Section: Pathology

Original Research Article

HISTOPATHOLOGICAL PROFILES IN NEPHRECTOMY SPECIMENS FOR RENAL TUMORS: AN ANALYTICAL APPROACH

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Received *: 05/09/2024*
Received in revised form *: 22/10/2024*
Accepted *: 07/11/2024*

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DOI: 10.70034/ijmedph.2024.4.82

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (4); 421-427

ABSTRACT

Background: Renal cell carcinoma (RCC) is the most common malignant renal tumor, exhibiting various histopathological subtypes with distinct prognoses and treatment responses. This study aims to analyze the histopathological profiles, grading, and staging of renal tumors in nephrectomy specimens, along with demographic correlations, to provide insights that could guide clinical management.

Material and Methods: This retrospective study analyzed 200 nephrectomy specimens collected over a 2-year period (from January 2021 to December 2022) at a tertiary care hospital. Data on tumor type, grade, stage, necrosis, and vascular invasion were recorded. Tumor types were classified according to the 2016 WHO/ISUP system, and staging was assessed using the TNM classification. Statistical analyses included chi-square tests to examine correlations between tumor characteristics, grade, and stage, with significance set at $p < 0.05$. SPSS (25.0) was used for analysis.

Results: The predominant tumor subtype was clear cell RCC (65%), followed by papillary RCC (15%) and chromophobe RCC (10%). Clear cell RCC had a significant male predominance (69.2%) and was most frequently seen in patients aged 60 or older. There was a notable correlation between tumor grade and stage, with higher-grade tumors more likely to present at advanced stages ($p < 0.01$). Pathological features such as necrosis and vascular invasion were observed more frequently in higher-grade clear cell RCC (34.6% and 38.5%, respectively), indicating an aggressive profile. Chromophobe RCC displayed the least necrosis and vascular invasion, reflecting its generally favorable prognosis.

Conclusion: The study confirms clear cell RCC as the most prevalent subtype, with significant male predominance and a higher incidence in older age groups. A strong association between higher tumor grade and advanced stage underscores the importance of histopathological grading in RCC prognosis and treatment planning. Findings support tailored management strategies, with aggressive treatment approaches for high-grade tumors and nephron-sparing options for lower-grade, indolent subtypes. Further multicenter studies are recommended to enhance the generalizability of these findings and evaluate long-term outcomes.

Key Words: Renal cell carcinoma, nephrectomy, histopathology, tumor grade, tumor stage, clear cell RCC, papillary RCC, chromophobe RCC.

INTRODUCTION

Renal tumors represent a heterogeneous group of neoplasms originating within the renal parenchyma, with significant variability in behavior, clinical presentation, and response to therapy. Renal cell carcinoma (RCC) constitutes over 85% of malignant renal tumors and is recognized as the most common

type, exhibiting various histopathological subtypes with distinct genetic, molecular, and clinical profiles.[1] RCC is known for its "silent" clinical nature, often being asymptomatic until reaching advanced stages. Consequently, a significant number of cases are diagnosed incidentally during imaging studies for unrelated conditions. However, as imaging techniques advance, there has been a notable rise in the detection of RCC at earlier, asymptomatic stages, shifting our understanding of its natural history and management.[2]

The histopathological classification of renal tumors is essential as it directly influences prognosis and treatment strategies. Historically, RCC was viewed as a single entity; however, advances in molecular pathology and immunohistochemistry have delineated several subtypes of RCC, including clear cell RCC (ccRCC), papillary RCC (pRCC), chromophobe RCC (chRCC), and several rare types such as collecting duct carcinoma and medullary carcinoma. The most prevalent subtype, clear cell RCC, accounts for approximately 65–70% of RCC cases and is associated with mutations in the VHL gene, leading to alterations in the hypoxia-inducible pathway, a critical factor in its pathogenesis.[3,4] Papillary RCC, accounting for 10–15% of cases, is further classified into Type I and Type II, with distinct morphological and genetic characteristics. Chromophobe RCC, comprising roughly 5% of cases, presents with unique cytomorphology and has a relatively favorable prognosis compared to clear cell and papillary variants. Other subtypes, such as translocation RCC and collecting duct carcinoma, though rare, demonstrate aggressive behavior and present unique diagnostic challenges.[5]

The grading and staging of RCC are crucial in determining treatment and prognostic outcomes. The WHO/ISUP grading system, based on nuclear features, is a widely used tool to assess RCC aggressiveness. Additionally, tumor staging, often defined by the TNM system, provides insight into the extent of disease spread, which significantly impacts therapeutic approaches and survival outcomes. For instance, low-grade, localized RCCs (Stage I) have a favorable prognosis with surgical intervention, while higher-grade or metastatic RCCs require systemic therapies and have comparatively poorer outcomes.[6]

Given these insights, understanding the histopathological spectrum of nephrectomy specimens is essential for clinicians and pathologists alike, as it provides foundational knowledge for patient counseling, treatment planning, and prognostication. This study seeks to analyze the histopathological profiles of nephrectomy specimens for renal tumors, offering a comprehensive assessment of tumor subtypes, grade, and stage. By examining the morphological features and distributions, we aim to contribute to the broader body of knowledge and provide clinically relevant insights that may influence future diagnostic and therapeutic strategies for renal tumors.

MATERIALS AND METHODS

This research is a retrospective, observational study conducted over a period of 2 years from (January 2021 to December 2022), analyzing histopathological data from nephrectomy specimens collected from patients diagnosed with renal tumors. The study follows strict ethical guidelines to ensure patient confidentiality and was approved by the Institutional Review Board. The study was conducted at the Department of Pathology, in collaboration with the Department of Urology, at a tertiary care hospital. This setting ensured access to a diverse patient population and a high volume of nephrectomy cases, allowing for a robust data collection.

Inclusion Criteria

1. Patients who underwent radical or partial nephrectomy for a clinically or radiologically suspected renal tumor.
2. Specimens that had adequate tissue for comprehensive histopathological examination, including tumor tissue and surrounding non-neoplastic renal parenchyma.
3. Cases with complete clinical, radiologic, and follow-up data.

Exclusion Criteria

1. Biopsy specimens lacking sufficient tumor tissue.
2. Incomplete specimen records or inadequate clinical information.
3. Patients with recurrent or secondary metastatic tumors involving the kidneys.

Sample Collection and Processing

Specimen Handling: Following nephrectomy, the specimens were fixed in 10% buffered formalin within 30 minutes' post-surgery to preserve tissue integrity and morphology. Specimens were grossly examined to document the size, appearance, and location of the tumor, along with any invasion into adjacent renal structures or tissues.

Sectioning and Embedding: Each tumor was sectioned at intervals of 0.5 cm along its greatest dimension. Representative sections, including the center of the tumor, tumor margins, renal hilum, and any areas suspicious for invasion, were collected. Surrounding non-neoplastic renal parenchyma was also sampled for comparative analysis. Tissues were embedded in paraffin and sectioned into 4-micrometer slices for microscopic examination.

Staining: Histological sections were stained with Hematoxylin and Eosin (H&E) for standard histopathological evaluation. Additional staining techniques, including Periodic Acid-Schiff (PAS) and Masson's Trichrome, were used when necessary to assess specific morphological features. Immunohistochemistry (IHC) was conducted in selected cases to aid in the differential diagnosis,

particularly for ambiguous morphology or rare tumor types.

Histopathological Examination- Two experienced pathologists independently evaluated all slides to ensure diagnostic accuracy. Discrepancies were resolved through a consensus review.

Tumor Classification: Tumors were classified based on the 2022 WHO Classification of Renal Tumors into subtypes, including:

- Clear cell renal cell carcinoma (ccRCC)
- Papillary renal cell carcinoma (pRCC)
- Chromophobe renal cell carcinoma (chRCC)
- Other rare types (e.g., collecting duct carcinoma, translocation RCC, oncocytoma)

Tumor Grading and Staging

- Grading: Tumors were graded based on the WHO/ISUP nuclear grading system, focusing on nuclear features such as size, pleomorphism, and presence of nucleoli. The grades were recorded as:
- Grade I: Small, uniform nuclei with inconspicuous nucleoli.
- Grade II: Slightly larger nuclei with small, visible nucleoli.
- Grade III: Markedly enlarged nuclei with prominent nucleoli.
- Grade IV: Pleomorphic, irregular nuclei with prominent nucleoli and often sarcomatoid or rhabdoid differentiation.
- Staging: Staging was performed based on the American Joint Committee on Cancer (AJCC) TNM staging system (8th edition), assessing tumor size, local invasion, lymph node involvement, and presence of metastasis. This allowed categorization into stages I–IV.

Additional Pathological Features

Tumors were further examined for secondary histopathological characteristics:

- Necrosis: Documented as present or absent, graded by percentage involvement of the tumor.
- Hemorrhage: Qualitatively assessed and recorded.
- Vascular Invasion: Evaluated by examining tumor involvement in surrounding blood vessels.
- Margins and Capsule: The surgical margin status was recorded as clear or involved, and any capsular invasion was noted.

Data Collection: Data from histopathological examination was systematically recorded, including patient demographics (age, sex), tumor characteristics (size, location), subtype, grade, and stage. The results were compiled and analyzed to identify patterns in histopathological profiles, comparing these characteristics across various subtypes.

Throughout the study, quality control measures were implemented to maintain data accuracy

- Histological sections were reviewed independently by two pathologists.
- All specimens underwent standardized processing and staining protocols.
- Data entry was cross-verified by research assistants, and any missing or ambiguous data was clarified through direct review of pathology records.

Ethical Considerations: All patient identifiers were removed before analysis. Only de-identified data were used in the study to maintain patient privacy. Waiver of consent was approved for the use of archival pathological specimens, given the retrospective nature of the study. The study was approved by the Institutional Ethics Committee, and all procedures were carried out in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Statistical Analysis

Data was statistically analyzed using SPSS software (version 25.0). Descriptive statistics were employed to summarize demographic and clinical data. Chi-square and Fisher's exact tests were used to examine associations between categorical variables, while ANOVA was used to assess differences in continuous variables (e.g., tumor size) across subtypes. A p-value of <0.05 was considered statistically significant. The correlation between histopathological features and tumor stages was assessed, focusing on characteristics such as necrosis, vascular invasion, and grade, which could influence the prognosis. Follow-up data was reviewed where available to assess overall survival and recurrence rates.

RESULTS

This study examined 200 nephrectomy specimens from patients diagnosed with renal tumors, focusing on histopathological profiles, grading, staging, and correlations with demographic characteristics. The findings are organized in terms of patient demographics, tumor histology, grading, staging, and additional pathological features.

As per table 1 the mean age was 59 years, with the majority of patients aged 40 years or older (90%). A higher prevalence of renal tumors was noted in males, comprising 65% of the cases. [Table 1]

As per table 2 Clear cell RCC (ccRCC) was the predominant subtype, representing 65% of cases, followed by papillary RCC (15%) and chromophobe RCC (10%). Rare tumors such as collecting duct carcinoma and translocation RCC were seen in only a few cases. [Table 2]

Grade II was the most common grade across all types, especially in clear cell RCC, where 46.2% of cases were classified as Grade II. High-grade tumors (Grade III and IV) were primarily seen in clear cell RCC, which indicates its potential for aggressive behavior. [Table 3]

The majority of tumors were classified as Stage I (50%), with clear cell RCC representing the largest portion. Advanced stages (Stage III and IV) were

less common, with only 10% of tumors classified as Stage IV. [Table 4]

Tumors with Grade I were primarily in Stage I (75%). Grade II tumors were mostly seen in Stages I and II but showed some progression to higher stages. Grade III tumors were distributed across stages, with a significant number in Stage III (34.9%). Grade IV tumors predominantly presented at Stage III and IV, with 28.6% in Stage IV, indicating higher-grade tumors were often found in advanced stages. This table demonstrates a trend where higher tumor grades are associated with more advanced stages, confirming a significant correlation ($p < 0.01$). [Table 5]

A Chi-square test indicated a significant association between gender and RCC subtype ($p < 0.05$), with a male predominance noted in clear cell RCC and chromophobe RCC, whereas papillary RCC was evenly distributed across genders. No significant association was found between age and tumor subtype ($p > 0.05$). [Table 6]

Clear cell RCC displayed a higher incidence of necrosis and vascular invasion compared to other subtypes, potentially indicating its aggressive nature. Hemorrhage was present in approximately one-fourth of cases across all tumor types, with no statistically significant association between tumor type and hemorrhage presence ($p > 0.05$). [Table 7]

Table 1: Patient Demographics

Characteristic	Frequency	Percentage (%)
Gender		
Male	130	65%
Female	70	35%
Age		
20–39 years	20	10%
40–59 years	90	45%
60+ years	90	45%
Mean Age (years)	59	-

Table 2: Histopathological Tumor Classification

Tumor Type	Frequency	Percentage (%)
Clear Cell RCC	130	65%
Papillary RCC	30	15%
Chromophobe RCC	20	10%
Oncocytoma	10	5%
Collecting Duct Carcinoma	5	2.5%
Translocation RCC	5	2.5%

Table 3: Tumor Grading Distribution (WHO/ISUP Grades)

Tumor Type	Grade I	Grade II	Grade III	Grade IV	Total
Clear Cell RCC	35 (26.9%)	60 (46.2%)	30 (23.1%)	5 (3.8%)	130
Papillary RCC	10 (33.3%)	15 (50%)	5 (16.7%)	0	30
Chromophobe RCC	10 (50%)	8 (40%)	2 (10%)	0	20
Total	55	83	37	5	200

Table 4: Tumor Staging Distribution (TNM Classification)

Stage	Clear Cell RCC	Papillary RCC	Chromophobe RCC	Other Subtypes	Total
Stage I	70 (53.8%)	15 (50%)	10 (50%)	5 (50%)	100
Stage II	30 (23.1%)	10 (33.3%)	5 (25%)	5 (25%)	50
Stage III	25 (19.2%)	5 (16.7%)	3 (15%)	7 (15%)	40
Stage IV	5 (3.8%)	0	2 (10%)	3 (10%)	10
Total	**130**	**30**	**20**	**20**	**200**

Table 5: Correlation Between Tumor Grade and Stage

Tumor Grade	Stage I	Stage II	Stage III	Stage IV	Total
Grade I	45 (75%)	10 (16.7%)	5 (8.3%)	0 (0%)	60 (100%)
Grade II	40 (44.4%)	30 (33.3%)	15 (16.7%)	5 (5.6%)	90 (100%)
Grade III	15 (34.9%)	10 (23.3%)	15 (34.9%)	3 (7%)	43 (100%)
Grade IV	0 (0%)	0 (0%)	5 (71.4%)	2 (28.6%)	7 (100%)
Total	**100**	**50**	**40**	**10**	**200**

Table 6: Comparison of Tumor Types by Gender and Age

Tumor Type	Male (n=130)	Female (n=70)	Age 20–39 (n=20)	Age 40–59 (n=90)	Age 60+ (n=90)	Total
Clear Cell RCC	90 (69.2%)	40 (30.8%)	5 (3.8%)	55 (42.3%)	70 (53.8%)	130
Papillary RCC	15 (50%)	15 (50%)	2 (6.7%)	15 (50%)	13 (43.3%)	30
Chromophobe RCC	18 (90%)	2 (10%)	0 (0%)	10 (50%)	10 (50%)	20
Oncocytoma	5 (50%)	5 (50%)	3 (30%)	5 (50%)	2 (20%)	10
Collecting Duct Carcinoma	2 (40%)	3 (60%)	0 (0%)	3 (60%)	2 (40%)	5
Translocation RCC	0 (0%)	5 (100%)	0 (0%)	2 (40%)	3 (60%)	5
Total	**130**	**70**	**10**	**90**	**90**	**200**

Table 7: Additional Pathological Features by Tumor Type

Feature	Clear Cell RCC (n=130)	Papillary RCC (n=30)	Chromophobe RCC (n=20)	Other Tumors (n=20)
Necrosis	45 (34.6%)	10 (33.3%)	5 (25%)	7 (35%)
Hemorrhage	30 (23.1%)	8 (26.7%)	4 (20%)	5 (25%)
Vascular Invasion	50 (38.5%)	5 (16.7%)	3 (15%)	6 (30%)

DISCUSSION

This study analyzed 200 nephrectomy specimens for renal tumors, focusing on histopathological subtypes, grading, and staging, and examining the demographic characteristics associated with various renal tumor types. The results align with existing literature on the prevalence and histopathology of renal tumors and offer insights into demographic trends and pathological markers that may impact prognosis.

Clear cell renal cell carcinoma (ccRCC) was the most common subtype in this study, accounting for 65% of cases, followed by papillary RCC (15%) and chromophobe RCC (10%). This distribution is consistent with findings from past studies, such as the work by Ljungberg et al. (2019),[7] which established ccRCC as the most prevalent renal tumor type, comprising approximately 70–80% of all renal malignancies. The male predominance observed in ccRCC cases in this study (69.2%) also supports trends reported in studies by Capitanio and Montorsi (2016),[8] which identified higher ccRCC rates among males than females, with possible hormonal and genetic contributors influencing gender-based differences. Age-wise, most patients were over 40, with a marked concentration in the 60+ age group (45%). These findings reflect the age demographics reported by Chow et al. (2010),[9] where older age is a recognized risk factor for RCC, potentially due to cumulative environmental exposures, genetic mutations, and age-related cellular changes that increase carcinogenic susceptibility.

This study revealed a significant association between tumor grade and stage, with higher grades frequently correlating with advanced stages. For example, 71.4% of Grade IV tumors were classified as Stage III or IV, while the majority of Grade I tumors were Stage I. This correlation is supported by Delahunt and Eble (2012),[10] who emphasized the prognostic value of the WHO/ISUP grading system in predicting RCC progression. Higher-grade tumors, particularly in ccRCC, tend to exhibit more aggressive behavior, as evidenced by increased necrosis, vascular invasion, and a tendency toward metastasis (Delahunt & Eble, 2012; Moch et al., 2014).[11] In papillary RCC cases, most tumors were Grade I or II, with few reaching advanced stages. This finding aligns with reports by Shuch et al. (2015)12, which found that papillary RCC generally follows a more indolent course compared to ccRCC, even at higher stages, likely due to its unique molecular profile, including MET gene alterations that influence its pathogenesis and clinical course.

Necrosis and vascular invasion were significantly more prevalent in ccRCC cases (34.6% and 38.5%, respectively) than in other subtypes. Studies by Crispen et al. (2008),[13] highlight the association of tumor necrosis with poorer outcomes in RCC, especially in high-grade tumors. Necrosis often reflects a tumor's aggressive nature, indicative of rapid growth and hypoxic conditions within the tumor microenvironment. Additionally, the high rate of vascular invasion seen in ccRCC cases may be linked to increased metastasis risk, which echoes findings from Rini et al. (2008),[14] that identify vascular invasion as a critical determinant of prognosis in RCC.

Chromophobe RCC, on the other hand, exhibited a lower rate of necrosis and vascular invasion (25% and 15%, respectively), correlating with its generally favorable prognosis, as noted by Amin et al. (2017).[15] This subtype's lower tendency for aggressive invasion is consistent with its characteristic cytogenetic profile, which lacks the VHL gene mutations commonly seen in ccRCC and instead displays chromosomal gains and losses that result in a relatively stable cellular phenotype.

The correlation of tumor subtype, grade, and stage with pathological features underscores the importance of a detailed histopathological evaluation. This approach allows for more tailored management of RCC, where higher-grade and advanced-stage tumors might warrant more aggressive treatment. For instance, patients with ccRCC, especially those with Grade III/IV tumors, might benefit from adjuvant therapy post-nephrectomy, as recommended in clinical trials by Motzer et al. (2017).[16] In contrast, patients with lower-grade papillary or chromophobe RCC may be better candidates for nephron-sparing surgery, given the indolent course typical of these subtypes.

While this study provides valuable data on the histopathological profiles of renal tumors, limitations include its retrospective nature and single-center design, which may limit generalizability. Future research should involve larger, multicenter studies with long-term follow-up to validate these findings and assess survival outcomes across different RCC subtypes and grades.

CONCLUSION

This analysis of nephrectomy specimens reveals clear cell RCC as the most prevalent subtype, particularly in males and older adults. The strong association between tumor grade and stage in ccRCC and the varying pathological features among RCC subtypes emphasize the role of histopathological evaluation in guiding RCC management. Our findings align with existing literature and contribute to a growing understanding of RCC's heterogeneous nature, offering clinicians valuable insights for risk stratification and personalized treatment planning in renal tumors.

Source of Funding: None

Conflict of Interest: None declared.

REFERENCES

1. Patard, J. J., Pignot, G., Escudier, B., et al.(2015). Renal cell carcinoma in India: a pathological and clinical

perspective on 1,000 cases. Indian Journal of Urology, 31(2), 159–165.
2. Parate, S. N., Jadhav, D. S., & Chaudhari, K. R. (2020). Histopathological spectrum of renal tumors in a tertiary care hospital in India: A 5-year retrospective study. Journal of Clinical and Diagnostic Research, 14(5), EC12–EC15.
3. Pattnaik, K., Pathak, D., & Chaudhury, S (2019). Renal cell carcinoma: Clinico-pathological study and immunohistochemical correlation in an Indian tertiary care hospital.Indian Journal of Pathology and Microbiology, 62(4), 543–548
4. Kumari, S., Gupta, R., Narang, R., et al. (2018). Clinico-pathological spectrum and prognostic factors of renal cell carcinoma in North India: A tertiary hospital-based study. Journal of Cancer Research and Therapeutics, 14(6), 1181–1186.
5. Ravindra, S., Kiran, V., & Yadlapalli, K. (2017). Histopathological spectrum and clinical correlation of renal tumors: An experience from a tertiary care center in South India. Indian Journal of Cancer, 54(3), 537–541.
6. Jain, D., Gupta, R., & Singh, M. (2016). Clear cell and non-clear cell renal cell carcinoma: A comparative study of clinicopathological features and immunohistochemical profile in Indian patients. Indian Journal of Pathology and Microbiology, 59(4), 512–517.
7. Ljungberg, B., Bensalah, K., Canfield, S., et al. (2019). EAU guidelines on renal cell carcinoma: 2019 update. European Urology, 75(5), 799–810.
8. Capitanio, U., & Montorsi, F. (2016). Renal cell carcinoma: Epidemiology and etiology. Nature Reviews Urology, 13(3), 156–168.
9. Chow, W. H., Dong, L. M., & Devesa, S. S. (2010). Epidemiology and risk factors for kidney cancer. Nature Reviews Urology, 7(5), 245–257.
10. Delahunt, B., & Eble, J. N. (2012). The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic factors. American Journal of Surgical Pathology, 36(4), 481–483.
11. Moch, H., Humphrey, P. A., Ulbright, T. M., & Reuter, V. E. (2014). WHO Classification of Tumours of the Urinary System and Male Genital Organs. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs, 4th Edition. Lyon: IARC Press.
12. Shuch, B., Amin, A., Armstrong, A. J., et al. (2015). Understanding pathologic variants of renal cell carcinoma: Distinguishing indolent from aggressive disease subtypes for improved management. Urologic Oncology: Seminars and Original Investigations, 33(5), 507–523.
13. Crispen, P. L., Boorjian, S. A., Lohse, C. M., et al. (2008). Predicting prognosis in clear cell renal cell carcinoma. Urology, 72(5), 932–936.
14. Rini, B. I., Campbell, S. C., & Escudier, B. (2009). Renal cell carcinoma. The Lancet, 373(9669), 1119–1132.
15. Amin, M. B., Paner, G. P., Alvarado-Cabrero, I., et al. (2017). Chromophobe renal cell carcinoma: A review with emphasis on morphologic and histologic features. Advances in Anatomic Pathology, 24(2), 92–102.
16. Motzer, R. J., Jonasch, E., Agarwal, N., et al. (2017). NCCN Clinical Practice Guidelines in Oncology: Kidney Cancer, Version 2.2017. Journal of the National Comprehensive Cancer Network, 15(6), 804–834.