

Histopathological Spectrum of Renal Cell Carcinoma and Its Correlation With Clinical Presentation, Imaging Findings, and Surgical Outcomes: A Multicenter Retrospective Observational Study

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Abstract

Introduction:

To evaluate the histopathological spectrum of renal cell carcinoma (RCC) and correlate histopathological subtypes and tumor characteristics with clinical presentation, imaging findings, pathological stage, and surgical outcomes.

Methods:

This multicenter retrospective observational study included 120 adults with histopathologically confirmed RCC who underwent radical or partial nephrectomy at Jagannath Medical College & Hospital, Puri, and Acharya Harihara Post Graduate Institute of Cancer, Cuttack. Clinical, radiological, operative, and histopathological records were reviewed. Histopathological assessment included tumor subtype, WHO/ISUP grade, pathological stage, and lymphovascular invasion. Associations with clinical, imaging, and postoperative variables were assessed using appropriate statistical tests.

Results:

Clear cell RCC was the predominant subtype (82, 68.3%), followed by papillary RCC (20, 16.7%) and chromophobe RCC (12, 10.0%). Hematuria (51.7%) and flank pain (45.0%) were the most common presentations, while 31.7% of tumors were detected incidentally. Tumor size >7 cm was significantly associated with advanced pathological stage, renal vein invasion, perinephric fat invasion, and enlarged lymph nodes ($p < 0.05$). High WHO/ISUP grade was significantly associated with advanced pathological stage ($p < 0.001$). Postoperative complications occurred in 15.0% of patients and were associated with larger tumor size, high grade, advanced stage, and renal vein invasion. Multivariate analysis identified tumor size >7 cm, high WHO/ISUP grade, stage III–IV disease, and renal vein invasion as significant predictors of postoperative complications.

Conclusion:

Clear cell RCC predominated, while tumor size, grade, stage, and vascular invasion were significantly associated with disease extent and postoperative outcomes.

Recommendation:

Integrated clinicoradiological and histopathological assessment should be considered for risk stratification and perioperative management of RCC.

Keywords: Renal cell carcinoma; Histopathology; Clear cell RCC; Nephrectomy; World Health Organization/International Society of Urological Pathology (WHO/ISUP) grading; Surgical outcomes.

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Introduction

Nearly 90% of all primary renal malignancies are renal cell carcinomas (RCCs), the most prevalent malignant tumour of the kidney in adults. RCC is among the top ten malignancies diagnosed globally, and its incidence has been continuously rising due to increased diagnosis of incidental renal masses and extensive use of cross-sectional imaging. Because of its biological variability and potential for metastatic spread, RCC continues to significantly contribute to cancer-related morbidity and mortality despite advancements in diagnostic imaging and surgical procedures (1).

A wide range of tumours originating from the renal tubular epithelium are included in renal cell carcinoma. Clear cell renal cell carcinoma (ccRCC), papillary renal cell carcinoma (pRCC), and chromophobe renal cell carcinoma (chRCC) account for the majority of instances among the several histological subtypes recognised by the World Health Organisation (WHO) 2022 Classification. Collecting duct carcinoma, medullary carcinoma, translocation-associated renal cell carcinoma, fumarate hydratase-deficient RCC, succinate dehydrogenase-deficient RCC, and a number of recently identified molecularly characterised tumours are examples of less prevalent types. Each subtype has distinctive morphological, immunohistochemical, genetic, and clinical characteristics that affect treatment choices and prognosis (2).

Over the past few decades, RCC's clinical presentation has changed significantly. Nowadays, only a small percentage of patients experience the classic triad of hematuria, flank discomfort, and palpable abdominal mass, since many tumours are discovered by accident during computed tomography (CT) or ultrasonography procedures carried out for unrelated illnesses. However, constitutional symptoms such as weight loss, fever, exhaustion, anaemia, or paraneoplastic syndromes brought on by ectopic hormone production may appear in patients with severe illness. Because metastatic illness has a far worse prognosis than localised tumours, which may be cured by surgical resection, early identification is still essential (3).

When it comes to RCC diagnosis, staging, and preoperative planning, radiological imaging is essential. While contrast-enhanced computed tomography (CECT) is still the preferred imaging modality for characterising renal masses and evaluating local extension, vascular invasion, lymph node involvement, and distant metastases, ultrasound is used as an initial screening tool. For some patients, especially those who have venous thrombus or are contraindicated for iodinated contrast, magnetic resonance imaging (MRI) offers extra information. However, histological analysis of nephrectomy tissues is necessary for a final diagnosis and prognostic assessment (4).

Tumour subtype identification, WHO/ISUP nuclear grading, pathological TNM staging, tumour necrosis,

sarcomatoid differentiation, rhabdoid characteristics, lymphovascular invasion, and surgical margin status are all included in the histopathological evaluation. Postoperative surveillance and adjuvant treatment options are guided by these indicators, which have established prognostic importance. Higher nuclear grade, advanced clinical stage, greater tumour size, and unfavourable histological features have all been linked to increased recurrence, metastasis, and worse survival, according to numerous studies (5).

The clinicopathological profile of RCC has been described in a number of studies, but there is still a dearth of regional data from eastern India. Additionally, in a multicenter context, few studies have thoroughly connected histological findings with clinical presentation, imaging features, and surgical outcomes. Finding prognostic factors that could affect long-term outcomes, enhancing treatment planning, and increasing diagnostic accuracy all depend on this information (6).

In order to assess the histological spectrum of renal cell carcinoma in patients receiving treatment at Jagannath Medical College and Hospital in Puri and Acharya Harihar Post Graduate Institute of Cancer in Cuttack, Odisha, the current multicenter retrospective observational study was conducted. Correlating histological subtypes with clinical presentation, radiographic findings, surgical management, and postoperative surgical outcomes was another goal of the study.

Materials and Methods

Study Design

This was a multicenter retrospective observational study conducted to evaluate the histopathological spectrum of renal cell carcinoma (RCC) and its association with clinical presentation, imaging findings, pathological characteristics, and surgical outcomes.

Study Setting

The study was conducted at Jagannath Medical College & Hospital, Puri, Odisha, India, and Acharya Harihar Post Graduate Institute of Cancer, Cuttack, Odisha, India. **The study involved the Departments of Pathology, Urology, and General Surgery** at the participating institutions. These departments provide diagnostic, surgical, oncological, and postoperative care services for patients with urological and other malignant diseases. Patients with suspected renal tumors undergo clinical evaluation and radiological assessment, followed by definitive surgical management and histopathological examination when indicated.

Study Duration

Medical records of eligible patients treated during the study period were retrospectively reviewed.

Study Population and Participant Selection

The study population comprised **adult patients aged ≥ 18 years with histopathologically confirmed RCC** who underwent radical or partial nephrectomy at either participating institution. Patients were identified from hospital records and pathology databases using the predefined eligibility criteria.

Patients were included if they had histopathologically confirmed RCC, had undergone radical or partial nephrectomy, had complete clinical, radiological, operative, and histopathological records, and had documented postoperative follow-up. Patients with benign renal tumors, metastatic nonrenal tumors, inadequate biopsy or histopathological material, those managed conservatively without surgery, and those with substantially incomplete records were excluded.

A total of **120 eligible patients** were included in the final analysis.

Data Collection

Data were retrospectively extracted from medical records using a predefined data collection format. The variables included age, sex, presenting symptoms, comorbidities, laboratory findings, tumor laterality, tumor size, ultrasonography findings, contrast-enhanced computed tomography findings, magnetic resonance imaging findings where available, operative procedure and findings, histopathological subtype, WHO/ISUP grade, pathological TNM stage according to the AJCC 8th edition, surgical margins, lymphovascular invasion, tumor necrosis, sarcomatoid differentiation, postoperative complications, and duration of hospital stay.

Histopathological Evaluation

Nephrectomy specimens were fixed in **10% neutral buffered formalin**, routinely grossed and processed, followed by hematoxylin and eosin staining. Histopathological examination was performed by experienced pathologists. Tumors were classified according to the **2022 WHO Classification of Tumours**, and grading was performed using the **WHO/ISUP grading system**. Relevant pathological features, including tumor subtype, grade, pathological stage, lymphovascular invasion, necrosis, and sarcomatoid differentiation, were recorded.

Statistical Analysis

Statistical analysis was performed using **IBM SPSS Statistics version 26.0**. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. The **independent-samples Student's t-test** was used to compare continuous variables between two groups, and **one-way analysis of variance (ANOVA)** was used when more

than two groups were compared. The **Pearson chi-square test** was used to assess associations between categorical variables when the expected cell frequencies were adequate; **Fisher's exact test** was used when the expected frequencies were small. **Multivariable logistic regression analysis** was performed to identify independent predictors of postoperative complications. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A **two-sided p-value < 0.05** was considered statistically significant.

Bias

To minimize selection bias, predefined inclusion and exclusion criteria were applied consistently to records from both participating institutions. Consecutive eligible patients identified from institutional medical and pathology records were considered for inclusion. To reduce information bias, data were extracted using a standardized data collection format, and histopathological diagnoses and grading were based on established WHO/ISUP criteria. Only records containing sufficient clinical, radiological, operative, and histopathological information were included in the final analysis. As this was a retrospective study, the possibility of residual selection and information bias could not be completely eliminated.

Ethical Considerations

The study was conducted in accordance with the **Declaration of Helsinki** and institutional ethical guidelines. Ethical approval was obtained from the Institutional Ethics Committees of both participating institutions before commencement of the study. Patient information was anonymized during data extraction and analysis, and confidentiality of medical records was maintained.

Results

The present multicenter study demonstrated that clear cell RCC was the predominant histopathological subtype. Hematuria and flank pain remained the most common clinical presentations, although incidental detection was increasingly frequent. Imaging findings showed excellent correlation with pathological stage, while high nuclear grade, larger tumor size, and vascular invasion were significantly associated with poorer surgical outcomes.

A total of 120 patients with histopathologically confirmed renal cell carcinoma (RCC) who underwent surgical treatment at the participating centers were included in the study. The mean age was 56.8 ± 11.9 years (range: 28–81 years), with a male predominance (72 males, 60.0%). Clear cell renal cell carcinoma (ccRCC) was the most common histopathological subtype. Radical nephrectomy was performed in the majority of patients. Histopathological grade and pathological stage showed significant associations with imaging characteristics and postoperative outcomes.

Table 1. Baseline demographic and clinicopathological characteristics (n=120)

Variable	Frequency (%)
Age (years)	
<40	14 (11.7)
40–59	58 (48.3)
≥60	48 (40.0)
Mean age (years)	56.8 ± 11.9
Sex	
Male	72 (60.0)
Female	48 (40.0)
Right kidney	66 (55.0)
Left kidney	54 (45.0)
Mean tumor size (cm)	6.7 ± 2.8

Most patients were older than 40 years, with a peak incidence between 40 and 59 years. RCC demonstrated a male predominance and slightly higher involvement of the right kidney. The average tumor size at presentation was 6.7 cm, indicating that many tumors were diagnosed at an intermediate stage.

Table 2. Clinical presentation of patients

Clinical feature	Frequency (%)
Hematuria	62 (51.7)
Flank pain	54 (45.0)
Incidental renal mass	38 (31.7)
Weight loss	24 (20.0)
Palpable abdominal mass	18 (15.0)
Fever	14 (11.7)
Classical triad	10 (8.3)

Hematuria was the most common presenting symptom, followed by flank pain. Nearly one-third of tumors were detected incidentally during imaging, reflecting increasing utilization of abdominal ultrasonography and CT. The classical triad was uncommon, occurring in only 8.3% of patients.

Table 3. Histopathological spectrum of renal cell carcinoma

Histological subtype	Frequency (%)
Clear cell RCC	82 (68.3)
Papillary RCC	20 (16.7)
Chromophobe RCC	12 (10.0)
Collecting duct carcinoma	3 (2.5)
Unclassified RCC	3 (2.5)

Clear cell RCC was the predominant histological subtype, accounting for more than two-thirds of all tumors. Papillary RCC and chromophobe RCC were the next most frequent subtypes, while rare variants collectively constituted only 5% of cases.

Table 4. Correlation of imaging findings with pathological stage

Imaging finding	Stage I–II (n=72)	Stage III–IV (n=48)	p-value
Tumor size >7 cm	18 (25.0%)	34 (70.8%)	<0.001
Renal vein invasion	5 (6.9%)	20 (41.7%)	<0.001
Perinephric fat invasion	8 (11.1%)	26 (54.2%)	<0.001
Enlarged lymph nodes	6 (8.3%)	18 (37.5%)	0.002

Advanced-stage tumors demonstrated significantly larger size, renal vein involvement, perinephric fat invasion, and regional lymphadenopathy on imaging. These radiological findings strongly correlated with pathological staging.

Table 5. Histopathological grade and pathological stage

Variable	Low grade (Grade I–II)	High grade (Grade III–IV)	p-value
Stage I	38	6	
Stage II	24	10	
Stage III	10	18	
Stage IV	4	10	<0.001

High WHO/ISUP nuclear grade was significantly associated with advanced pathological stage. Patients with Grade III–IV tumors were considerably more likely to present with Stage III–IV disease.

Table 6. Surgical procedures and postoperative outcomes

Variable	Frequency (%)
Radical nephrectomy	88 (73.3)
Partial nephrectomy	32 (26.7)
Mean operative time (minutes)	152 ± 32
Mean hospital stay (days)	6.8 ± 2.4
Overall postoperative complications	18 (15.0)
Major complications (Clavien–Dindo ≥III)	6 (5.0)

Radical nephrectomy was the most frequently performed procedure. Surgical outcomes were favorable, with relatively short hospital stays and a low incidence of major postoperative complications.

Table 7. Predictors of postoperative complications

Variable	Complications (%)	No complications (%)	p-value
Tumor size >7 cm	14	38	0.001
High-grade RCC	12	32	0.003
Stage III–IV	13	35	0.002
Clear cell RCC	14	68	0.418

Larger tumors, higher nuclear grade, and advanced pathological stage were significantly associated with postoperative complications. Histological subtype alone did not significantly influence early surgical outcomes.

Table 8. Multivariate logistic regression analysis for adverse surgical outcome

Variable	Adjusted OR	95% CI	p-value
Tumor size >7 cm	3.18	1.42–7.12	0.004
High WHO/ISUP grade	2.86	1.24–6.58	0.012
Stage III–IV disease	3.94	1.65–9.43	0.002
Renal vein invasion	2.52	1.10–5.79	0.028

Multivariate analysis identified tumor size greater than 7 cm, high WHO/ISUP grade, advanced pathological stage, and renal vein invasion as independent predictors of adverse postoperative outcomes.

Discussion

Renal cell carcinoma (RCC) is a physiologically complex cancer with a wide range of histological subgroups and inconsistent clinical manifestations. About two-thirds of all instances in the current multicenter retrospective analysis were clear cell RCC, with papillary and chromophobe RCC

coming in second and third. Clear cell RCC consistently accounts for 65–75% of renal epithelial malignancies, which is in line with the WHO 2022 categorisation and global epidemiological data. Changes in the von Hippel–Lindau (VHL) tumour suppressor pathway, which promotes tumour angiogenesis and development, are primarily responsible for the prevalence of clear cell RCC (7).

In line with reports from India and other nations, the patients' mean age was 56.8 years, with a noticeable male predominance. Greater exposure to smoking, obesity, hypertension, and occupational carcinogens—all known

risk factors for RCC—has been linked to male predominance. The bulk of patients arrived after their fourth decade of life, confirming earlier findings that RCC primarily affects middle-aged and older adults (8).

In the current study, hematuria and flank pain continued to be the most frequent presenting symptoms. However, during radiological evaluation for unrelated abdominal problems, over one-third of tumours were unintentionally discovered. Because ultrasonography and contrast-enhanced computed tomography (CECT) are widely available, the percentage of accidentally discovered kidney masses is rising. Improved long-term survival and a rise in localised tumours amenable to nephron-sparing surgery are results of earlier identification (9).

The pathological stage and imaging results showed a strong correlation. Advanced pathological stage was substantially correlated with tumours larger than 7 cm, renal vein invasion, perinephric fat infiltration, and enlarged regional lymph nodes. These findings highlight how important preoperative imaging is for risk assessment and surgery planning. Because of its great sensitivity in detecting local extension and vascular involvement, CECT remains the primary imaging modality for staging RCC (10).

The gold standard for conclusive diagnosis and prognostic assessment is still histopathological investigation. High WHO/ISUP nuclear grade was strongly correlated with advanced pathological stage and surgical complications in this study. Higher vascular invasion and a higher chance of locally progressed disease were among the more aggressive biological behaviours displayed by high-grade tumours. These results support the predictive significance of WHO/ISUP grading, which is now a crucial part of standard pathology reporting (11).

Radical nephrectomy remained the most regularly performed surgical technique because a major proportion of malignancies were large or locally advanced upon diagnosis. However, in certain patients with localised disease, partial nephrectomy was successfully carried out, which is in line with current guidelines that favour nephron-sparing techniques wherever they are theoretically possible. Overall surgical results were satisfactory, with acceptable hospital stays and low rates of serious postoperative complications (12).

Adverse surgical outcomes were found to be independently predicted by tumour size larger than 7 cm, advanced pathological stage, high nuclear grade, and renal vein invasion, according to multivariate analysis. The UCLA Integrated Staging System (UISS) and SSIGN score are two examples of validated prognostic models that include similar prognostic markers that have been consistently identified in recent literature. Understanding these pathological risk factors makes it easier to choose individuals who might benefit from adjuvant systemic

therapy and to conduct tailored postoperative surveillance (13).

This study's multicenter design, thorough clinicopathological correlation, and standardised histological evaluation in accordance with the WHO 2022 classification are among its strong points. However, significant drawbacks include the retrospective design, lack of quality-of-life assessment, insufficient molecular characterisation, and lack of a long-term survival study. Future prospective multicenter studies integrating histology with molecular biomarkers, genetic profiling, and long-term oncological outcomes are required to better customise care of renal cell carcinoma. Overall, the current results confirm that nuclear grade, pathological stage, histological subtype, and imaging features continue to be important predictors of prognosis and surgical outcomes in RCC patients (14, 15).

Conclusion

The current multicenter retrospective analysis demonstrates the wide range of histological features of renal cell carcinoma (RCC) and underlines the intimate connection between radiological findings, clinical presentation, histopathological features, and surgical outcomes. The most common subtype was clear cell renal cell carcinoma, which was followed by papillary and chromophobe RCC. The most common presenting symptoms continued to be hematuria and flank pain, despite an increasing number of tumours being found by accident through imaging. Adverse surgical outcomes and postoperative complications were found to be significantly correlated with histopathological characteristics, specifically WHO/ISUP nuclear grade, pathological stage, tumour size, and vascular invasion. Accurate surgical planning and risk assessment were made possible by the strong correlation between preoperative imaging results and pathological staging. While nephron-sparing surgery produced satisfactory results in carefully chosen patients with localised illness, radical nephrectomy continued to be the most common surgical technique. For precise diagnosis, prognostic classification, and postoperative care, a thorough histological evaluation is still essential. It is anticipated that the integration of contemporary imaging methods with standardised pathological evaluation and molecular classification will enhance long-term survival, surveillance tactics, and individualised treatment for patients with renal cell carcinoma. The integration of pathology, imaging, and risk assessment for tailored management is still emphasised in recent guidelines.

Generalizability

The findings of this multicenter retrospective observational study provide clinically relevant information regarding the histopathological spectrum of renal cell carcinoma and its

association with tumor characteristics, pathological stage, and postoperative outcomes. The predominance of clear cell RCC and the observed associations of larger tumor size, higher WHO/ISUP grade, advanced pathological stage, and renal vein invasion with postoperative complications may be applicable to similar tertiary-care hospitals managing patients with RCC. However, generalizability to other populations should be considered cautiously because the study was conducted at two institutions in Odisha and included only patients who underwent surgical treatment. The findings may therefore not directly represent patients managed conservatively, patients from primary or secondary healthcare settings, or populations with different demographic and clinical characteristics. Prospective multicenter studies involving diverse geographical and healthcare settings are required to further validate these findings.

Conclusion

This multicenter retrospective observational study demonstrated a broad histopathological spectrum of RCC, with clear cell RCC being the predominant subtype. Larger tumor size, higher WHO/ISUP grade, advanced pathological stage, and renal vein invasion were significantly associated with adverse pathological characteristics and postoperative complications. The findings emphasize the importance of integrating clinical, radiological, surgical, and histopathological assessment in the evaluation and management of patients with RCC.

Limitations

The study has several limitations. First, its retrospective design may have resulted in selection and information bias because the analysis depended on the completeness and accuracy of existing medical records. Second, the study was conducted at only two institutions and included a relatively small sample of 120 patients, which may limit the generalizability of the findings. Third, only patients who underwent radical or partial nephrectomy were included; therefore, the findings may not be applicable to patients managed conservatively or with nonsurgical approaches. Fourth, molecular and genetic characteristics of the tumors were not assessed. Fifth, quality-of-life measures and long-term survival outcomes were not evaluated. Finally, the study focused primarily on short-term postoperative outcomes, and prospective studies with longer follow-up are required to confirm the observed associations.

Recommendations

Future studies should include larger, prospective, multicenter cohorts with longer follow-up to validate the associations between histopathological characteristics and clinical outcomes. Incorporation of molecular and genetic

tumor profiling may provide additional information regarding tumor biology and prognosis. Standardized collection of clinical, radiological, pathological, and patient-reported outcome data may also improve risk stratification and facilitate comparison across different healthcare settings.

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List of Abbreviations

- **RCC** – Renal cell carcinoma
- **WHO** – World Health Organization
- **ISUP** – International Society of Urological Pathology
- **LVI** – Lymphovascular invasion
- **TNM** – Tumor, Node, Metastasis
- **AJCC** – American Joint Committee on Cancer
- **USG** – Ultrasonography
- **CECT** – Contrast-enhanced computed tomography
- **MRI** – Magnetic resonance imaging
- **SPSS** – Statistical Package for the Social Sciences
- **OR** – Odds ratio
- **CI** – Confidence interval

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Conflict of Interest

The authors declare that they have no conflict of interest related to this study.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to institutional policies and applicable ethical and confidentiality requirements.

Author Contributions

Sujata Pujari: Conceptualization, study design, histopathological evaluation, data interpretation, manuscript preparation, and critical revision of the manuscript.

Original Article

Jeeban Jyoti Mishra: Study coordination, clinical and surgical data collection, interpretation of clinical and operative findings, and critical revision of the manuscript.

Dr. Datteswar Hota: Surgical expertise, interpretation of urological and operative findings, critical review of the manuscript, and final approval of the version to be published.

All authors: Reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work.

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