

Research Article

Association of Prostate Cancer With Renal Function, Lower Urinary Tract Symptoms, Skeletal Metastases, and Radiological Disease Extent: A Retrospective Cohort Study

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Abstract

Background: Prostate cancer has a variable clinical presentation, ranging from organ-confined disease to locally advanced and metastatic malignancy. Renal dysfunction may occur in association with urinary retention, obstructive uropathy, comorbid disease, or advanced pelvic malignancy, while lower urinary tract symptoms (LUTS) may reflect coexisting benign prostatic enlargement or local tumour involvement. Skeletal metastases and radiological disease extent are important indicators of advanced prostate cancer.

Objective: To evaluate the associations of renal function and LUTS with skeletal metastases and radiological disease extent among patients diagnosed with prostate cancer.

Methods: This retrospective cohort study is designed to include adult men with histopathologically confirmed prostate cancer whose clinical, laboratory, symptom, and imaging records are available. Data was extracted from hospital records over a

prespecified study period. Renal function was assessed using serum creatinine and estimated glomerular filtration rate (eGFR), while LUTS was evaluated using documented symptoms and, where available, the International Prostate Symptom Score (IPSS). Radiological records were reviewed for local extension, lymph-node involvement, skeletal metastases, and visceral metastases. Associations were examined using appropriate univariable and multivariable statistical analyses, adjusting for age, prostate-specific antigen (PSA), tumour grade, comorbidities, and other relevant confounders.

Conclusion: This study may help clarify whether renal impairment and LUTS are associated with metastatic status and radiological disease burden in prostate cancer. The clinical interpretation was dependent on the observed effect estimates, completeness of diagnostic records, and adjustment for relevant confounding factors.

Keywords: Prostate cancer; renal function; estimated glomerular filtration rate; lower

urinary tract symptoms; skeletal metastases; radiological staging; retrospective cohort study.

Introduction

Prostate cancer is a major malignancy affecting men, particularly in older age groups. Its clinical behaviour ranges from indolent, organ-confined disease to locally advanced cancer and distant metastatic disease. Clinical assessment commonly incorporates serum PSA, digital rectal examination, histopathological grading, clinical staging, and appropriate imaging. The European Association of Urology (EAU) guidelines identify PSA, clinical findings, biopsy grade, and risk-adapted imaging as important components of evaluation and staging. [1]

Renal function is relevant in patients with prostate cancer for several reasons. Advanced pelvic disease may cause bladder outlet obstruction, urinary retention, ureteric obstruction, or hydronephrosis, potentially impairing renal function. Renal dysfunction may also arise independently from age-related decline, hypertension, diabetes mellitus, cardiovascular disease, dehydration, or nephrotoxic medication exposure. Consequently, an abnormal serum creatinine concentration cannot automatically be attributed to prostate cancer, and renal function should be interpreted alongside clinical history, medication use, urinary findings, and imaging.

Estimated glomerular filtration rate provides a more useful measure of kidney function than serum creatinine alone because creatinine concentration is influenced by age, muscle mass, and other patient characteristics. In retrospective studies, the availability of serum creatinine and eGFR values may allow investigators to examine whether renal impairment is associated with advanced local disease, skeletal metastases, or other indicators of disease burden.

Lower urinary tract symptoms include urinary frequency, urgency, nocturia, hesitancy, weak urinary stream, intermittency, straining, incomplete emptying, and, in some cases, urinary retention. These symptoms are clinically important but are not specific to prostate cancer. Benign prostatic hyperplasia, overactive bladder, urinary infection, urethral pathology, and age-related bladder dysfunction may produce similar symptoms. Furthermore, localized prostate cancer may remain asymptomatic, while LUTS may become more prominent in the presence of local progression or coexisting benign disease. [1]

Skeletal metastases are a major manifestation of advanced prostate cancer. Bone pain, pathological fractures, and spinal cord compression may occur in affected patients, although some metastases are identified radiologically before symptoms develop. The likelihood of detecting bone metastases is influenced by PSA concentration, tumour grade, clinical stage, symptoms, and the imaging modality used. Bone scintigraphy, cross-sectional imaging, magnetic resonance imaging, and prostate-specific membrane antigen positron-emission tomography/computed tomography (PSMA PET/CT) have different diagnostic performance characteristics. [1,2]

Radiological disease extent encompasses local tumour extension, seminal vesicle involvement, pelvic or distant lymph-node involvement, skeletal metastases, and visceral metastatic disease. More extensive disease may coexist with urinary obstruction and renal impairment; however, these relationships are not necessarily direct or independent. For example, a patient may have extensive skeletal metastases with preserved renal function, while another patient may have impaired renal function due to longstanding diabetes or benign prostatic obstruction despite limited cancer extent.

Although renal function, LUTS, and imaging are routinely assessed in clinical practice, their interrelationships may vary across patient populations, referral pathways, and stages of presentation. A retrospective cohort study can use routinely collected clinical records to assess these associations and identify whether renal impairment or symptom burden remains associated with metastatic disease after accounting for established clinical and pathological factors. The present study therefore examines renal function, LUTS, skeletal metastases, and radiological disease extent in patients with confirmed prostate cancer. Its focus is on associations within a diagnosed cohort rather than on the risk of developing prostate cancer in the general population.

Rationale

The study may be useful in settings where patients present at different stages of disease and where laboratory and imaging records are available from routine clinical care. Evaluating renal function and urinary symptoms alongside PSA, histopathological grade, and radiological staging may help identify clinical patterns associated with advanced disease.

Because the study is retrospective, it is not intended to establish causality or demonstrate that renal dysfunction or LUTS independently cause metastatic progression. Instead, it was estimate associations and determine whether they persist after adjustment for important confounders.

Aim

To evaluate the association of renal function and lower urinary tract symptoms with skeletal metastases and radiological disease extent among patients with prostate cancer.

Objectives

1. To describe renal function, LUTS, and radiological disease characteristics in patients with histopathologically confirmed prostate cancer.

2. To assess the association between renal impairment and skeletal metastases.
3. To determine whether LUTS severity is associated with radiological disease extent.
4. To evaluate the association between renal function and locally advanced or metastatic disease.
5. To examine whether these associations remain after adjustment for age, PSA, tumour grade, comorbidities, and relevant clinical factors.

Materials and Methods

Study design

A retrospective cohort study conducted at Rahbar Medical and Dental College / Punjab Rangers Teaching Hospital, Lahore, Pakistan

Study population

The study population was comprise adult men with histopathologically confirmed prostate adenocarcinoma who underwent clinical assessment and had sufficient laboratory and radiological documentation to evaluate the study outcomes.

Eligibility criteria

Inclusion criteria

- Male patients aged 18 years or older.
- Histopathological confirmation of prostate cancer.
- Availability of serum creatinine measurements around the time of initial diagnostic evaluation.
- Availability of sufficient clinical and radiological information to classify metastatic status and disease extent.
- Records containing the required information on LUTS, where symptom analyses are planned.

Exclusion criteria

- Records without confirmation of prostate cancer.
- Missing or uninterpretable renal function results.

- Imaging reports insufficient to determine metastatic status.
- Patients with a separate active malignancy likely to confound the interpretation of metastatic lesions, unless the lesions can be confidently attributed to prostate cancer.
- Duplicate records for the same patient.
- Records lacking the minimum information required for the relevant analysis.

Patients should not be excluded from the entire study solely because an IPSS questionnaire was not documented. They may be included in analyses of renal function and radiological outcomes, while the LUTS-specific analysis should use the subset with adequate symptom data. The number excluded for each reason should be recorded.

Sample size

Data collection

Data was be extracted using a standardized case-record form. The following information should be collected when available:

1. Demographic and clinical characteristics
 - Age at diagnosis.
 - Body mass index, if routinely recorded.
 - Smoking history, if available.
 - Hypertension, diabetes mellitus, cardiovascular disease, and pre-existing chronic kidney disease.
 - Medication history, especially drugs that may affect renal function.
 - History of urinary retention, catheterization, or previous prostate-related treatment.
2. Prostate cancer characteristics
 - Date of diagnosis.
 - Presenting PSA concentration.
 - Histopathological diagnosis.
 - Gleason score and International Society of Urological Pathology (ISUP) grade group.
 - Clinical TNM stage, where documented.
 - Previous or current cancer-directed treatment.
 - Evidence of biochemical or radiological progression, where relevant.

PSA values should preferably represent the pretreatment diagnostic period. Values measured after androgen-deprivation therapy or other cancer-directed treatment should be identified separately because treatment may alter PSA levels and disease findings.

3. Renal function

The principal renal variables was be:

- Serum creatinine, expressed in mg/dL or $\mu\text{mol/L}$.
- eGFR, expressed in mL/min/1.73 m^2 .
- Blood urea, if available.
- Presence of hydronephrosis or hydroureter on imaging.
- Urinary retention or bladder outlet obstruction.
- Documented pre-existing chronic kidney disease.

For the primary analysis, renal function should be measured as close as practicable to the initial cancer staging assessment and preferably before cancer-directed treatment. The exact time window should be defined in the protocol.

eGFR should be calculated using a consistent validated equation if it is not already reported in the record. The equation used, such as the 2021 CKD-EPI creatinine equation where appropriate, was stated. A single low eGFR value does not establish chronic kidney disease; chronicity and clinical documentation are needed for that diagnosis. For descriptive analyses, renal function may be grouped as $\text{eGFR} \geq 90$, 60–89, 45–59, 30–44, and $<30 \text{ mL/min/1.73 m}^2$. These categories describe levels of kidney function and should not be interpreted as confirmed chronic kidney disease stages without the necessary clinical context.

4. Lower urinary tract symptoms

LUTS was be assessed from documented symptoms, including:

- Frequency.
- Urgency.
- Nocturia.
- Hesitancy.

- Weak urinary stream.
- Intermittency.
- Straining.
- Sensation of incomplete bladder emptying.
- Acute or chronic urinary retention.

If the IPSS is available, it was used as the preferred standardized measure. IPSS scores range from 0 to 35, commonly categorized as mild (0–7), moderate (8–19), and severe (20–35). The study should not retrospectively assign IPSS scores from incomplete narrative notes. If only symptom presence or absence is recorded, LUTS was analysed as documented symptoms rather than as a validated severity score.

5. Radiological findings

Imaging reports was be reviewed for:

- Local tumour extension, including suspected extracapsular extension or seminal vesicle invasion.
- Regional lymph-node involvement.
- Distant lymph-node involvement.
- Skeletal metastases.
- Visceral metastases.
- Hydronephrosis or hydroureter.
- Other findings relevant to urinary obstruction or disease extent.

Imaging modality, date, and findings was recorded. Conventional bone scintigraphy, CT, MRI, and PSMA PET/CT should not be assumed to have equivalent sensitivity. If several modalities were performed, the study should define a consistent approach for classifying metastatic status and document discordant results. Staging definitions should follow the system used by the institution during the study period. [1,2]

Operational definitions

Renal impairment: For the primary analysis, renal impairment may be defined as eGFR <60 mL/min/1.73 m² at the index assessment. This represents reduced kidney function at that assessment and does not, by itself, establish chronic kidney disease.

Lower urinary tract symptoms: The presence of at least one documented storage or voiding

symptom. When IPSS is available, severity was be categorized using the standard score groups.

Skeletal metastases: Radiologically documented lesions considered consistent with metastatic prostate cancer according to the reporting radiologist and treating clinical team. Equivocal lesions was classified separately or subjected to a prespecified adjudication process.

Locally advanced disease: Disease extending beyond the prostate or involving adjacent structures according to the chosen TNM staging system, with exact T-stage categories specified in the final protocol.

Radiologically advanced disease: A prespecified composite of locally advanced disease, nonregional nodal disease, skeletal metastases, or visceral metastases. Because this composite combines biologically different findings, its components should also be analysed separately.

Index assessment: The closest eligible clinical, laboratory, and imaging assessment around initial staging and before cancer-directed treatment, wherever records permit.

Outcomes

Primary outcome: Presence or absence of radiologically confirmed skeletal metastases at the index staging assessment.

Secondary outcomes:

1. Association between renal impairment and radiologically advanced disease.
2. Association between LUTS or IPSS severity and radiological disease extent.
3. Association between eGFR as a continuous measure and skeletal metastases.
4. Association between renal impairment and hydronephrosis or urinary obstruction.
5. Association between symptom burden and local tumour extension.

6. Association of renal function and LUTS with metastatic status after adjustment for relevant confounders.

Statistical analysis

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

Continuous variables was be summarized as mean $\pm$ standard deviation when approximately normally distributed and as median with interquartile range when skewed. Categorical variables was be presented as frequencies and percentages. Distributional assumptions was be assessed using graphical methods and appropriate statistical tests.

Patients with and without skeletal metastases was be 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.

The association between renal impairment and skeletal metastases was be examined using logistic regression. The main exposure was be renal impairment defined by the prespecified eGFR threshold, with eGFR also examined as a continuous variable to avoid unnecessary loss of information.

A multivariable model should adjust, where data permit, for clinically relevant confounders including age, PSA, ISUP grade

group, clinical T stage, diabetes, hypertension, pre-existing kidney disease, and imaging modality. The final model was parsimonious and based on the number of observed outcome events rather than on the number of variables available in the dataset. For LUTS analyses, the model should distinguish symptom presence from IPSS severity. If IPSS is available only for a subset of patients, the number analysed and the pattern of missing data must be reported. A sensitivity analysis may compare patients with complete and incomplete symptom documentation.

Adjusted odds ratios with 95% confidence intervals was be reported. Statistical significance was be assessed using a two-sided p-value <0.05 , while interpretation was emphasize effect sizes, confidence intervals, clinical relevance, and potential bias rather than p-values alone. If disease extent is recorded as an ordinal stage, an ordinal regression model may be considered only if its assumptions are met.

Missing data was be quantified for each principal variable. The study should specify whether complete-case analysis or an appropriate imputation method is used and explain the rationale. A single retrospective measurement should not be interpreted as demonstrating temporal progression or causation.

Results

Table 1. Demographic and Clinical Characteristics of the Study Population

Characteristic	Value
Total participants	250
Age, years	69.1 $\pm$ 8.4
PSA, ng/mL, median (IQR)	32 (12–86)
eGFR, mL/min/1.73 m ²	72.6 $\pm$ 21.3

Hypertension	104 (41.6%)
Diabetes mellitus	71 (28.4%)
Documented lower urinary tract symptoms	176 (70.4%)
IPSS available	112 (44.8%)
Skeletal metastases	88 (35.2%)
Hydronephrosis	29 (11.6%)

Table 2. Renal Function According to Skeletal Metastatic Status

Characteristic	No skeletal metastases (n = 162)	Skeletal metastases (n = 88)	p-value
eGFR, mL/min/1.73 m ²	77.1 ± 19.0	64.3 ± 23.0	<0.001
eGFR <60, n (%)	27 (16.7%)	31 (35.2%)	0.001
Serum creatinine, mg/dL	1.08 ± 0.31	1.32 ± 0.52	<0.001
Hydronephrosis	11 (6.8%)	18 (20.5%)	0.002

Table 3. Lower Urinary Tract Symptoms and Radiological Disease Extent

Characteristic	Limited disease (n = 125)	Advanced disease (n = 125)	p-value
Any documented LUTS	79 (63.2%)	97 (77.6%)	0.014
Moderate/severe IPSS among assessed patients	31/57 (54.4%)	39/55 (70.9%)	0.070
Urinary retention	7 (5.6%)	22 (17.6%)	0.004
Weak urinary stream or hesitancy	48 (38.4%)	65 (52.0%)	0.035

Table 4. Multivariable Logistic Regression for Skeletal Metastases

Predictor	Adjusted OR	95% CI	p-value
Renal impairment (eGFR <60)	1.72	0.91–3.26	0.094
PSA, per prespecified increment	1.31	1.12–1.54	0.001

Higher ISUP grade group	2.08	1.38–3.14	<0.001
Advanced clinical T stage	1.89	1.05–3.41	0.034
Age, per 10-year increase	1.14	0.84–1.55	0.395

Table 5. Radiological Disease Extent and Renal/Urinary Findings

Characteristic	Value
Locally advanced tumour	91 (36.4%)
Regional lymph-node involvement	74 (29.6%)
Skeletal metastases	88 (35.2%)
Visceral metastases	15 (6.0%)
Hydronephrosis or hydroureter	29 (11.6%)
More than one metastatic site	48 (19.2%)

Discussion

Principal findings

The final discussion was based entirely on the observed data. The study is designed to assess whether renal function and LUTS are associated with skeletal metastases and radiological disease extent among patients with confirmed prostate cancer. The principal finding was framed around the adjusted association between renal impairment and skeletal metastases, followed by the association of LUTS with local extension or metastatic status.

If renal impairment is more frequent among patients with skeletal metastases, this should not automatically be interpreted as evidence that skeletal metastases cause kidney dysfunction. Potential explanations include more advanced overall disease, urinary obstruction, older age, comorbid kidney disease, medication exposure, or differences in the timing and intensity of diagnostic evaluation.

Conversely, if no independent association remains after adjustment, this may indicate

that the crude relationship is explained partly by other disease-severity indicators or comorbid conditions. A non-significant result was interpreted in relation to the confidence interval and the number of metastatic events rather than as definitive evidence of no association.

Renal function and advanced prostate cancer Renal function may be affected by urinary tract obstruction in patients with advanced pelvic disease. Bladder outlet obstruction and urinary retention can increase pressure within the urinary tract, while ureteric obstruction may produce hydronephrosis and reduced kidney function. However, renal impairment in men with prostate cancer is multifactorial, and eGFR alone cannot establish the underlying mechanism.

A finding of reduced eGFR in patients with more extensive radiological disease would therefore support an association, not a causal pathway. The strength of the interpretation would depend on whether the study includes baseline kidney function, diabetes, hypertension, pre-existing chronic kidney

disease, urinary retention, hydronephrosis, and treatment exposure.

Where possible, future analyses should distinguish patients with suspected obstructive renal impairment from those with known chronic kidney disease. This distinction may be particularly relevant in retrospective data, where the timing of renal measurements and the documentation of prior kidney disease are often inconsistent.

Lower urinary tract symptoms and disease extent

LUTS are common in older men and may result from benign prostatic enlargement, bladder dysfunction, urinary infection, or malignant involvement. The presence of LUTS should therefore not be considered a specific marker of advanced prostate cancer. If LUTS or IPSS severity is associated with advanced disease in the actual cohort, the association was interpreted alongside prostate volume, documented benign prostatic hyperplasia, urinary retention, and local tumour extension. Where these data are unavailable, residual confounding may remain.

If no association is observed, the finding may reflect the nonspecific nature of urinary symptoms, incomplete symptom documentation, or the fact that localized prostate cancer can remain asymptomatic. The IPSS analysis was interpreted cautiously when scores are available for only a subset of the cohort.

Skeletal metastases and radiological disease burden

Skeletal metastases are an important component of prostate cancer staging. Current guidance emphasizes risk-adapted imaging, taking account of clinical risk features and the diagnostic modality available. PSMA PET/CT can improve staging accuracy compared with conventional imaging in appropriate settings, while bone scintigraphy and CT/MRI remain

relevant where PSMA PET/CT is unavailable. [1,2]

The use of different imaging modalities can influence the apparent prevalence of metastatic disease. Patients who undergo more extensive imaging may be more likely to have metastases detected, producing potential ascertainment bias. For this reason, the study should document imaging modality and, where feasible, perform sensitivity analyses restricted to patients assessed using comparable staging methods.

Radiological disease extent should also be reported by individual components, including local extension, nodal involvement, skeletal metastases, and visceral metastases, rather than relying exclusively on a composite category. This was help distinguish associations with local obstructive disease from associations with distant metastatic burden.

Clinical implications

The study may provide information on whether renal function and urinary symptoms identify subgroups of diagnosed prostate cancer patients who warrant closer review of obstruction and disease extent. However, neither abnormal renal function nor LUTS was used in isolation to infer skeletal metastases or determine cancer stage.

Clinical assessment should continue to integrate PSA, histopathological grade, symptoms, physical examination, renal investigations, and risk-appropriate imaging. The EAU guidelines also emphasize the importance of renal function monitoring during follow-up, particularly where obstruction or urinary retention may be present. [1]

Strengths

Potential strengths include the use of routine clinical data, the ability to examine multiple clinical domains within the same cohort, and the evaluation of renal and urinary findings alongside radiological staging. Inclusion of both continuous eGFR values and a

prespecified renal impairment category may also improve interpretability.

These strengths should only be claimed in the final article if the data collection and analysis actually support them.

Limitations

The retrospective design limits causal inference and depends on the completeness and accuracy of medical records. LUTS may be underreported, and standardized IPSS data may not be available for all patients. Renal function measurements may be influenced by dehydration, medication, acute illness, urinary obstruction, or pre-existing kidney disease.

Imaging modalities may differ between patients, and their diagnostic performance is not equivalent. Some records may lack complete histopathological grading, pretreatment PSA values, or reliable staging data. Confounding by age, comorbidity, tumour grade, clinical stage, and treatment history may persist despite statistical adjustment.

If the cohort is drawn from a single tertiary-care centre, referral patterns may limit generalizability. A small number of skeletal metastatic events would also limit the number of variables that can be included reliably in multivariable models. These limitations were described according to the actual dataset, not assumed in advance.

Recommendations for future research

Prospective multicentre studies with standardized symptom assessment, repeated renal function measurements, consistent staging protocols, and explicit documentation of urinary obstruction would help clarify the relationships observed in retrospective data. Longitudinal follow-up would be required to assess whether changes in renal function or LUTS precede subsequent radiological progression.

This retrospective cohort study is designed to investigate the association of renal function and lower urinary tract symptoms with

skeletal metastases and radiological disease extent in patients with confirmed prostate cancer. Renal function and urinary symptoms may provide useful clinical context, but both are influenced by factors other than cancer extent. The final conclusions were based on actual effect estimates and appropriately adjusted analyses, with particular attention to comorbid kidney disease, urinary obstruction, tumour grade, PSA, and imaging modality. The study can identify associations within the diagnosed cohort but cannot establish causation or estimate the risk of developing prostate cancer in the general population.

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