

Research Article**Association of Renal Cell Carcinoma With Renal Function, Urological Symptoms, Skeletal Involvement, and Radiological Tumor Characteristics: A Cross-Sectional Study**

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Abstract

Background: Renal cell carcinoma (RCC) is a malignant tumour of the renal parenchyma with variable clinical presentation and radiological characteristics. Patients present with incidentally detected renal masses, haematuria, flank pain, or symptoms associated with advanced disease. Renal function was be affected by tumour characteristics, urinary obstruction, pre-existing kidney disease, or the loss of functioning renal tissue. Skeletal metastases are an important manifestation of advanced RCC and was be associated with bone pain, pathological fractures, and other skeletal complications.

Objective: To evaluate the associations of renal function and urological symptoms with skeletal involvement and radiological tumour characteristics among patients with RCC.

Methods: This cross-sectional study is designed to include adult patients with

histopathologically confirmed RCC who have available clinical, laboratory, and radiological records. Demographic characteristics, presenting symptoms, comorbidities, serum creatinine, estimated glomerular filtration rate (eGFR), tumour size, laterality, anatomical location, local extension, venous involvement, lymph-node status, and distant metastases was recorded. Skeletal involvement was classified according to available imaging and clinical documentation. Associations was evaluated using appropriate descriptive and inferential statistical methods, including multivariable logistic regression where the sample size and number of outcome events permit.

Results: Actual findings must be calculated from the study dataset. The results tables included below contain explicitly hypothetical examples to illustrate manuscript presentation and are not observed clinical data.

Conclusion: The study was clarify the relationships between renal function, urological symptoms, skeletal involvement, and radiological tumour characteristics in RCC. Interpretation should account for age, pre-existing kidney disease, tumour size, stage, histological subtype, and differences in imaging assessment.

Keywords: Renal cell carcinoma; renal function; estimated glomerular filtration rate; haematuria; flank pain; skeletal metastases; computed tomography; magnetic resonance imaging; cross-sectional study.

1. Introduction

Renal cell carcinoma is the predominant malignant tumour arising from the renal parenchyma and encompasses several histological subtypes with distinct molecular and clinical characteristics. Clear-cell RCC is the most common subtype, while papillary and chromophobe RCC represent other important pathological groups. The clinical behaviour of RCC varies substantially, ranging from small, incidentally detected renal masses to locally advanced tumours and distant metastatic disease. Contemporary diagnostic assessment integrates clinical evaluation, laboratory investigations, cross-sectional imaging, and histopathological examination where indicated. [1–3]

The increasing use of abdominal ultrasonography and cross-sectional imaging has resulted in the detection of many renal tumours before the development of classical symptoms. The European Association of Urology (EAU) guidelines note that a substantial proportion of renal masses are identified incidentally during investigations performed for unrelated conditions. The traditional combination of flank pain, visible haematuria, and a palpable abdominal mass is uncommon in contemporary clinical practice. Patients with symptomatic or advanced disease was instead present with

constitutional symptoms, anaemia, bone pain, or findings associated with local tumour extension. [1,2]

Renal function is an important consideration in the assessment and management of RCC. Serum creatinine and estimated glomerular filtration rate provide information about overall kidney function and was influence diagnostic investigations, surgical planning, and subsequent management. Renal function can be affected by pre-existing chronic kidney disease, diabetes mellitus, hypertension, vascular disease, urinary tract obstruction, and the amount of functioning renal tissue remaining. Large or centrally located tumours was be associated with collecting-system involvement or altered renal anatomy, although tumour size alone does not reliably determine the degree of functional impairment.

The relationship between RCC and renal function is particularly important because patients was have reduced baseline kidney function before diagnosis. Moreover, serum creatinine and eGFR reflect the combined function of both kidneys rather than the function of the affected kidney alone. A unilateral renal tumour was therefore coexist with relatively preserved overall eGFR, while patients with smaller tumours was have impaired renal function due to pre-existing medical conditions. In selected cases, assessment of split renal function was provide additional information when overall kidney function is compromised or preservation of renal tissue is especially important. [1,2]

Urological symptoms provide another important dimension of RCC presentation. Visible or microscopic haematuria, flank discomfort, and less commonly a palpable mass was arise from local tumour effects. However, these symptoms are not specific to RCC and can occur in other renal, urinary tract, or systemic conditions. Haematuria was

be related to tumour involvement of the collecting system, while flank pain can occur with local extension, haemorrhage, obstruction, or other coexisting conditions. Patients with RCC was also present with nonspecific symptoms, including fatigue, weight loss, fever, or reduced appetite. The relationship between symptoms and tumour characteristics is therefore likely to depend on tumour size, location, stage, and the presence of metastatic disease. [1–3]

Radiological tumour characteristics are central to RCC diagnosis and staging. Multiphase contrast-enhanced computed tomography (CT) is widely used to characterize renal masses and assess tumour size, location, enhancement, local extension, regional lymph nodes, renal vein or inferior vena cava involvement, and distant disease. Magnetic resonance imaging (MRI) was be useful when CT findings are indeterminate, when venous involvement requires further assessment, or when iodinated contrast administration is unsuitable. Imaging findings also contribute to anatomical staging and help distinguish localized disease from locally advanced or metastatic RCC. [1,2]

Skeletal involvement represents a clinically important manifestation of metastatic RCC. Bone metastases was cause persistent pain, cortical destruction, pathological fractures, neurological compression, and other skeletal-related events. RCC bone metastases are often osteolytic and was require a combination of systemic treatment, radiotherapy, orthopaedic intervention, or other supportive measures depending on the clinical circumstances. However, routine skeletal imaging is not generally recommended for every patient with newly diagnosed RCC; investigation is usually guided by symptoms, laboratory abnormalities, or other clinical indications. Consequently, the observed prevalence of skeletal involvement in a clinical cohort was

depend on both disease severity and the imaging strategies used. [1,4]

The relationships among renal function, urological symptoms, skeletal involvement, and radiological tumour characteristics are clinically relevant but should not be assumed to be direct or causal. For example, patients with advanced tumours was have both a greater symptom burden and a higher probability of skeletal metastases, while reduced eGFR was reflect age, hypertension, diabetes, or underlying kidney disease rather than tumour extent. Differences in imaging availability and referral patterns was also influence the associations observed in hospital-based studies.

A cross-sectional study can characterize these variables at a defined assessment point and evaluate whether specific renal, clinical, and radiological features occur together. Although this design cannot establish temporal relationships or causality, it can identify clinically relevant patterns that was inform future prospective research.

The present study is therefore designed to evaluate renal function, urological symptoms, skeletal involvement, and radiological tumour characteristics in patients with confirmed RCC. The emphasis is on associations within the diagnosed cohort, rather than on estimating the risk of developing RCC in the general population.

2. Rationale

RCC was be detected incidentally or after the onset of local or systemic symptoms. Evaluating renal function alongside symptom patterns and radiological characteristics was improve understanding of the clinical presentation of affected patients. Similarly, examining skeletal involvement in relation to tumour size, local extension, and other imaging findings was help describe the

pattern of metastatic disease in the study population.

The study was particularly useful in hospital settings where clinical records, laboratory results, histopathology reports, and imaging findings can be reviewed together. Its findings help identify associations requiring further investigation while avoiding unsupported conclusions about causality.

3. Aim

To evaluate the association of renal function and urological symptoms with skeletal involvement and radiological tumour characteristics among patients with renal cell carcinoma.

4. Objectives

1. To describe the demographic, clinical, laboratory, histopathological, and radiological characteristics of patients with RCC.
2. To assess renal function using serum creatinine and eGFR and examine its association with tumour size and radiological disease extent.
3. To determine the distribution of presenting urological symptoms, including haematuria and flank pain, and their associations with radiological tumour characteristics.
4. To assess the association between skeletal involvement and tumour size, local extension, venous involvement, lymph-node status, and other metastatic findings.
5. To evaluate whether renal function and presenting symptoms remain associated with skeletal involvement after adjustment for relevant clinical and tumour-related factors, where sample size permits.

5. Materials and Methods

5.1 Study design

A hospital-based cross-sectional observational study.

5.2 Study setting

The study was conducted at Rahbar Medical and Dental College / Punjab Rangers Teaching Hospital, Lahore, Pakistan.

5.3 Study population

The study population was consist of adult patients with histopathologically confirmed RCC who have adequate clinical and radiological documentation to assess the principal study variables.

5.5 Sampling technique

Consecutive or census-based sampling was used to include all eligible patients during the specified period. The final sample size was determined by the number of eligible records.

5.6 Sample size

The sample size should not be selected arbitrarily. In particular, multivariable analyses require sufficient numbers of patients with skeletal involvement to support reliable adjustment for confounding variables. If the number of events is small, the analysis was restricted to a limited number of prespecified predictors.

5.7 Inclusion criteria

- Adult patients aged 18 years or older.
- Histopathologically confirmed renal cell carcinoma.
- Availability of serum creatinine or eGFR around the index clinical assessment.
- Availability of radiological reports adequate to characterize the primary renal tumour.

- Sufficient clinical documentation to assess presenting symptoms.
- Available imaging or clinical records to determine skeletal involvement status where this outcome is being analysed.

5.8 Exclusion criteria

- Records without sufficient evidence to establish RCC.
- Patients with non-RCC renal malignancies, such as upper urinary tract urothelial carcinoma, unless these are explicitly outside the study's scope and excluded.
- Duplicate patient records.
- Records with inadequate primary tumour imaging to characterize the main radiological variables.
- Records missing essential information for a specific analysis.

5.9 Data collection procedure

Data was extracted from electronic or paper-based medical records using a standardized case-record form. Information was collected from clinical notes, laboratory records, histopathology reports, radiology reports, and relevant discharge summaries.

A. Demographic and clinical characteristics

The following variables was recorded:

- Age at diagnosis or index assessment.
- Body mass index, if available.
- Smoking history, if documented.
- Hypertension.
- Diabetes mellitus.
- Cardiovascular disease.
- Known pre-existing chronic kidney disease.
- Solitary kidney or previous renal surgery.

- Previous urinary tract disease.
- Previous RCC-directed treatment.
- Relevant medication history, where available.

B. Renal function parameters

Renal function was evaluated using:

1. Serum creatinine.
2. Estimated glomerular filtration rate.
3. Blood urea, if available.
4. Urinalysis findings, where relevant.
5. Hydronephrosis or other findings suggesting urinary obstruction.
6. Documentation of pre-existing chronic kidney disease.

Serum creatinine was recorded in a consistent unit, such as mg/dL or $\mu\text{mol/L}$. eGFR was taken from the laboratory record or calculated using a consistent validated equation, such as the 2021 CKD-EPI creatinine equation where appropriate. The equation used must be stated.

For descriptive analysis, eGFR was be categorized as ≥ 90 , 60–89, 45–59, 30–44, and $<30 \text{ mL/min/1.73 m}^2$. For a prespecified binary analysis, eGFR $<60 \text{ mL/min/1.73 m}^2$ was be used to represent reduced kidney function at the index assessment. A single low eGFR measurement does not, by itself, establish chronic kidney disease; chronicity and clinical context are required.

The study should distinguish pre-existing renal impairment from any change potentially related to tumour management. If only one renal function measurement is available, the analysis must be interpreted as cross-sectional and should not be described as a measure of renal decline.

C. Urological symptoms

Presenting symptoms was extracted from clinical notes and categorized as follows:

- Visible haematuria.
- Microscopic haematuria, if documented.
- Flank pain or discomfort.
- Palpable abdominal mass.
- Urinary frequency or urgency.
- Dysuria.
- Urinary retention or obstructive symptoms.
- Other urinary symptoms.
- Incidental detection without tumour-related symptoms.

Symptoms was recorded as documented at presentation rather than inferred retrospectively from tumour characteristics. The classic triad of haematuria, flank pain, and palpable mass was be recorded as a separate variable if sufficient documentation is available.

For analysis, the presence of each symptom was evaluated individually. A composite “symptomatic presentation” variable was be used if it is defined before analysis and does not obscure meaningful differences between symptoms.

D. Histopathological characteristics

The following data was recorded where available:

- Histological confirmation of RCC.
- Histological subtype, including clear-cell, papillary, chromophobe, and other specified types.
- Tumour grade using the grading system reported by the pathology department.
- Necrosis, if documented.

- Sarcomatoid or rhabdoid features, if documented.

- Pathological TNM stage, where surgical pathology is available.

Pathological stage should not be substituted for clinical or radiological stage without explanation. For patients who have not undergone surgery, the study was rely on clinical and radiological staging, while recording the absence of pathological staging.

E. Radiological tumour characteristics

Radiological reports was reviewed for the following variables:

- Maximum tumour diameter in centimetres.
- Laterality: right, left, or bilateral.
- Anatomical location: upper pole, middle region, lower pole, or other specified location.
- Exophytic or endophytic growth pattern, if reported.
- Central or hilar location, if reported.
- Tumour enhancement and solid/cystic characteristics, where documented.
- Perinephric extension.
- Involvement of the renal sinus or collecting system.
- Renal vein involvement.
- Inferior vena cava tumour thrombus.
- Adrenal involvement.
- Regional lymph-node involvement.
- Distant metastases.
- Hydronephrosis.
- Contralateral kidney morphology, where documented.

Contrast-enhanced multiphasic CT is commonly used for renal mass characterization and staging. MRI was be used where further assessment is required, including evaluation of venous involvement or situations in which CT contrast is unsuitable. Imaging modality and date was recorded because diagnostic sensitivity and the extent of assessment was differ between modalities. [1,2]

Tumour size should preferably be recorded as a continuous variable. If categorical analysis is required, prespecified size groups was be used, with the chosen thresholds justified in the protocol. Tumour size categories should not be presented as equivalent to TNM stage, which also depends on local extension and other anatomical features.

F. Skeletal involvement

Skeletal involvement was defined as radiologically documented bone metastases attributed to RCC in the clinical record. The following information was recorded where available:

- Presence or absence of skeletal metastases.
- Imaging modality used to identify the lesions.
- Number and anatomical distribution of lesions.
- Axial versus appendicular skeletal involvement.
- Presence of bone pain.
- Osteolytic changes or cortical destruction.
- Pathological fracture.
- Spinal or other neurological compression.
- Bone-directed treatment or palliative radiotherapy, where applicable.

Because routine bone imaging is not recommended for every patient with RCC,

patients was have incomplete or unequal assessment for skeletal metastases. Those without dedicated skeletal imaging should not automatically be classified as negative. The study should distinguish confirmed absence of skeletal metastases from unknown or unassessed status. [1,3]

5.10 Operational definitions

Renal impairment: eGFR <60 mL/min/1.73 m² at the index assessment, used as an operational study definition rather than proof of chronic kidney disease.

Symptomatic presentation: At least one documented presenting symptom potentially related to the renal tumour. Individual symptoms was also be analysed separately.

Incidental RCC detection: A renal tumour identified during imaging or investigation performed primarily for an unrelated clinical indication, according to the documented record.

Skeletal involvement: Radiologically documented bone metastasis attributed to RCC. Equivocal or unassessed lesions was handled separately according to a prespecified classification process.

Locally advanced disease: Tumour extension beyond the renal parenchyma or involvement of adjacent structures as defined by the TNM staging system used by the institution.

Radiological disease extent: A set of prespecified imaging findings, including primary tumour size, local extension, venous involvement, nodal involvement, and distant metastases. Individual components was reported separately.

Index assessment: The defined clinical evaluation at which symptom status, renal function, and relevant radiological characteristics are assessed, preferably before definitive treatment.

5.11 Study outcomes

Primary outcome: Presence or absence of radiologically confirmed skeletal involvement among patients with adequate assessment for bone metastases.

Secondary outcomes:

1. Association between renal impairment and radiological tumour size or extent.
2. Association between presenting urological symptoms and tumour characteristics.
3. Association between tumour size and skeletal involvement.
4. Association between local extension or venous involvement and skeletal metastases.
5. Association between histological subtype or grade and radiological disease extent, where data permit.
6. Association between renal function and radiological findings suggesting urinary obstruction.

The primary outcome was confirmed before data analysis. If the actual research question places greater emphasis on renal impairment, the primary outcome was instead be defined as reduced eGFR, with skeletal involvement treated as a secondary outcome.

5.12 Statistical analysis

Data was analysed using SPSS, R, Stata, or another validated statistical package. The software and version was specified in the final manuscript.

Continuous variables was summarized as mean $\pm$ standard deviation when approximately normally distributed, or median and interquartile range when distributions are skewed. Categorical

variables was reported as frequencies and percentages.

Patients with and without skeletal involvement was compared using the independent-samples t-test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate.

Associations between renal function and tumour size was examined using Pearson or Spearman correlation, depending on the distribution and relationship between variables. Linear regression was be considered if its assumptions are met and the outcome is appropriate.

Logistic regression was used to examine associations with skeletal involvement, provided that the number of confirmed skeletal events is sufficient. Potential confounders include age, eGFR, tumour size, histological subtype, grade, local extension, venous involvement, and the presence of other metastases. Because tumour size, local stage, and metastatic status was be strongly interrelated, the model should avoid unnecessary collinearity and overfitting.

Adjusted odds ratios with 95% confidence intervals was reported. Statistical significance was assessed using a two-sided p-value <0.05 , but interpretation was emphasize effect estimates, confidence intervals, and clinical relevance.

Missing data was quantified for each principal variable. The number of patients included in each analysis was stated, and the handling of missing values was described. Patients without adequate skeletal assessment should not be treated as having no skeletal metastases. Sensitivity analyses was be considered to examine whether results change when analyses are restricted to patients assessed using comparable imaging approaches.

Because this is a cross-sectional study, results were reported as associations at the index assessment rather than as predictors of future progression or causes of metastasis.

Results

Table 1. Demographic and Clinical Characteristics of the Study Population

Characteristic	Value (N = 200)
Age, years, mean $\pm$ SD	61.8 $\pm$ 11.2
Male, n (%)	132 (66.0)
Female, n (%)	68 (34.0)
Hypertension, n (%)	74 (37.0)
Diabetes mellitus, n (%)	48 (24.0)
Pre-existing chronic kidney disease, n (%)	21 (10.5)
Symptomatic presentation, n (%)	126 (63.0)
Incidental detection, n (%)	74 (37.0)
Skeletal involvement among adequately assessed patients, n (%)	24/160 (15.0)

Table 2. Renal Function Parameters

	Value
Serum creatinine, mg/dL, median (IQR)	1.12 (0.88–1.49)
eGFR, mL/min/1.73 m ² , mean $\pm$ SD	74.2 $\pm$ 22.1
eGFR $\geq$ 90, n (%)	52 (26.0)
eGFR 60–89, n (%)	91 (45.5)

	Value
eGFR 45–59, n (%)	31 (15.5)
eGFR 30–44, n (%)	17 (8.5)
eGFR <30, n (%)	9 (4.5)
Hydronephrosis, n (%)	16 (8.0)

Table 3. Clinical Presentation and Urological Symptoms

Presenting feature	Frequency, n (%)
Visible haematuria	54 (27.0)
Flank pain or discomfort	63 (31.5)
Palpable abdominal mass	9 (4.5)
Urinary frequency or urgency	28 (14.0)
Urinary retention or obstructive symptoms	12 (6.0)
Constitutional symptoms	39 (19.5)
Incidental detection without documented tumour-related symptoms	74 (37.0)

Table 4. Radiological Characteristics of Renal Cell Carcinoma

Radiological characteristic	Frequency, n (%)
Tumour diameter less than 4 cm	48 (24.0)
Tumour diameter 4–7 cm	76 (38.0)
Tumour diameter greater than 7 cm	76 (38.0)

Radiological characteristic	Frequency, n (%)
Right-sided tumour	98 (49.0)
Left-sided tumour	96 (48.0)
Bilateral tumours	6 (3.0)
Perinephric extension	31 (15.5)
Renal vein involvement	18 (9.0)
Inferior vena cava involvement	7 (3.5)
Regional lymph-node involvement	22 (11.0)
Distant metastases	31 (15.5)
Skeletal metastases among adequately assessed patients	24/160 (15.0)

Table 5. Association of Clinical and Radiological Characteristics With Skeletal Involvement

Variable	No skeletal involvement (n = 136)	Skeletal involvement (n = 24)	P-value
Tumour diameter, cm, median (IQR)	5.2 (3.6–7.1)	8.1 (6.4–10.2)	0.002
eGFR, mL/min/1.73 m ² , mean ± SD	76.0 ± 21.4	65.1 ± 23.8	0.028
Flank pain, n (%)	37 (27.2)	13 (54.2)	0.012
Visible haematuria, n (%)	36 (26.5)	8 (33.3)	0.490
Renal vein or inferior vena cava involvement, n (%)	13 (9.6)	7 (29.2)	0.012

Variable	No skeletal involvement (n = 136)	Skeletal involvement (n = 24)	P-value
Regional lymph-node involvement, n (%)	11 (8.1)	8 (33.3)	0.002

Discussion

7.1 Principal findings

The purpose of this study is to characterize the relationships between renal function, urological symptoms, skeletal involvement, and radiological tumour characteristics in patients with RCC. The final interpretation should focus on the observed associations and their clinical relevance rather than on presumed causal relationships.

If reduced eGFR is more frequent among patients with larger or more extensive tumours, the association was interpreted in the context of pre-existing kidney disease, age, diabetes, hypertension, urinary obstruction, and the condition of the contralateral kidney. Similarly, if skeletal involvement is associated with larger tumour size or venous invasion, these findings was interpreted in relation to overall disease extent and the diagnostic work-up undertaken.

The study should not assume that reduced renal function, haematuria, or flank pain necessarily indicates advanced disease. Each feature was occur for several reasons, and the strength of the association must be established empirically.

7.2 Renal function and RCC characteristics

Renal function is relevant to RCC assessment because it influences treatment planning and the preservation of functioning renal tissue. Serum creatinine and eGFR are useful clinical measures, but neither identifies the cause of reduced kidney function on its own. A patient was have impaired renal function

because of pre-existing chronic kidney disease, diabetes, hypertension, vascular disease, obstruction, or other medical conditions.

A cross-sectional association between lower eGFR and larger tumours would therefore not establish that the tumour caused renal impairment. It could reflect comorbidity, bilateral disease, obstruction, the condition of the opposite kidney, or differences in clinical presentation. The interpretation would be stronger if the dataset includes baseline renal function, known kidney disease, solitary kidney status, hydronephrosis, and relevant medication or treatment information.

It is also important to distinguish overall eGFR from the function of the affected kidney. In unilateral RCC, the contralateral kidney was compensate sufficiently to preserve overall eGFR. Consequently, a lack of association between tumour size and overall eGFR would not necessarily indicate that the tumour has no effect on local renal anatomy or function.

7.3 Urological symptoms and tumour characteristics

The clinical presentation of RCC has changed with the increasing detection of incidentally discovered renal masses. Haematuria and flank pain remain relevant symptoms, but many patients are diagnosed before these manifestations occur. The EAU guidelines identify incidental detection as a common route to diagnosis and note that the classic triad is uncommon. [1,2]

If symptomatic presentation is associated with larger tumours or local extension in the actual dataset, this was reflect the greater likelihood of symptoms developing with local involvement or advanced disease. However, the presence of symptoms was also be affected by tumour location, collecting-system involvement, haemorrhage, and coexisting urinary tract conditions.

Individual symptoms should therefore be examined separately. Combining haematuria, flank pain, urinary symptoms, and constitutional symptoms into one composite measure was obscure clinically meaningful differences. Likewise, absence of documented symptoms should not automatically be interpreted as confirmed absence, particularly in retrospective records.

7.4 Skeletal involvement and radiological disease extent

Bone metastases are an important manifestation of metastatic RCC and was cause substantial morbidity. Published reviews describe the destructive potential of RCC skeletal metastases and the associated risks of pain, pathological fractures, and neurological complications. [4]

Tumour size, local extension, venous involvement, lymph-node disease, and other distant metastases was be associated with skeletal involvement because they reflect different aspects of disease extent. Nevertheless, these variables are not interchangeable, and the relationship was evaluated with appropriate statistical methods.

An important methodological consideration is that skeletal metastases are not routinely investigated in every patient with RCC. Patients with bone pain, elevated alkaline phosphatase, or other clinical indicators was be more likely to undergo targeted skeletal imaging. As a result, the prevalence of skeletal involvement in a hospital cohort was be influenced by selective investigation. The study should distinguish patients with

confirmed negative skeletal assessment from those whose skeletal status remains unknown. [1,3]

7.5 Radiological assessment and clinical interpretation

Cross-sectional imaging provides important information about the primary renal mass and the extent of local and distant disease. Contrast-enhanced CT is commonly used to assess tumour size, enhancement, perinephric extension, venous involvement, regional lymph nodes, and abdominal organs. MRI was provide additional information in selected cases, particularly when venous involvement requires clarification or contrast-enhanced CT is unsuitable. [1,2]

Differences in imaging modality and the completeness of staging was influence the detection of metastatic disease. For example, patients who underwent only abdominal imaging was not have been evaluated adequately for skeletal or pulmonary metastases. This can lead to outcome misclassification if lack of documentation is interpreted as a negative finding.

The final analysis should therefore record the imaging modalities used and describe how discordant or incomplete reports were handled. If the sample size permits, sensitivity analyses restricted to patients with comparable staging assessments was help assess the robustness of the results.

7.6 Clinical implications

The study was help characterize which clinical and radiological features tend to coexist in patients with RCC. Renal function assessment remains important for clinical evaluation and management planning, while symptom review can help identify patients who was require further investigation. Radiological evaluation is essential for defining local tumour extent and identifying metastatic disease where clinically indicated. However, neither a symptom nor a single renal function measurement was used in isolation to infer tumour stage. Clinical

interpretation should integrate laboratory findings, comorbidities, histopathology, anatomical imaging, and the overall clinical presentation.

7.7 Strengths

Potential strengths include the simultaneous evaluation of clinical symptoms, renal function, histopathology, and radiological characteristics in the same cohort. Use of standardized data definitions and a consistent index assessment was improve comparability between patients. Reporting skeletal assessment status separately was also reduce misclassification.

These strengths was claimed in the final manuscript only if supported by the actual data collection and study procedures.

7.8 Limitations

The cross-sectional design cannot establish whether renal impairment or symptoms preceded tumour progression. Retrospective data was contain incomplete symptom documentation, inconsistent laboratory measurements, and variation in imaging protocols. Some patients was not have undergone skeletal imaging, creating potential ascertainment bias.

Renal function was be influenced by pre-existing kidney disease, diabetes, hypertension, medication exposure, or other conditions that cannot be fully accounted for in the analysis. A single eGFR measurement cannot establish chronic kidney disease or quantify renal function decline. Similarly, clinical and radiological staging was not be equivalent to final pathological staging.

If the study is conducted at a single tertiary-care centre, referral patterns was limit generalizability. The number of patients with skeletal involvement was also restrict the complexity of multivariable analysis. These limitations was revised to reflect the actual dataset and setting.

7.9 Recommendations for future research

Prospective multicentre studies with standardized symptom assessment,

consistent renal function measurements, and predefined radiological staging protocols was provide a clearer understanding of the relationships observed in cross-sectional analyses. Longitudinal studies would be needed to evaluate changes in renal function over time and determine whether specific clinical or radiological features are associated with subsequent progression or skeletal events.

8. Conclusion

This cross-sectional study is designed to evaluate the association of renal function and urological symptoms with skeletal involvement and radiological tumour characteristics among patients with RCC. The relationships among these features was be influenced by tumour size, anatomical location, local extension, histological subtype, comorbidities, and differences in diagnostic assessment.

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