclerosis complex (TSC), as multiple hepatic angiomyolipomas are considered a hallmark of this condition. Multiple hepatic angiomyolipomas are frequently observed in patients with TSC, particularly in those with bilateral diffuse renal angiomyolipomas [92].

***I. Conservative treatment***

Klompenhouwer et al. estimated a cumulative growth rate of 0.77 cm per year in patients who underwent conservative management with biopsy-proven HEAML. Based on these findings, the authors proposed active surveillance at one year if the lesion is definitively diagnosed as HEAML. However, if imaging and biopsy findings remain inconclusive, surgical resection should be performed. In patients with TSC, more frequent surveillance is recommended [13].

***II. Active treatment***

*a) Embolization*

There are not many cases of HAML resolved with embolization. Some of the ones for which it was opted for this technique presented hemorrage and had the diameter ranging from 2.5 cm to 12.5 cm. In some cases, this procedure was followed by surgical resection [40].

In a retrospective study, three patients with histologically confirmed large HAML (11, 12, and 17 cm) underwent therapeutic arterial embolization, showing no progression after an average follow-up of 12.7 months. The risk of spontaneous hemorrhage appears to be lower in HAML rather than in renal AML, which is typically supplied by a single vessel and associated with aneurysms. Given the soft consistency of large AML, similar to hepatic adenomas or HCC, there is some bleeding risk. Considering its safety and effectiveness in preventing severe complications, embolization is a reasonable approach, particularly for large, peripherally located tumors. Embolization may also have a palliative role, while chemotherapy has minimal impact in AML treatment. The metastatic disease can be treated with systemic chemotherapy, hepatic artery embolization, or embolization plus intra-arterial chemotherapy. Given the soft consistency of large AML, similar to hepatic adenomas or HCC, there is some bleeding risk. Considering its safety and effectiveness in preventing severe complications, embolization is a reasonable approach, particularly for large, peripherally located tumors. Embolization may also have a palliative role, while chemotherapy has minimal impact in AML treatment [91].

*b) Surgical treatment*

Surgical resection is indicated in symptomatic patients, in cases where tumors exhibit an aggressive pattern (e.g., significant changes in size on imaging, high proliferation activity, or an atypical epithelioid pattern on liver biopsy), in biopsy-confirmed HEAMLs larger than 5 cm, and when imaging or histological findings remain inconclusive. In all other cases, a conservative approach may be considered [40]. Surgical resection should also be considered in cases of inconclusive biopsy results, progressive symptoms, or tumor growth during follow-up. Most importantly, given the rarity of this disease, shared decision-making and multidisciplinary consultation in expert centers remain crucial for optimal management [64].

*c) Systemic therapy*

Pharmacological treatment represents a viable therapeutic alternative. Everolimus has demonstrated efficacy in a clinical trial involving patients with TSC-associated hepatic angiomyolipoma (TSC-HAML) or sporadic angiomyolipoma (AML) with lesions smaller than 3 cm. The study reported a reduction in lesion size of more than 50% in 42% of patients [85].

**CONCLUSION:**

Angiomyolipomas, both renal and hepatic, present a spectrum of clinical and pathological features, requiring a multidisciplinary approach for diagnosis and management. Advances in imaging and immunohistochemistry have improved diagnostic accuracy. The recognition of malignant potential has shifted treatment paradigms, emphasizing the need for personalized strategies. Further research is needed in order to develop a standard protocol of care.

NOTES: *All authors contributed equally to this work.

**Conflicts of Interest:** The authors declare no conflicts of interest regarding the publication of this paper.

**References**


1. W. F. Dienierenturomorenbei der Tuberosen Hirsklerose Zeigler Beite. Z Path Anat UZ allg Path. 1911; 50: 235-282.
2. Ishak K. Mesenchymal tumors of the liver. In Okuda K, Peters R, editors. Hepatocellular carcinoma. New York: Wiley Medical; 1976. p. 247-307.
3. Krawczyk M., Ziarkiewicz-Wróblewska B., Wróblewski T., et al. PEComa-A Rare Liver Tumor. J Clin Med. 2021; 10(8): 1756.
4. Dalle I., Sciot R., de Vos R., et al. Malignant angiomyolipoma of the liver: a hitherto unreported variant. Histopathology. 2000; 36(5): 443-50.
5. Skelton W., Leslie S., Publishing. Renal Angiomyolipoma. In. Treasure Island (FL): StatPearls Publishing; 2025.Tsui WM, Colombari R, Portmann BC, et al. Hepatic angiomyolipoma: a clinicopathologic study of 30 cases and delineation of unusual morphologic variants. *Am J Surg Pathol*. 1999; 23:34–48.
6. Cai PQ, Wu YP, Xie CM, et al. Hepatic angiomyolipoma: CT and MR imaging findings with clinical-pathologic comparison. *Abdom Imaging*. 2013;38(3):482-9.
7. Yang CY, Ho MC, Jeng YM, et al. Management of hepatic angiomyolipoma. *J Gastrointest Surg*. 2007;11(4):452-7.
8. Jeon TY, Kim SH, Lim HK, et al. Assessment of triple-phase CT findings for the differentiation of fat-deficient hepatic angiomyolipoma from hepatocellular carcinoma in non-cirrhotic liver. *Eur J Radiol*. (2010) 73:601–6.
9. Liu W, Wang J, Huang Q, et al. Comparison of MRI Features of Epithelioid Hepatic Angiomyolipoma and Hepatocellular Carcinoma: Imaging Data From Two Centers. *Front Oncol*. 2018; 8:600.
10. Çalışkan S, Gümrükçü G, Özsoy E, et al. Renal angiomyolipoma. *Rev Assoc Med Bras*. 2019; 65:977–981.
11. Shepherd CW, Gomez MR, Lie JT, et al. Causes of death in patients with tuberous sclerosis. *Mayo Clin Proc*. 1991; 66:792–796.
12. Klompenhouwer AJ, Verver D, Janki S, et al. Management of hepatic angiomyolipoma: A systematic review. *Liver Int*. 2017;37(9):1272-1280
13. Junhao L, Hongxia Z, Jiajun G, et al. Hepatic epithelioid angiomyolipoma: magnetic resonance imaging characteristics. *Abdom Radiol (NY)*. 2023;48(3):913-924.
14. Flum AS, Hamoui N, Said MA, et al. Update on the diagnosis and

management of renal angiomyolipoma. *J Urol*. 2017; 195(4): 834–846.
15. Halpenny D, Snow A, McNeill G, et al. The radiological diagnosis and treatment of renal angiomyolipoma-current status. *Clin Radiol*. 2010; 65(2): 99–108.
16. Logue, LG, Acker, R, et al. Best cases from the AFIP: Angiomyolipomas in tuberous sclerosis. *Radiographics*. 2003; 23(1): 241–246.
17. Jinzaki M, Silverman SG, Akita H, et al. Renal angiomyolipoma: a radiological classification and update on recent developments in diagnosis and management. *Abdom Imaging*. 2014;39(3):588-604.
18. Komarowska H, Bednarek-Rajewska K, Kański M, et al. Epithelioid angiomyolipoma mimicking adrenal cortical carcinoma: A diagnostic pitfall. *Oncol Lett.* 2015;10(4):2130-2134.
19. Zhu J, Li H, Ding L, et al. Imaging appearance of renal epithelioid angiomyolipoma: A case report and literature review. *Medicine (Baltimore)*. 2018;97(1): e9563.
20. Benincasa A, Pinto A, Lamberti F, et al. A rare case of spontaneous rupture of epithelioid angiomyolipoma. *Urol Case Rep*. 2021 Mar 19; 38:101645.
21. Yang JW, Liang C, Yang L. Advancements in the diagnosis and treatment of renal epithelioid angiomyolipoma: A narrative review. *Kaohsiung J Med Sci.* 2022;38(10):925-932.
22. Du S, Li Y, Mao Y, et al. Diagnosis and treatment of hepatic angiomyolipoma. Hepatobiliary *Surg Nutr*. 2012;1(1):19-24.
23. Parfitt JR, Bella AJ, Izawa JI, et al. Malignant neoplasm of perivascular epithelioid cells of the liver. *Arch Pathol Lab Med* 2006;130: 1219-1222.
24. Pan CC, Chung MY, Ng KF, et al. Constant allelic alteration on chromosome 16p (TSC2 gene) in perivascular epithelioid cell tumour (PEComa): genetic evidence for the relationship of PEComa with angiomyolipoma. *J Pathol*. 2008; 214(3): 387–93.
25. Pirson, Y. Tuberous sclerosis complex-associated kidney angiomyolipoma: From contemplation to action. *Nephrol Dial Transplant*. 2013; 28(7): 1680–1685.
26. Rappold PM, Zucker M, Yoo A, et al. Mp39-09 genomic characterization of aggressive sporadic epithelioid angiomyolipoma. *J Urol*. 2021; 206: e708.
27. Sobiborowicz A, Czarnecka AM, Szumera-Ciećkiewicz A, et al. Diagnosis and treatment of malignant PEComa tumours. *Oncol Clin Pract*. 2020; 16: 22–33.
28. Shon W, Kim J, Sukov W, et al. Malignant TFE3-rearranged perivascular epithelioid cell neoplasm (PEComa) presenting as a subcutaneous mass. *Br J Dermatol*. 2016;174(3): 617–20.
29. Brakemeier S, Bachmann F, Budde K. Treatment of renal angiomyolipoma in tuberous sclerosis complex (TSC) patients. *Pediatr Nephrol*. 2017;32(7):1137-1144
30. O'Callaghan FJ, Noakes MJ, Martyn CN, et al. An epidemiological study of renal pathology in tuberous sclerosis complex. *BJU Int.* 2004;94(6):853-7.
31. Aydin H, Magi-Galluzzi C, Lane BR, et al. Renal Angiomyolipoma: Clinicopathologic Study of 194 Cases with Emphasis on the Epithelioid Histology and Tuberous Sclerosis Association. *Am J Surg Pathol.* 2009;33(2):289-297.
32. Rabenou RA, Charles HW. Differentiation of Sporadic Versus Tuberous Sclerosis Complex-Associated Angiomyolipoma. *AJR Am J Roentgenol*. 2015;205(2):292-301.
33. Wang XT, Xia QY, Ye SB, et al. RNA sequencing of Xp11 translocation-associated cancers reveals novel gene fusions and distinctive clinicopathologic

correlations. *Mod Pathol*. 2018; 31(9): 1346–60.
34. Thiravit S, Teerasamit W, Thiravit P. The different faces of renal angiomyolipomas on radiologic imaging: a pictorial review. *Br J Radiol*. 2018;91(1084):20170533.
35. Vos N, Oyen R. Renal Angiomyolipoma: The Good, the Bad, and the Ugly. *J Belg Soc Radiol.* 2018;102(1):41.
36. Huang Z, Zhou P, Li S, et al. Hepatic Angiomyolipoma: Clinical Features and Imaging Findings of Quantitative Contrast-Enhanced Ultrasound Perfusion Analysis and Magnetic Resonance Imaging. *J Ultrasound Med* 2020; 39: 2111-2122
37. Jung DH, Hwang S, Hong SM, et al. Clinicopathological correlation of hepatic angiomyolipoma: a series of 23 resection cases. *ANZ J Surg* 2018; 88: E60-E65
38. Maebayashi T, Abe K, Aizawa T, et al. Improving recognition of hepatic perivascular epithelioid cell tumor: Case report and literature review. *World J Gastroenterol.* 20157;21(17):5432-41.
39. Calame P, Tyrode G, Weil Verhoeven D, et al. Clinical characteristics and outcomes of patients with hepatic angiomyolipoma: A literature review. *World J Gastroenterol*. 2021;27(19):2299-2311.
40. Nese N, Martignoni G, Fletcher CD, 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.
41. Kingswood JC, Belousova E, Benedik MP, et al. Renal angiomyolipoma in patients with tuberous sclerosis complex: findings from the TuberOus SClerosis registry to increase disease Awareness. *Nephrol Dial Transplant.* 2019;34(3):502-508.
42. Park SG, Park BK. New radiologic classification of renal angiomyolipoma: frequently asked questions. *Clin Imaging*. 2019; 55:156-160
43. Vekeman F, Magestro M, Karner P, et al. Kidney involvement in tuberous sclerosis complex: the impact on healthcare resource use and costs. *J Med Econ*. 2015;18(12):1060-70
44. Eijkemans MJ, van der Wal W, Reijnders LJ, et al. Long-term Follow-up Assessing Renal Angiomyolipoma Treatment Patterns, Morbidity, and Mortality: An Observational Study in Tuberous Sclerosis Complex Patients in the Netherlands. *Am J Kidney Dis*. 2015;66(4):638-45.
45. Folpe AL, Mentzel T, Lehr HA, et al. Perivascular epithelioid cell neoplasms of soft tissue and gynecologic origin: a clinicopathologic study of 26 cases and review of the literature. *Am J Surg Pathol*. 2005;29(12):1558-75.
46. Thway K, Fisher C. PEComa: morphology and genetics of a complex tumor family. *Ann Diagn Pathol.* 2015;19(5):359-368.
47. Tsai CC, Wu WJ, Li CC, et al. Epithelioid angiomyolipoma of the kidney mimicking renal cell carcinoma: a clinicopathologic analysis of cases and literature review. *Kaohsiung J Med Sci*. 2009;25(3):133-40
48. He W, Cheville JC, Sadow PM, Gopalan A, Fine SW, Al-Ahmadie HA, Chen YB, Oliva E, Russo P, Reuter VE, Tickoo SK. Epithelioid angiomyolipoma of the kidney: pathological features and clinical outcome in a series of consecutively resected tumors. *Mod Pathol*. 2013 Oct;26(10):1355-64.
49. Nonomura A, Enomoto Y, Takeda M, et al. Angiomyolipoma of the liver: a reappraisal of morphological features and delineation of new characteristic histological features from the clinicopathological findings of 55 tumours in 47 patients. *Histopathology.* 2012;61(5):863-880
50. Liu Y, Wang J, Lin XY, et al. Inflammatory angiomyolipoma of the

liver: a rare hepatic tumor. *Diagn Pathol*. 2012; 7:122.
51. Agaimy A, Märkl B. Inflammatory angiomyolipoma of the liver: an unusual case suggesting relationship to IgG4-related pseudotumor. *Int J Clin Exp Pathol*. 2013;6(4):771-9.
52. Mao JX, Yuan H, Sun KY, Liu C, Fu H, Ding GS, Guo WY, Teng F. Pooled analysis of hepatic inflammatory angiomyolipoma. *Clin Res Hepatol Gastroenterol* 2020;44: e145-e151
53. Dong W, Liu L, He J, Zhu X, Wan Z, Xiao W, Li Y: Hepatic epithelioid angiomyolipoma: a malignant potential tumor and literature review. *Int J Clin Exp Med*. 2017,10:3928-31.
54. Zhang X, Chen J, Huang B, et al. Case report: hepatic epithelioid angiomyolipoma with elevated alphafetoprotein and a history of breast cancer. *Front Surg.* 2022; 9:991228.
55. Alotaibi A, AlGhazawi S, Alghthami M, et al. Hepatic Angiomyolipoma in Patients with Inflammatory Breast Cancer: A Case Report. *Cureus.* 2024;16(6): e62651.
56. Terris B, Fléjou JF, Picot R, et al. Hepatic angiomyolipoma. A report of four cases with immunohistochemical and DNA-flow cytometric studies. *Arch Pathol Lab Med.* 1996;120(1):68-72.
57. Jiang TA, Zhao QY, Chen MY, et al. Diagnostic analysis of hepatic angiomyolipoma. *Hepatobiliary Pancreat Dis Int*. 2005;4(1):152-5.
58. Ren N, Qin LX, Tang ZY, et al. Diagnosis and treatment of hepatic angiomyolipoma in 26 cases. World J Gastroenterol. 2003 Aug;9(8):1856-8.
59. Nonomura A, Enomoto Y, Takeda M, et al. Invasive growth of hepatic angiomyolipoma; a hitherto unreported ominous histological feature. *Histopathology*. 2006;48(7):831-5.
60. Azawi NH, Tolouee SA, Madsen M, et al. Core needle biopsy clarify the histology of the small renal masses and may prevent overtreatment. *Int Urol Nephrol*. 2018; 50(7): 1205–9.
61. Brimo F, Robinson B, Guo C, et al. Renal epithelioid angiomyolipoma with atypia: a series of 40 cases with emphasis on clinicopathologic prognostic indicators of malignancy. *Am J Surg Pathol*. 2010; 34(5): 715–22.
62. Lei JH, Liu LR, Wei Q, et al. A four-year follow-up study of renal epithelioid Angiomyolipoma: a multi-center experience and literature review. *Sci Rep*. 2015; 5: 10030.
63. Klompenhouwer AJ, Dwarkasing RS, Doukas M, et al. Hepatic angiomyolipoma: an international multicenter analysis on diagnosis, management and outcome. HPB (Oxford). 2020;22(4):622-629.
64. Stone CH, Lee MW, Amin MB, et al. Renal angiomyolipoma: further immunophenotypic characterization of an expanding morphologic spectrum. *Arch Pathol Lab Med*. 2001;125(6):751-8.
65. Hwang I, Yu E, Cho KJ. Hepatic angiomyolipoma with variable histologic features: 8 cases resembling hepatocellular carcinoma or inflammatory pseudotumor. *Korean J Gastroenterol.* 2012;60(4):242-8.
66. Gupta RK, Nowitz M, Wakefield SJ. Fine-needle aspiration cytology of renal angiomyolipoma: report of a case with immunocytochemical and electron microscopic findings. *Diagn Cytopathol*. 1998;18(4):297-300.
67. Caliò A, Brunelli M, Gobbo S, et al. Cathepsin K: a novel diagnostic and predictive biomarker for renal tumors. *Cancers (Basel)*. 2021;13(10): 2441
68. Martignoni G, Pea M, Reghellin D, et al. Perivascular epithelioid cell tumor (PEComa) in the genitourinary tract. Adv Anat Pathol. 2007;14(1):36-41.
69. Vij M, Calderaro J. Pathologic and molecular features of hepatocellular

carcinoma: An update. *World J Hepatol.* 2021;13(4):393-410.
70. Azimpouran M, Vazifekhah S, Moslemi F, et al. Immunohistochemical profile of uterine leiomyomas; a comparison between different subtypes. *Niger Med J.* 2016;57(1):54-8.
71. Kuusk T, Biancari F, Lane B, et al. Treatment of renal angiomyolipoma: pooled analysis of individual patient data. *BMC Urol.* 2015 Dec 28; 15:123.
72. Fernández-Pello S, Hora M, Kuusk T, 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.
73. Jung Y, Choi MJ, Kim BM, et al. Transarterial Embolization for Sporadic Renal Angiomyolipoma: Patient Selection and Technical Considerations for Optimal Therapeutic Outcomes. *Taehan Yongsang Uihakhoe Chi*. 2022;83(3):559-581.
74. Bhatt JR, Richard PO, Kim NS, 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.
75. Maclean DFW, Sultana R, Radwan R, et al. Is the follow-up of small renal angiomyolipomas a necessary precaution? *Clin Radiol.* 2014; 69:822–6.
76. Seyam RM, Bissada NK, Kattan SA, et al. Changing trends in presentation, diagnosis and management of renal angiomyolipoma: comparison of sporadic and tuberous sclerosis complex-associated forms. *Urology*. 2008; 72:1077–82.
77. Yamakado K, Tanaka N, Nakagawa T, et al. Renal angiomyolipoma: Relationships between tumor size, aneurysm formation, and rupture. *Radiology.* 2002; 225:78–82.
78. Xu XF, Hu XH, Zuo QMet al. A scoring system based on clinical features for the prediction of sporadic renal angiomyolipoma rupture and hemorrhage. *Medicine (Baltimore).* 2020;99(20):e20167.
79. Kiefer RM, Stavropoulos SW. The Role of Interventional Radiology Techniques in the Management of Renal Angiomyolipomas. *Curr Urol Rep*. 2017;18(5):36.
80. Seyam RM, Alkhudair WK, Kattan SA, et al. The Risks of Renal Angiomyolipoma: Reviewing the Evidence. *J Kidney Cancer VHL*. 2017 Oct 16;4(4):13-25.
81. Abdelsalam ME, Ahrar K. Ablation of Small Renal Masses. *Tech Vasc Interv Radiol.* 2020;23(2):100674
82. Prevoo, W, van den Bosch, MAAJ and Horenblas, S. Radiofrequency ablation for treatment of sporadic angiomyolipoma. *Urology*. 2017; 72(1): 188–191.
83. Msezane L, Chang A, Shikanov S, Deklaj T, Katz MH, Shalhav AL, et al. Laparoscopic nephron-sparing surgery in the management of angiomyolipoma: A single center experience. *J Endourol.* 2010; 24:583–7.
84. Bissler JJ, Kingswood JC, Radzikowska E, et al. Everolimus for angiomyolipoma associated with tuberous sclerosis complex or sporadic lymphangioleiomyomatosis (EXIST-2): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2013;381(9869):817-24.
85. Henske E.P., Jozwiak S., Kingswood J.C., et al. Tuberous sclerosis complex. *Nat. Rev. Diease Prim*. 2016; 2:1–18. doi:
86. Hatano T, Matsu-Ura T, Mori KI, et al. Effect of everolimus treatment for regrown renal angiomyolipoma associated with tuberous sclerosis complex after transcatheter arterial embolization. Int J Clin Oncol. 2018 Dec;23(6):1134-1139.

87. Sanfilippo R, Jones RL, Blay JY, et al. : Role of chemotherapy, VEGFR inhibitors, and mTOR inhibitors in advanced perivascular epithelioid cell tumors (PEComas). *Clin Cancer Res* 2019; 25:5295-5300.
88. Czarnecka AM, Skoczylas J, Bartnik E, et al. Management Strategies for Adults with Locally Advanced, Unresectable or Metastatic Malignant Perivascular Epithelioid Cell Tumor (PEComa): Challenges and Solutions. *Cancer Manag Res*. 2023; 15:615-623.
89. Wagner AJ, Ravi V, Riedel RF, et al. Phase II Trial of *nab*-Sirolimus in Patients with Advanced Malignant Perivascular Epithelioid Cell Tumors (AMPECT): Long-Term Efficacy and Safety Update. *J Clin Oncol*. 2024;42(13):1472-1476.
90. Butte JM, Do RK, Shia J, et al. Liver angiomyolipomas: a clinical, radiologic, and pathologic analysis of 22 patients from a single center. *Surgery*. 2011; 150:557–567.
91. Fricke BL, Donnelly LF, Casper KA, et al. Frequency and imaging appearance of hepatic angiomyolipomas in pediatric and adult patients with tuberous sclerosis. *AJR Am J Roentgenol*. 2004;182(4):1027-30.