



# Renal Epithelioid Angiomyolipoma: Genomic Characterization and Malignant Potential

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## Introduction

Renal angiomyolipomas (AMLs) are one of the most common benign kidney tumors diagnosed. They account for about 1% of surgically resected renal lesions and affect women more than men [1]. Majority of AMLs are found incidentally, but patients may present with relatively nonspecific symptoms such as flank pain, hematuria, and abdominal pain. Grossly, these tumors are highly vascular and grow exophytically, making retroperitoneal bleeding the most dangerous complication in affected patients [2,3]. Histologically, these tumors consist of dysmorphic blood vessels, spindled smooth muscle cells, and adipocytes [4]. AMLs are traditionally grouped into two categories: classic and syndromic. Classic AMLs account for 80% of cases, and syndromic AMLs account for 20%. Associated syndromes include tuberous sclerosis and lymphangioleiomyomatosis [5].

Epithelioid AMLs (eAMLs) are a third category that can arise from any types of AMLs. They are distinguished from other AMLs due to the presence of epithelioid cells [4]. This rare variant has been classified by the World Health Organization as a potentially malignant mesenchymal neoplasm that metastasizes in one-third of cases [6]. However, conflicting reports have brought in to question their true malignant potential [7]. Due to eAMLs overall rarity, few studies have characterized this entity. In this study, we further define eAML by describing its genomic alterations and malignant potential by comparing it to a cohort of AML patients at a large-volume cancer center.

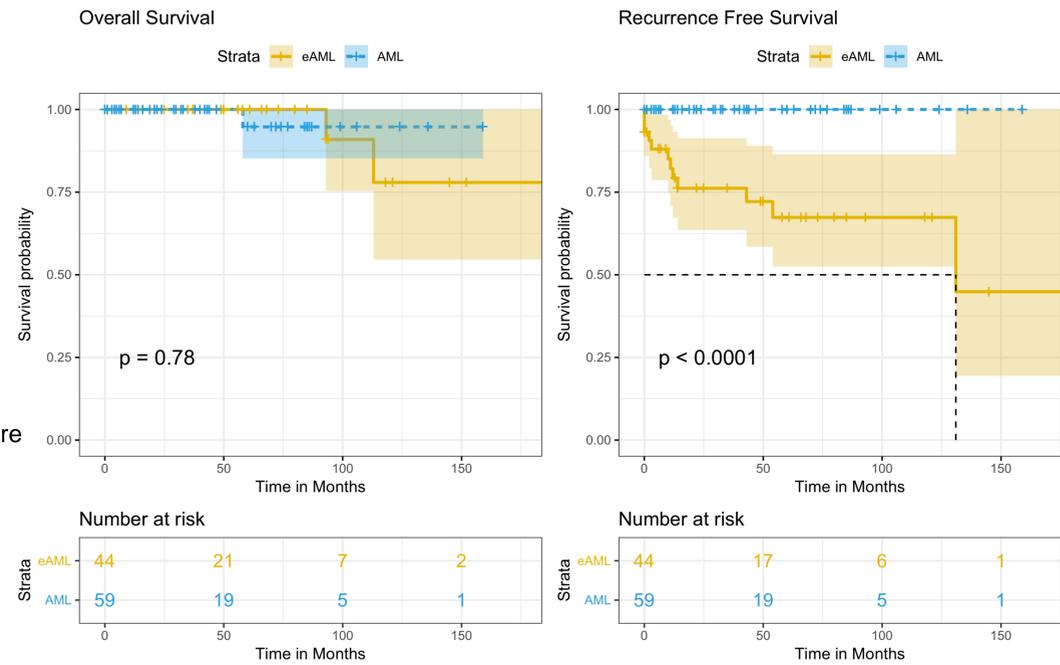
## Method

- Prospectively maintained kidney cancer database queried for all patients with eAML and AML who underwent nephrectomy between 1994 and 2008 at the Memorial Sloan Kettering Cancer Center.
- Patients separated into two histologic groups: eAML and AML.
- Clinicopathologic features and genomic alterations analyzed and compared.
- Descriptive statistics performed using Mann-Whitney U test and Chi-squared test. All statistical analyses performed using R 3.5.2 with significance set at <0.05.
- Overall survival (OS) and recurrence-free survival (RFS) data analyzed using Kaplan-Meier method with significance determined by log-rank tests.
- Genomic data gathered for 6 eAML and 10 AML patients.

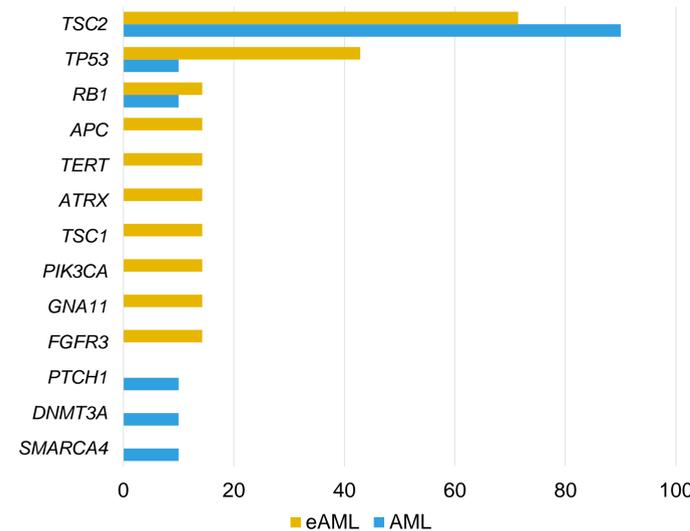
## Results

- Median RFS was worse in eAML than in AML patients.
- Patients with eAML had larger tumors and more underwent radical nephrectomy.
- Patients with eAML metastasized more.**
- Patients with eAML had more heterogeneous mutations.
- TSC2** was the most frequently mutated gene in both groups.

**Figure 1:** Overall and Recurrence-Free Survival in eAML and AML Patients



**Figure 2:** Percent Comparison of Mutational Landscape Between eAML and AML



**Table 1:**

	Epithelioid AML	AML	p
<b>Patients (n)</b>	44	59	
<b>Age (Median [IQR])</b>	58.00 [43.57, 64.29]	53.00 [48.00, 63.50]	0.963
<b>Sex (%)</b>			0.126
Women	30 (68.2)	49 (83.1)	
Men	14 (31.8)	10 (16.9)	
<b>BMI (Median [IQR])</b>	26.30 [23.90, 28.90]	27.50 [23.90, 31.65]	0.331
<b>Symptoms (%)</b>			0.597
Incidental	23 (54.8)	33 (62.3)	
Symptomatic	19 (45.2)	20 (37.7)	
<b>Type of Nephrectomy (%)</b>			0.014
Partial	23 (54.8)	47 (79.7)	
Radical	19 (45.2)	12 (20.3)	
<b>Laterality (%)</b>			0.586
Left	21 (47.7)	32 (55.2)	
Right	23 (52.3)	26 (44.8)	
<b>Single Lesion (%)</b>	42 (95.5)	50 (84.7)	0.156
<b>Tumor Size (Median [IQR])</b>	4.00 [2.50, 8.80]	2.00 [1.45, 2.80]	<0.001
<b>Positive Margins (%)</b>	3 (8.6)	5 (8.5)	1
<b>Metastasized (%)</b>	12 (27.3)	0 (0.0)	<0.001

## Discussion

- Out of 103 patients, 44 had eAML and 59 had AML.
- Women in their fifth and sixth decade were more commonly diagnosed than men, Table 1.
- Patients with eAML had larger tumors ( $p < 0.001$ ) and underwent radical nephrectomy more often ( $p = 0.014$ ).
- Twelve (27.3%) eAML patients metastasized, while no metastases were observed in AML patients.
- Median RFS for eAML patients was 131 months, and median RFS was not reached in AML patients ( $p < 0.0001$ ), Figure 1.
- The most frequently mutated gene across both groups expectedly was *TSC2*, a mutation commonly found in AMLs.
- The mutational burden in eAMLs was heterogeneous compared to AMLs, with more mutations observed within *TP53* (43%), *RB1* (14%), *APC* (14%), *TERT* (14%), *ATRX* (14%), *TSC1* (14%), *PIK3CA* (14%), *GNA11* (14%), and *FGFR3* (14%), Figure 2.

## Conclusion

- Patients with eAML were observed to have larger tumors and metastasized at a higher rate than patients with AML.
- A greater frequency of eAML patients underwent radical nephrectomy.
- The mutational burden across eAML was notable for a more heterogeneity, with largest mutations in *TSC2* and *TP53* genes.
- Further investigation into the impact of mutational burden on metastatic potential is warranted.

## References

- Fittschen et al. *Abdom Imaging*. 2014.
- Lee et al. *J Formos Med Assoc*. 2018.
- Rimon et al. *Clin Radiol*. 2006.
- Jinzaki, et al. *Abdom Imaging*. 2014.
- Vos et al. *J Belgian Soc of Radiol*. 2018.
- Amin. *WHO Classification of Tumours*, IARC Press. 2004.
- He et al. *Mod Pathol*. 2013.

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