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Clinicopathological Features of Primary Renal Mesenchymal Neoplasms in Adults: A Cross-sectional Study

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Abstract:

Background
Primary renal mesenchymal neoplasms are rare non-epithelial tumors of the kidney exhibiting diverse histopathological patterns and variable biological behavior. Owing to their rarity and overlapping clinicoradiological features, accurate diagnosis remains challenging. The present study was conducted to evaluate the clinicopathological spectrum, radiological features, immunohistochemical profile, and predictors of malignancy among adult patients with primary renal mesenchymal neoplasms.

Methods
This hospital-based cross-sectional study included 564 adult patients diagnosed with primary renal mesenchymal neoplasms at a tertiary care center. Demographic, clinical, radiological, histopathological, and immunohistochemical data were analyzed. Tumors were classified according to standard histopathological criteria and immunohistochemical findings. Comparative analysis between benign and malignant tumors was performed using appropriate statistical tests, and multivariate logistic regression analysis was used to identify predictors of malignancy.

Results
The mean age of patients was 48.7 ± 13.6 years, with male predominance (58.2%). Flank pain was the most common presenting symptom (66.0%). Angiomyolipoma was the commonest tumor subtype (50.7%), while leiomyosarcoma was the predominant malignant neoplasm (12.8%). Malignant tumors occurred in significantly older patients and were associated with larger tumor size, hematuria, necrosis, vascular invasion, and perinephric fat involvement ($p<0.001$). Tumor size >7 cm (OR=4.96), necrosis on imaging (OR=5.62), and vascular invasion (OR=6.18) emerged as significant independent predictors of malignancy. Immunohistochemistry aided accurate differentiation among spindle-cell renal tumors.

Conclusion
Primary renal mesenchymal neoplasms demonstrate a broad clinicopathological and immunohistochemical spectrum. Larger tumor size, hematuria, necrosis, and vascular invasion were strongly associated with malignant behavior. Integrated clinicoradiological, histopathological, and immunohistochemical evaluation is essential for accurate diagnosis and prognostic assessment of these rare renal tumors.

Keywords:
Primary renal mesenchymal neoplasms; angiomyolipoma; renal sarcoma; leiomyosarcoma; immunohistochemistry

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Introduction

Primary renal mesenchymal neoplasms are a rare and heterogeneous group of non-epithelial tumors arising from the mesenchymal components of the kidney, including smooth muscle, adipose tissue, fibrous tissue, vascular elements, and primitive mesenchyme [1]. Unlike the far more common renal cell carcinomas, which constitute nearly 85–90% of adult renal malignancies, primary mesenchymal tumors account for less than 5% of all renal neoplasms in adults [2]. These tumors encompass a broad histopathological spectrum ranging from benign lesions such as angiomyolipoma and leiomyoma to highly aggressive malignant neoplasms including leiomyosarcoma, liposarcoma, malignant peripheral nerve sheath tumor, synovial sarcoma, and undifferentiated pleomorphic sarcoma [3,4].

The clinicopathological evaluation of renal mesenchymal neoplasms remains challenging because of their rarity, overlapping radiological appearances, and diverse biological behavior [4]. Most patients present with nonspecific clinical manifestations such as flank pain, abdominal mass, hematuria, weight loss, or incidentally detected renal masses during imaging performed for unrelated conditions [5]. Advances in ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) have increased the incidental detection of renal masses; however, imaging alone is often insufficient to accurately differentiate mesenchymal tumors from renal cell carcinoma or other spindle-cell lesions of the kidney [6]. Consequently, definitive diagnosis relies heavily on histopathological examination supplemented by immunohistochemistry and, in selected cases, molecular studies [6].

Among adult renal mesenchymal tumors, angiomyolipoma is the most frequently encountered benign lesion and represents approximately 0.3–3% of all renal masses [7]. Although generally benign, larger angiomyolipomas may lead to spontaneous hemorrhage and significant morbidity. In contrast, renal sarcomas are exceedingly uncommon, accounting for nearly 1–2% of adult malignant renal tumors, but they are associated with aggressive clinical behavior and poor prognosis [8]. Leiomyosarcoma is considered the most common subtype of primary renal sarcoma and often demonstrates high rates of local recurrence and distant metastasis [9]. Due to the rarity of these tumors, most available literature consists of isolated case reports and small retrospective series, resulting in limited understanding regarding their epidemiology, clinicopathological characteristics, treatment outcomes, and prognostic determinants [9].

Histopathological assessment plays a central role in characterizing these neoplasms because several lesions exhibit overlapping spindle-cell morphology. Immunohistochemical markers such as smooth muscle actin (SMA), desmin, HMB-45, Melan-A, CD34, S-100, cytokeratin, and TLE1 aid in distinguishing among different mesenchymal tumors and in differentiating them from sarcomatoid renal cell carcinoma and metastatic spindle-cell malignancies [10]. Recent advances in molecular pathology have further improved diagnostic accuracy, particularly for tumors such as synovial sarcoma harboring the characteristic SYT-SSX translocation [11].

Given the rarity and histological diversity of adult primary renal mesenchymal neoplasms, there is a paucity of comprehensive clinicopathological studies from developing countries and tertiary care centers [10,11]. Detailed evaluation of demographic patterns, clinical presentation, radiological findings, histopathological spectrum, immunohistochemical profile, and associated outcomes may contribute to improved diagnostic precision and therapeutic planning. Therefore, the present study was aimed to analyze the clinicopathological features of primary renal mesenchymal neoplasms in adults in a tertiary care setting.

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Material and methods

Study Design and Setting

This hospital-based cross-sectional observational study was conducted in the Department of Pathology in collaboration with the Departments of Urology and Radiodiagnosis at a tertiary care teaching hospital over a period of 5 years from March 2021 to February 2025. The study was undertaken to evaluate the clinicopathological characteristics of primary renal mesenchymal neoplasms diagnosed in adult patients presenting to the institution during the study period. The study protocol was reviewed and approved by the Institutional Ethics Committee prior to commencement, and all procedures were performed in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

Study Population

The study included adult patients aged 18 years and above who were diagnosed histopathologically with primary renal mesenchymal neoplasms on nephrectomy specimens, partial nephrectomy specimens, trucut biopsies, or excision specimens received in the Department of Pathology during the study period. Both benign and malignant mesenchymal tumors originating primarily from the kidney were included. Cases with secondary involvement of the kidney by retroperitoneal sarcomas, metastatic mesenchymal tumors, sarcomatoid renal cell carcinoma, Wilms tumor, and inadequate or poorly preserved tissue specimens were excluded from the study. Cases with incomplete clinicopathological data were also excluded.

Data Collection

Detailed demographic, clinical, radiological, and pathological data were collected from hospital medical records, pathology requisition forms, imaging records, operative notes, and histopathology archives. The demographic variables included age, sex, and relevant comorbidities. Clinical parameters such as presenting complaints, duration of symptoms, side and location of renal mass, associated constitutional symptoms, and incidental radiological detection were recorded. Radiological findings from ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) were reviewed wherever available to assess tumor size, location, heterogeneity, necrosis, hemorrhage, vascular involvement, and local extension.

Histopathological Examination

All surgical and biopsy specimens were fixed in 10% neutral buffered formalin immediately after receipt in the pathology department. Gross examination was performed according to standard pathological protocols, and details regarding tumor size, weight, external surface, cut surface appearance, areas of necrosis, hemorrhage, cystic degeneration, and involvement of renal pelvis, capsule, perinephric fat, renal vein, or adjacent structures were documented. Representative tissue sections were processed routinely, embedded in paraffin, sectioned at 3–5 µm thickness, and stained with hematoxylin and eosin (H&E).

Microscopic evaluation was carried out independently by experienced pathologists to assess tumor architecture, cellular morphology, mitotic activity, nuclear atypia, necrosis, vascular invasion, stromal characteristics, and margin status. Tumors were classified according to the latest World Health Organization (WHO) classification of tumors of the urinary system and male genital organs. Histological grading of malignant mesenchymal tumors was performed using standard grading criteria wherever applicable.

Immunohistochemistry

Immunohistochemical analysis was performed in selected cases where histomorphological findings alone were insufficient for definitive diagnosis or differentiation from other spindle-cell lesions.

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Formalin-fixed paraffin-embedded tissue sections were subjected to immunohistochemical staining using appropriate antibody panels based on the differential diagnosis. Commonly used markers included smooth muscle actin (SMA), desmin, HMB-45, Melan-A, S-100, CD34, cytokeratin, epithelial membrane antigen (EMA), vimentin, CD117, TLE1, and Ki-67 proliferation index. Interpretation of immunostaining was performed by assessing the pattern, intensity, and percentage of tumor cell positivity. Final diagnosis was established by correlating histopathological and immunohistochemical findings.

Outcome Measures

The primary outcome measures of the study included the spectrum and frequency of various primary renal mesenchymal neoplasms in adults and their clinicopathological characteristics. Secondary outcome measures included correlation of histopathological diagnosis with demographic profile, clinical presentation, radiological findings, tumor size, laterality, and immunohistochemical profile.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on data distribution, while categorical variables were presented as frequencies and percentages. Associations between clinicopathological variables were assessed using Chi-square test or Fisher's exact test for categorical variables and Student's t-test or Mann–Whitney U test for continuous variables as appropriate. A p-value of <0.05 was considered statistically significant.

Results

Among the 564 patients included in the study, the majority belonged to the 46–60 years age group (37.9%), followed by 31–45 years (29.8%), with a mean age of 48.7 ± 13.6 years. Male predominance was observed, with males constituting 58.2% of cases. Most patients were from rural areas (59.6%). Flank pain was the most common presenting symptom, reported in 66.0% of patients, followed by hematuria (38.7%), abdominal mass (25.9%), and weight loss or loss of appetite (23.4%). Fever was present in 12.1% of cases, while 22.0% of tumors were detected incidentally during radiological evaluation. The right kidney was slightly more frequently involved (53.5%) compared to the left kidney (45.0%), whereas bilateral tumors were rare (1.4%). Most tumors measured between 4–7 cm (43.6%), followed by tumors larger than 7 cm (35.5%), with an overall mean tumor size of 6.9 ± 3.2 cm (Table 1).

Table 1. Baseline Demographic and Clinicoradiological Characteristics of Adult Patients with Primary Renal Mesenchymal Neoplasms (n=564).

Variable	Frequency (%)/Mean ± SD
Age Group (years)	
18–30	**74 (13.1)**
31–45	**168 (29.8)**
46–60	**214 (37.9)**
>60	**108 (19.1)**
Mean (years)	**48.7 ± 13.6**
Gender	

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Male	**328 (58.2)**
Female	**236 (41.8)**
Residence	
Rural	**336 (59.6)**
Urban	**228 (40.4)**
Presenting Symptoms*	
Flank pain	**372 (66.0)**
Hematuria	**218 (38.7)**
Abdominal mass	**146 (25.9)**
Weight loss/appetite loss	**132 (23.4)**
Fever	**68 (12.1)**
Incidental radiological detection	**124 (22.0)**
Laterality	
Right kidney	**302 (53.5)**
Left kidney	**254 (45.0)**
Bilateral	**8 (1.4)**
Tumor Size	
<4 cm	**118 (20.9)**
4–7 cm	**246 (43.6)**
>7 cm	**200 (35.5)**
Tumor size (cm)	**6.9 ± 3.2**

Histopathological examination revealed angiomyolipoma as the most common renal mesenchymal neoplasm, accounting for 50.7% of cases. Leiomyoma was the second most common benign tumor (9.6%), followed by solitary fibrous tumor (6.7%), fibroma (4.6%), and hemangioma (3.2%). Among malignant tumors, leiomyosarcoma was the predominant subtype, representing 12.8% of all neoplasms. Other malignant tumors included liposarcoma (4.3%), synovial sarcoma (2.8%), undifferentiated pleomorphic sarcoma (2.1%), malignant peripheral nerve sheath tumor (1.4%), and primitive neuroectodermal tumor/Ewing sarcoma (1.1%). Rare mesenchymal tumors collectively constituted 0.7% of cases (Table 2).

Table 2. Histopathological Spectrum of Primary Renal Mesenchymal Neoplasms in Adults (n=564).

Histopathological Diagnosis	Frequency (%)
Angiomyolipoma	**286 (50.7)**
Leiomyoma	**54 (9.6)**
Solitary fibrous tumor	**38 (6.7)**
Fibroma	**26 (4.6)**
Hemangioma	**18 (3.2)**
Leiomyosarcoma	**72 (12.8)**
Liposarcoma	**24 (4.3)**
Synovial sarcoma	**16 (2.8)**
Undifferentiated pleomorphic sarcoma	**12 (2.1)**
Malignant peripheral nerve sheath tumor	**8 (1.4)**

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Primitive neuroectodermal tumor/Ewing sarcoma	**6 (1.1)**
Other rare mesenchymal tumors	**4 (0.7)**

Immunohistochemical evaluation demonstrated distinct marker expression patterns among various renal mesenchymal neoplasms. Angiomyolipomas showed positivity for HMB-45, Melan-A, and SMA with low proliferative activity (Ki-67: 2–5%). Leiomyomas were strongly positive for SMA and desmin with minimal proliferative index (<2%). Solitary fibrous tumors demonstrated CD34, STAT6, and Bcl-2 positivity with low Ki-67 labeling (3–7%). Malignant tumors exhibited comparatively higher proliferative activity, particularly undifferentiated pleomorphic sarcoma (35–60%) and PNET/Ewing sarcoma (40–70%). Synovial sarcoma showed positivity for TLE1, EMA, and cytokeratin, while MPNST demonstrated focal S-100 and SOX10 positivity. These findings supported histopathological diagnosis and differentiation among spindle-cell renal neoplasms (Table 3).

Table 3. Immunohistochemical Profile and Ki-67 Proliferation Index of Major Renal Mesenchymal Neoplasms.

Tumor Type	Important Positive Immunohistochemical Markers	Ki-67 Proliferation Index (%)
Angiomyolipoma	**HMB-45, Melan-A, SMA**	**2–5**
Leiomyoma	**SMA, Desmin**	**<2**
Solitary fibrous tumor	**CD34, STAT6, Bcl-2**	**3–7**
Leiomyosarcoma	**SMA, Desmin, Vimentin**	**18–42**
Synovial sarcoma	**TLE1, EMA, Cytokeratin**	**20–48**
Malignant peripheral nerve sheath tumor (MPNST)	**S-100 (focal), SOX10, Vimentin**	**22–40**
Undifferentiated pleomorphic sarcoma (UPS)	**Vimentin, CD68 (focal)**	**35–60**
Primitive neuroectodermal tumor / Ewing sarcoma (PNET/Ewing sarcoma)	**CD99, FLI1, NKX2.2**	**40–70**

Among the 142 malignant renal mesenchymal neoplasms, high-grade tumors constituted the largest proportion (39.4%), followed by intermediate-grade (36.6%) and low-grade lesions (23.9%). Mitotic activity greater than 10 per 10 high-power fields was observed in 36.6% of cases. Tumor necrosis was identified in 62.0% of malignant tumors, while vascular invasion and perinephric fat invasion were present in 31.0% and 40.8% of cases, respectively. Lymph node metastasis was documented in 18.3% of patients, and distant metastasis at diagnosis was noted in 12.7%. Radiologically, heterogeneous enhancement was the most common imaging feature (56.4%), followed by fat-containing lesions (46.8%). Intratumoral necrosis was observed in 24.1% of cases, whereas hemorrhage and calcification were seen in 14.5% and 8.5%, respectively. Renal vein involvement and inferior vena cava extension were identified in 6.0% and 2.1% of tumors. Most lesions demonstrated well-circumscribed margins (68.8%), while infiltrative margins were observed in 31.2% of cases (Table 4).

Table 4. Histopathological Characteristics of Malignant Primary Renal Mesenchymal Neoplasms (n=142) and Radiological Features of Primary Renal Mesenchymal Neoplasms in Adults n=564).

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Variable	Frequency (%)
Histological Grade	
Low grade	**34 (23.9)**
Intermediate grade	**52 (36.6)**
High grade	**56 (39.4)**
Mitotic Activity	
<5/10 HPF	**42 (29.6)**
5–10/10 HPF	**48 (33.8)**
>10/10 HPF	**52 (36.6)**
Tumor Necrosis	**88 (62.0)**
Vascular invasion	**44 (31.0)**
Perinephric fat invasion	**58 (40.8)**
Lymph node metastasis	**26 (18.3)**
Distant metastasis at diagnosis	**18 (12.7)**
Imaging Feature	
Heterogeneous enhancement	**318 (56.4)**
Fat-containing lesion	**264 (46.8)**
Intratumoral necrosis	**136 (24.1)**
Calcification	**48 (8.5)**
Hemorrhage	**82 (14.5)**
Renal vein involvement	**34 (6.0)**
Inferior vena cava extension	**12 (2.1)**
Perinephric extension	**74 (13.1)**
Well-circumscribed margins	**388 (68.8)**
Infiltrative margins	**176 (31.2)**

Malignant renal mesenchymal neoplasms occurred in significantly older patients compared to benign tumors (57.1 ± 11.4 vs 45.8 ± 12.9 years; p<0.001) and demonstrated a greater male predominance (70.4% vs 54.0%; p=0.001). Tumors larger than 7 cm were significantly more frequent among malignant neoplasms (64.8% vs 25.6%; p<0.001). Hematuria and constitutional symptoms such as weight loss or appetite loss were markedly more common in malignant tumors (60.6% and 49.3%, respectively) compared to benign lesions (31.3% and 14.7%; p<0.001). Necrosis on imaging or gross pathology, vascular invasion, and perinephric fat involvement were significantly associated with malignant tumors (all p<0.001). In contrast, incidental diagnosis was more frequently observed in benign neoplasms (27.0% vs 7.0%; p<0.001) (Table 5).

Table 5. Comparison of Clinicopathological Features Between Benign and Malignant Renal Mesenchymal Neoplasms.

Variable	Benign Tumors (n=422)	Malignant Tumors (n=142)	p-value
	Frequency (%)/Mean ± SD		
Mean age (years)	**45.8 ± 12.9**	**57.1 ± 11.4**	**<0.001**

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Male	**228 (54.0%)**	**100 (70.4%)**	**0.001**
Tumor size >7 cm	**108 (25.6%)**	**92 (64.8%)**	**<0.001**
Tumor Size			
<4 cm	**112 (26.5%)**	**6 (4.2%)**	**<0.001**
4–7 cm	**202 (47.9%)**	**44 (31.0%)**	
>7 cm	**108 (25.6%)**	**92 (64.8%)**	
Hematuria	**132 (31.3%)**	**86 (60.6%)**	**<0.001**
Weight loss/appetite loss	**62 (14.7%)**	**70 (49.3%)**	**<0.001**
Necrosis on imaging/gross pathology	**48 (11.4%)**	**88 (62.0%)**	**<0.001**
Vascular invasion	**12 (2.8%)**	**44 (31.0%)**	**<0.001**
Perinephric fat involvement	**18 (4.3%)**	**58 (40.8%)**	**<0.001**
Incidental diagnosis	**114 (27.0%)**	**10 (7.0%)**	**<0.001**

Multivariate logistic regression analysis identified several independent predictors of malignancy among renal mesenchymal neoplasms. Age greater than 50 years was associated with a two-fold increased risk of malignancy (OR=2.14; 95% CI: 1.38–3.42; p=0.001). Male gender was also significantly associated with malignant tumors (OR=1.72; 95% CI: 1.08–2.73; p=0.022). Tumor size greater than 7 cm emerged as a strong predictor of malignancy, increasing the odds nearly five-fold (OR=4.96; 95% CI: 3.01–8.14; p<0.001). Similarly, hematuria, necrosis on imaging, and vascular invasion showed significant positive associations with malignant behavior. Vascular invasion demonstrated the strongest association with malignancy (OR=6.18; 95% CI: 3.02–12.64; p<0.001). Conversely, incidentally detected tumors were significantly less likely to be malignant (OR=0.42; 95% CI: 0.19–0.88; p=0.028) (Table 6).

Table 6. Multivariate Logistic Regression Analysis of Factors Associated with Malignant Renal Mesenchymal Neoplasms.

Variable	Odds Ratio (OR)	95% CI	p-value
Age >50 years	**2.14**	**1.38–3.42**	**0.001**
Male	**1.72**	**1.08–2.73**	**0.022**
Tumor size >7 cm	**4.96**	**3.01–8.14**	**<0.001**
Hematuria	**2.48**	**1.56–3.95**	**<0.001**
Necrosis on imaging	**5.62**	**3.34–9.45**	**<0.001**
Vascular invasion	**6.18**	**3.02–12.64**	**<0.001**
Incidental diagnosis	**0.42**	**0.19–0.88**	**0.028**

Discussion

Primary renal mesenchymal neoplasms constitute a rare and histologically diverse group of renal tumors, posing significant diagnostic and therapeutic challenges because of their overlapping clinical, radiological, and pathological characteristics. In the present study comprising 564 adult cases, benign tumors predominated over malignant lesions, with angiomyolipoma emerging as the most common

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histological subtype. These findings are consistent with previous studies by Padmanabhan et al., and Suresh et al., reporting that mesenchymal tumors account for less than 5% of all renal neoplasms, with the majority being benign in nature [12,13]. The relatively large sample size in the present study provides a broader overview of the clinicopathological spectrum of these uncommon tumors in the Indian population.

The mean age of patients in the present study was 48.7 ± 13.6 years, with the highest frequency observed in the 46–60 years age group. Malignant tumors occurred at a significantly older age compared to benign tumors (57.1 ± 11.4 vs 45.8 ± 12.9 years; $p<0.001$). Similar age-related trends have been documented in previous studies by Mandrekar et al., and Kalyani et al., particularly for renal leiomyosarcoma and other high-grade sarcomas, which are more frequently encountered in the fifth and sixth decades of life [14,15]. The older age distribution among malignant tumors may reflect the cumulative effect of progressive genetic alterations, chronic inflammation, and prolonged environmental exposure contributing to malignant transformation [15]. A male predominance was observed overall (58.2%), and malignant tumors demonstrated significantly higher male representation (70.4%; $p=0.001$). Although angiomyolipoma is classically more common in females due to hormonal influences and association with tuberous sclerosis complex, aggressive mesenchymal sarcomas have been reported more frequently in males in several institutional series [16].

Clinically, flank pain was the most common presenting symptom (66.0%), followed by hematuria (38.7%) and abdominal mass (25.9%). These findings correlate with the classical symptomatology of renal masses described in earlier radiological and pathological studies by Gunawardena et al., and Woo et al., [17,18]. Hematuria and constitutional symptoms such as weight loss were significantly associated with malignant tumors in the present study ($p<0.001$). This observation may be explained by the infiltrative and highly vascular nature of malignant sarcomas, leading to destruction of renal parenchyma, hemorrhage, and systemic inflammatory response [19]. Additionally, malignant tumors frequently exhibited necrosis and vascular invasion, which may contribute to constitutional manifestations through cytokine-mediated metabolic effects [20]. Interestingly, incidental radiological detection was significantly more common in benign tumors (27.0% vs 7.0%; $p<0.001$), reflecting the increasing use of abdominal ultrasonography and computed tomography in routine clinical practice. Similar observations have been reported in contemporary imaging-based studies by Vinay et al., and Ray et al., where small benign angiomyolipomas and leiomyomas are increasingly identified during unrelated abdominal evaluations [21,22].

Histopathologically, angiomyolipoma accounted for more than half of all tumors (50.7%), reaffirming its status as the most common adult renal mesenchymal neoplasm. Previous studies by Ray et al., and Jinzaki et al., have similarly identified angiomyolipoma as the predominant mesenchymal renal tumor, often associated with characteristic triphasic morphology comprising adipose tissue, blood vessels, and smooth muscle cells [22,23]. Leiomyoma and solitary fibrous tumor represented the next most common benign lesions. Among malignant neoplasms, leiomyosarcoma was the most frequent subtype (12.8%), which aligns with previous studies by Jinzaki et al., and Gürsoy et al., identifying renal leiomyosarcoma as the commonest primary renal sarcoma [23,24]. The predominance of leiomyosarcoma may be attributed to the abundance of smooth muscle elements within renal vasculature and renal pelvis from which these tumors arise [24]. Rare tumors such as synovial sarcoma, malignant peripheral nerve sheath tumor, and primitive neuroectodermal tumor were infrequently encountered, highlighting the histological heterogeneity of renal mesenchymal neoplasms.

Tumor size demonstrated a strong association with malignant behavior in the present study. Tumors

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larger than 7 cm were significantly more frequent among malignant neoplasms (64.8% vs 25.6%; p<0.001), and multivariate analysis identified tumor size >7 cm as an independent predictor of malignancy (OR=4.96, p<0.001). Similar observations have been reported in studies by Seyam et al., and Rallis et al., evaluating renal sarcomas and epithelioid angiomyolipomas, where larger tumor size correlates with aggressive biological behavior, increased mitotic activity, and metastatic potential [25,26]. Larger tumors are more likely to develop hypoxia-induced angiogenesis, necrosis, and local tissue invasion, thereby contributing to malignant progression and adverse prognosis [26].

The radiological findings observed in this study were also noteworthy. Heterogeneous enhancement was the most common imaging feature (56.4%), while fat-containing lesions were identified in 46.8% of cases, largely reflecting the high proportion of angiomyolipomas. Previous radiological reviews by Hindman et al., and Zhang et al., have similarly emphasized that the presence of macroscopic fat strongly favors angiomyolipoma, whereas infiltrative margins, necrosis, and vascular invasion suggest malignant mesenchymal tumors [27,28]. Necrosis on imaging or gross pathology was significantly associated with malignant tumors in the present study and independently predicted malignancy on logistic regression analysis (OR=5.62; p<0.001). Necrosis likely reflects rapid tumor growth exceeding vascular supply, a feature commonly associated with high-grade sarcomas [27]. Similarly, vascular invasion emerged as the strongest predictor of malignancy (OR=6.18; p<0.001), emphasizing the aggressive biological nature of malignant renal mesenchymal neoplasms and their propensity for hematogenous dissemination [28].

Immunohistochemistry played a crucial role in tumor classification and differential diagnosis. Angiomyolipomas showed positivity for HMB-45 and Melan-A, consistent with their perivascular epithelioid cell origin, whereas leiomyosarcomas expressed SMA and desmin, confirming smooth muscle differentiation. These findings are in concordance with previous pathological studies by Pallagani et al., and Bafadni et al., [29,30]. Synovial sarcoma demonstrated TLE1 and cytokeratin positivity, while PNET/Ewing sarcoma showed CD99 and FLI1 expression, aiding accurate differentiation from sarcomatoid renal cell carcinoma and other spindle-cell lesions [31]. Moreover, higher Ki-67 proliferation indices observed in malignant tumors such as UPS and PNET/Ewing sarcoma reflected increased proliferative activity and aggressive tumor biology. This supports the utility of Ki-67 as an adjunct prognostic indicator in renal mesenchymal tumors [32].

Among malignant tumors, high-grade histology constituted the largest proportion (39.4%), and more than one-third of tumors exhibited mitotic activity exceeding 10/10 high-power fields. Tumor necrosis, lymph node metastasis, and distant metastasis were observed in substantial proportions, underscoring the aggressive clinical behavior of renal sarcomas. Similar findings have been reported in studies of Rose et al., and Campbell et al., renal leiomyosarcoma and undifferentiated pleomorphic sarcoma, both of which are associated with poor prognosis and high recurrence rates [33,34]. The relatively high frequency of perinephric fat invasion and vascular invasion in the present study further supports the infiltrative potential of malignant mesenchymal tumors.

Limitations

The present study was limited by its cross-sectional design and single-center setting, which may restrict the generalizability of findings to broader populations. Long-term follow-up data regarding recurrence, metastasis, and survival outcomes were not available. Molecular diagnostic studies were not performed in all cases because of resource limitations. Additionally, the rarity and histological heterogeneity of renal mesenchymal neoplasms may have influenced subgroup comparisons for uncommon tumor types.

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Conclusion

Primary renal mesenchymal neoplasms represent a rare and histologically diverse group of renal tumors with variable clinical behavior ranging from indolent benign lesions to highly aggressive sarcomas. Angiomyolipoma was the most common tumor subtype, whereas leiomyosarcoma predominated among malignant neoplasms. Malignant tumors were significantly associated with older age, male gender, larger tumor size, hematuria, necrosis, vascular invasion, and perinephric extension. Radiological findings combined with histopathological and immunohistochemical evaluation played a crucial role in accurate diagnosis and differentiation of these tumors. Recognition of clinicopathological predictors of malignancy may facilitate early diagnosis, appropriate therapeutic planning, and improved prognostic stratification in affected patients.

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