Cureus
Part of SPRINGER NATURE

Open Access Original Article

Preoperative Predictors of Pathological Upstaging to pT3a in Clinically Localized Renal Cell Carcinoma: A Retrospective Cohort Study

Amit K. Patel [1], Archit Garg [1], Sandesh G. Nair [1], Vishwajeet Singh [1]

1. Urology, King George's Medical University, Lucknow, IND

Corresponding author: Vishwajeet Singh, vishwajeetsingh72@yahoo.com

Review began 10/17/2026
Review ended 11/04/2026
Published 11/09/2026

© Copyright 2026
Patel et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.119362

Abstract

Objective: To evaluate the predictive value of preoperative anatomical imaging features compared with maximum tumor diameter for identifying occult pathological T3a (pT3a) upstaging in clinically localized (cT1) renal cell carcinoma (RCC).

Methods: This retrospective cohort study included 350 patients with cT1 RCC undergoing surgical treatment at a tertiary referral center. Preoperative radiological variables, including maximum tumor diameter, hilar proximity, main renal vessel contact, and tumor growth pattern, were analyzed. Independent predictors of pathological upstaging were identified using multivariable logistic regression. Model performance was evaluated using receiver operating characteristic (ROC) analysis, DeLong comparison, calibration testing, and bootstrap internal validation.

Results: Occult pT3a upstaging occurred in 51 patients (14.6%). On multivariable analysis, hilar proximity (adjusted odds ratio (aOR): 21.84, $p < 0.001$), main renal vessel contact (aOR: 12.96, $p < 0.001$), and endophytic growth pattern (aOR: 6.88, $p < 0.001$) were strong independent predictors of pathological upstaging. Maximum tumor diameter >4 cm was also independently associated with pT3a disease (aOR: 2.42, $p = 0.024$). The multivariable model demonstrated excellent discrimination in this cohort (AUC: 0.93), significantly outperforming tumor size alone (AUC: 0.61; DeLong $p < 0.001$).

Conclusions: Preoperative anatomical imaging characteristics, particularly hilar proximity, main renal vessel contact, and endophytic growth pattern, are important predictors of occult pT3a upstaging in clinical T1 RCC. Incorporation of these readily identifiable features into a multivariable model improved risk stratification beyond tumor size alone in this single-center cohort and may aid preoperative counseling and surgical planning; external validation is warranted before clinical application.

Categories: Therapeutics, Urology, Oncology
Keywords: hilar proximity, partial nephrectomy, pathological upstaging, preoperative imaging, pt3a, renal cell carcinoma, renal nephrometry score, renal sinus invasion

Introduction

The widespread use of high-resolution cross-sectional imaging has led to a marked increase in the incidental detection of clinically localized (cT1) renal cell carcinoma (RCC) [1]. The surgical management of clinically localized renal tumors has progressively shifted from radical nephrectomy toward partial nephrectomy whenever technically feasible, aiming to preserve renal function without compromising oncological outcomes [2].

Despite this paradigm shift, a persistent clinical challenge remains: the unexpected identification of pathological T3a (pT3a) disease following resection of presumed cT1 tumors. Occult upstaging, defined by microscopic invasion into perirenal fat, renal sinus fat, or segmental renal vein branches, occurs in approximately 10-15% of cases [3,4]. This finding is clinically significant, as pT3a disease has been associated with increased rates of recurrence, a higher likelihood of positive surgical margins, and inferior survival outcomes compared with organ-confined tumors [5-7].

Accurate preoperative identification of patients at risk of occult upstaging is therefore critical for surgical planning, selection of operative approach, and patient counseling. Traditionally, risk stratification has relied heavily on maximum tumor diameter, which forms the basis of the cT1a (≤4 cm) and cT1b (4-7 cm) staging framework [2]. However, increasing evidence suggests that tumor size alone is an imperfect surrogate for biological aggressiveness and local invasiveness [8,9]. The R.E.N.A.L. nephrometry score provides a standardized assessment of renal tumor anatomical complexity and assists in surgical planning [10,11]. However, it was not originally designed to assess tumor biological aggressiveness or predict pathological upstaging.

From an anatomical standpoint, the renal sinus represents a region of relative vulnerability, lacking the dense fibrous barrier present in the peripheral renal parenchyma and thereby facilitating tumor extension into surrounding structures [1,12]. Consequently, the spatial relationship between the tumor and central renal anatomy, particularly hilar proximity, contact with the main renal vessels, and an endophytic growth pattern, may play a pivotal role in predicting occult invasion beyond the renal capsule.

In this context, the present study aimed to evaluate the predictive value of preoperative radiological features in comparison with tumor size and to develop a multivariable model for identifying pathological upstaging in patients with clinically localized RCC.

Materials And Methods

Study design and setting

This retrospective, single-center observational cohort study was conducted at the Department of Urology, King George's Medical University, Lucknow, India, a high-volume tertiary referral center with a substantial RCC caseload [13]. The study protocol was reviewed and approved by the Institutional Ethics Committee (IEC) at its meeting held on May 13, 2026 (Approval no.: 275/Ethics/2026; Reference code: 152nd ECM IIA/P6; eRIB application no.: KGMUA00061). Given the retrospective design of the study, the requirement for individual informed consent was waived.

Patient Selection

Consecutive patients who underwent partial or radical nephrectomy at our institution between January 2014 and December 2025 were screened for eligibility. Inclusion criteria were: (1) aged 18 years or older; (2) surgical treatment of a renal mass with histopathologically confirmed RCC; (3) clinical stage cT1 (tumor ⩽7 cm) on preoperative imaging, as defined below; (4) availability of preoperative contrast-enhanced CT and/or MRI for review; and (5) complete histopathological data allowing assignment of the final pathological T stage. Exclusion criteria were: (1) clinical or radiological evidence of nodal (cN+) or distant metastatic (M1) disease; (2) tumors >7 cm; (3) benign histology; and (4) incomplete clinical, imaging, or pathology records. Demographic, clinical, perioperative, and pathological data were retrieved from institutional records. All 350 patients included in the analysis had a final pathological stage of pT1 or pT3a.

Clinical Staging

Clinical stage was assigned from preoperative contrast-enhanced CT and/or MRI according to the American Joint Committee on Cancer (AJCC) 8th edition TNM classification [14]. Clinical T1 (cT1) was defined as a tumor ⩽7 cm in greatest dimension that appeared confined to the kidney, subdivided into cT1a (⩽4 cm) and cT1b (>4 to ⩽7 cm) [2]. Patients were considered clinically localized when there was no radiological evidence of perinephric or renal sinus fat invasion, renal vein or inferior vena cava tumor thrombus, regional lymph node involvement (cN0), or distant metastasis (cM0).

Sample Size

The sample size was determined by the number of outcome events available for multivariable modeling rather than by a formal power calculation. Of 350 consecutive eligible patients, 51 experienced pathological upstaging to pT3a. With four prespecified predictors in the final multivariable model, this yielded approximately 12.8 events per predictor, supporting the adequacy of the cohort for model development.

Outcome Definition

Pathological upstaging was defined as a final pathological stage of pT3a in a patient who had been classified as cT1 on preoperative imaging. Patients were categorized into non-upstaged (pT1; tumor ⩽7 cm and confined to the kidney) and upstaged (pT3a) groups based on final histopathology of the surgical specimen. The primary outcome was pathological upstaging, defined according to the American Joint Committee on Cancer (AJCC) 8th edition TNM (tumor, node, and metastasis) criteria for pathological stage pT3a as tumor extension into the renal vein or its segmental branches, or invasion of the perirenal and/or renal sinus fat [14]. Isolated pelvicalyceal system invasion, also included in the AJCC 8th edition pT3a definition, was not separately captured as a distinct outcome category in this study's pathological ascertainment.

Radiological Assessment

Preoperative contrast-enhanced imaging (CT and/or MRI) was reviewed using predefined radiological criteria. The assessed variables included maximum tumor diameter, hilar proximity, contact with the main renal vessels, and tumor growth pattern. Hilar proximity was defined as a tumor located within ⩽4 mm of the renal sinus or main hilar vessels on preoperative imaging (Figure *1*). This was a study-specific anatomical definition and was analyzed separately from the standard R.E.N.A.L. nephrometry N component. Contact with the main renal vessels was defined as direct tumor abutment against a main renal vessel with loss of

the intervening perivascular fat plane (Figure 2). The ⩽4 mm threshold was selected with reference to the highest-complexity category of the N component of the R.E.N.A.L. nephrometry system, which measures nearness to the renal sinus or collecting system [10]. However, the present study used a broader, study-specific definition of hilar proximity that also included nearness to the main hilar vessels. This definition is not equivalent to the standard N component. In the original R.E.N.A.L. system, direct tumor contact with the main renal artery or vein is indicated separately by the hilar suffix, which does not contribute to the numerical score.

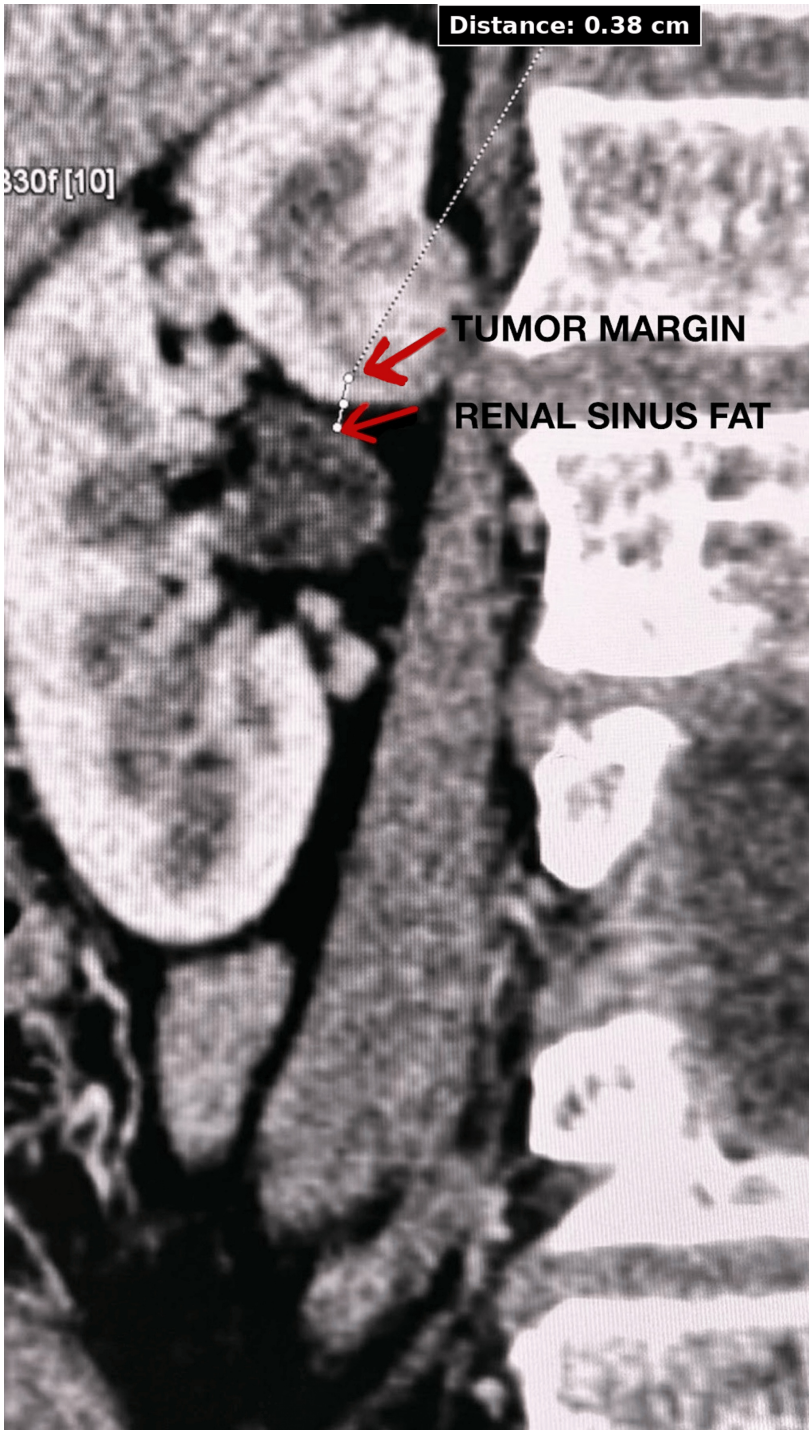


FIGURE 1: Measurement of hilar proximity on contrast-enhanced CT.

Representative coronal contrast-enhanced CT demonstrating the measurement used to define hilar proximity. The shortest distance between the renal tumor margin and the renal sinus was 3.8 mm, meeting the prespecified criterion of ≤4 mm.

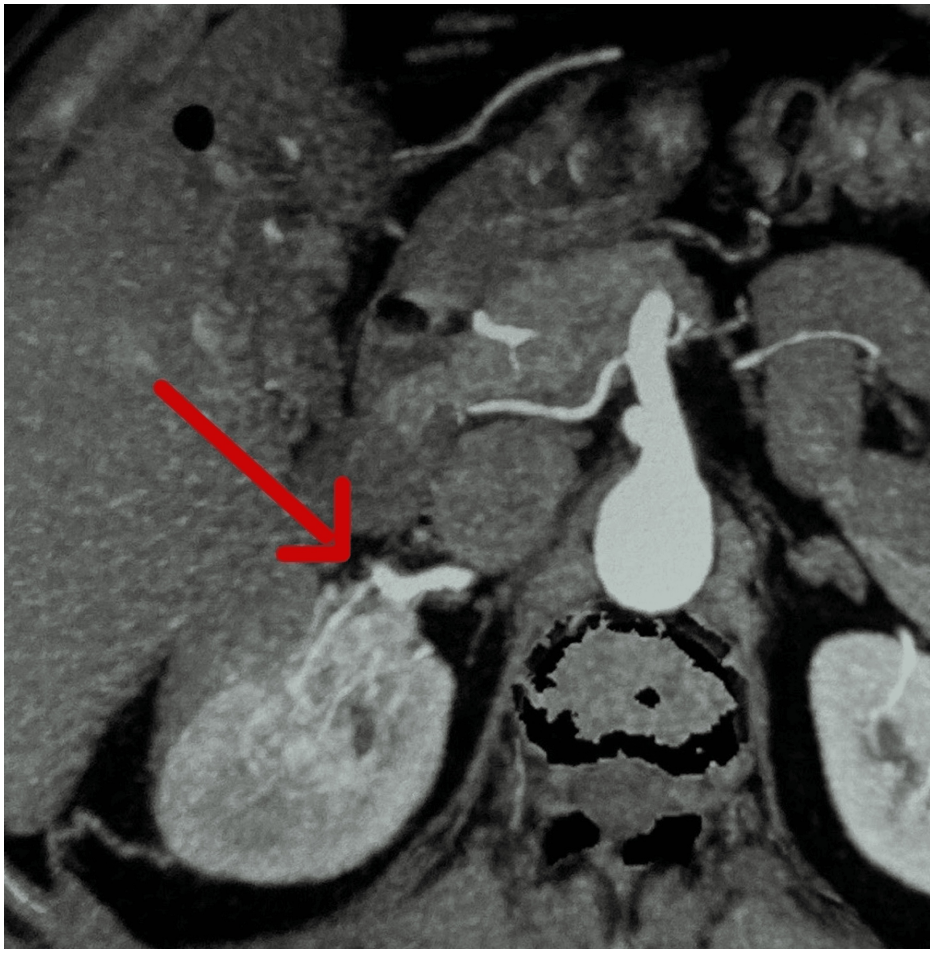


FIGURE 2: Main renal vessel contact on contrast-enhanced CT.

Representative axial contrast-enhanced CT demonstrating direct contact between the renal mass and a main renal hilar vessel (arrow), with loss of the intervening perivascular fat plane.

Endophytic growth was defined as <50% of the tumor extending beyond the renal contour, indicating that >50% of the tumor was located within the renal parenchyma, in accordance with the R.E.N.A.L. nephrometry system (Figure *3*). Imaging was independently assessed according to these predefined criteria by two board-certified urologists with five and seven years of clinical experience, respectively, who were blinded to the final pathological stage. Discordant assessments were resolved by consensus.

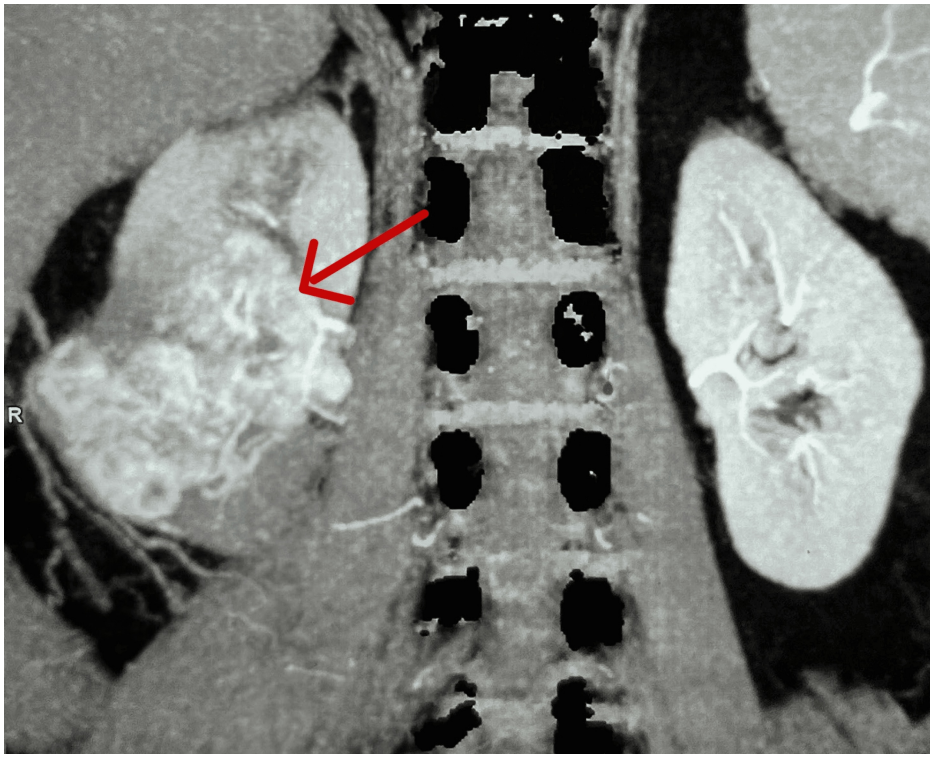


FIGURE 3: Endophytic growth pattern on contrast-enhanced CT.

Representative coronal contrast-enhanced CT demonstrating a predominantly endophytic renal mass (arrow). Less than 50% of the tumor extends beyond the renal contour, indicating that more than 50% of the tumor is intrarenal.

Imaging parameters and R.E.N.A.L. nephrometry scoring

The following imaging parameters were recorded for each tumor: maximum tumor diameter (cm); laterality; hilar proximity; contact with the main renal vessels; growth pattern (exophytic or endophytic); and the R.E.N.A.L. nephrometry score and its components. The R.E.N.A.L. score was calculated from the same preoperative imaging as described by Kutikov and Uzzo [10]. Its five components are: (R)adius, the maximal tumor diameter (⩽4 cm, 1 point; >4 to <7 cm, 2 points; ⩾7 cm, 3 points); (E)xophytic/endophytic properties (⩾50% exophytic, 1 point; <50% exophytic, 2 points; entirely endophytic, 3 points); (N)earness of the deepest portion of the tumor to the collecting system or renal sinus (⩾7 mm, 1 point; >4 to <7 mm, 2 points; ⩽4 mm, 3 points); (A)nterior or posterior location relative to the coronal plane of the kidney (a descriptive suffix that carries no points); and (L)ocation relative to the polar lines (entirely above or below a polar line, 1 point; tumor crossing a polar line, 2 points; more than 50% of the tumor crossing a polar line, crossing the axial renal midline, or lying entirely between the polar lines, 3 points). Points for the R, E, N, and L components were summed (range: 4-12) and categorized as low (4-6), moderate (7-9), or high (10-12) complexity [10]. For the multivariable analysis, the exophytic/endophytic component was dichotomized as endophytic (<50% exophytic) versus exophytic (⩾50% exophytic). Radiological invasion of the renal sinus fat was not entered as a predictor because tumors with such findings would not be classified as cT1; invasion of the renal sinus fat, perirenal fat, or segmental renal vein branches was instead ascertained histopathologically as part of the outcome definition.

Histopathological Assessment

Histopathological characteristics, including tumor subtype, International Society of Urological Pathology (ISUP) grade, lymphovascular invasion, surgical margin status, and site of invasion, were recorded for descriptive analysis. ISUP grade was assigned to the 315 clear cell and papillary RCCs. The 35 chromophobe RCCs were not graded, in line with the ISUP recommendation that chromophobe RCC should not be graded [15]; these ungraded tumors therefore do not represent missing or incomplete pathology data.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics, version 31 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical variables as frequencies (percentages). Differences between the pT1 and pT3a groups were assessed using the independent t-test or Mann-Whitney U test for continuous variables. For categorical

variables, Pearson's chi-square test (without continuity correction) was used, and Fisher's exact test was used when any expected cell count was <5; the three R.E.N.A.L. complexity categories were compared using a 3 × 2 chi-square test. Cases with missing ISUP grade were not imputed, and analyses involving ISUP grade used the available cases only. Crude (univariable) and adjusted (multivariable) odds ratios were estimated using binary logistic regression and are reported with Wald 95% confidence intervals (CI), Wald χ^2 statistics (1 degree of freedom), and p-values. A two-sided $p < 0.05$ was considered statistically significant.

Multivariable Model Development

Variables demonstrating $p < 0.10$ on univariable analysis, along with clinically relevant covariates, were entered into a forced-entry multivariable logistic regression model to identify independent predictors of pathological upstaging; associations were reported as odds ratios (OR) and adjusted odds ratios (aOR) with 95% CI. Although R.E.N.A.L. nephrometry complexity was associated with upstaging on univariable analysis, its individual anatomical components, rather than the composite score, were entered into the multivariable model, consistent with the study objective of evaluating the incremental predictive value of specific, clinically interpretable imaging characteristics. The final multivariable model comprised four predictors: maximum tumor diameter (>4 cm vs. ≤4 cm), hilar proximity, main renal vessel contact, and endophytic growth pattern.

ROC Curve Analysis and Internal Validation

Receiver operating characteristic (ROC) curve analysis was performed using data from 350 patients to evaluate discrimination of occult pT3a upstaging. The final multivariable model and maximum tumor diameter as a continuous variable were compared using the area under the ROC curve (AUC). Empirical ROC curves were constructed from the predicted probabilities of the fitted multivariable logistic regression model and from the observed continuous maximum tumor diameters, with occult pT3a upstaging as the outcome (pT3a = 1; pT1 = 0). For descriptive and univariable analysis, maximum tumor diameter was categorized according to the clinical T1a/T1b threshold of 4 cm; for ROC analysis, the original continuous tumor diameter was retained to evaluate discrimination across the full range of possible thresholds. Because both ROC curves were derived from the same patients, their AUCs were compared using the DeLong test for correlated ROC curves. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test, and internal validation was performed using bootstrap resampling (1000 iterations) to estimate optimism-corrected performance. As the model was developed and evaluated within the same cohort, the reported AUC represents apparent discrimination that may be optimistic, notwithstanding bootstrap correction; external validation in an independent cohort is required before clinical application.

Results

Baseline demographic and preoperative tumor characteristics

A total of 350 patients with clinically localized (cT1) renal masses were included. The mean age was 51.8 ± 14.7 years, with the highest proportion of patients aged 50-59 years (30.0%) and a male predominance (76.6%). The mean maximum tumor diameter was 3.7 ± 1.5 cm; 62.9% of tumors were cT1a (≤4 cm) and 37.1% were cT1b (>4 cm). According to the R.E.N.A.L. nephrometry score, 68.0% of tumors were predominantly exophytic, while moderate complexity was most common (55.7%). Hilar proximity was present in 24.0% of patients, and direct contact with the main renal vessels was observed in 14.0% (49/350) (Table *1*).

Characteristic	Value
Age (years)	
Mean ± SD	51.8 ± 14.7
Range	18-84
<30	28 (8.0%)
30-39	39 (11.1%)
40-49	70 (20.0%)
50-59	105 (30.0%)
60-69	78 (22.3%)
≥70	30 (8.6%)
Gender	
Male	268 (76.6%)
Female	82 (23.4%)
Maximum tumor diameter (cm)	
Mean ± SD	3.7 ± 1.5
≤4 cm (cT1a)	220 (62.9%)
>4-7 cm (cT1b)	130 (37.1%)
Tumor laterality	
Left	185 (52.9%)
Right	165 (47.1%)
Tumor growth pattern	
Exophytic (≥50% exophytic component)	238 (68.0%)
Endophytic (<50% exophytic component)	112 (32.0%)
Hilar proximity	
Yes	84 (24.0%)
No	266 (76.0%)
Contact with main renal vessels	
Yes	49 (14.0%)
No	301 (86.0%)
R.E.N.A.L. nephrometry complexity	
Low (4-6)	125 (35.7%)
Moderate (7-9)	195 (55.7%)
High (10-12)	30 (8.6%)

TABLE 1: Baseline demographic and preoperative tumor characteristics (N = 350).

Data are presented as n (%) unless otherwise specified.

SD: standard deviation; cT1a: clinical stage T1a; cT1b: clinical stage T1b; R.E.N.A.L.: Radius, Exophytic/endophytic, Nearness to collecting system or sinus, Anterior/posterior, and Location.

Surgical Management and Pathological Outcomes

Partial nephrectomy was performed in 73.7% (258/350) of patients, with laparoscopic surgery accounting for 74.9% of procedures. The mean operative time was 162.5 ± 19.2 minutes, estimated blood loss was 279.0 ± 67.7 mL, and warm ischemia time was 18.7 ± 4.8 minutes. Clear cell RCC was the predominant histological subtype (75.1%), and ISUP grade 2 was the most frequent grade (51.1%).

Pathological upstaging to pT3a occurred in 51 patients (14.6%). Among surgically treated patients, pT3a disease was identified in 6/258 (2.3%) undergoing partial nephrectomy and 45/92 (48.9%) undergoing radical nephrectomy; because surgical approach was not randomly assigned, these differences most likely reflect preoperative tumor complexity and selection of the operative approach rather than an effect of the procedure itself (Table *2*).

Characteristic	Value
Type of surgery	
Partial nephrectomy	258 (73.7%)
Radical nephrectomy	92 (26.3%)
Surgical approach	
Laparoscopic	262 (74.9%)
Open	88 (25.1%)
Operative parameters	
Operative time (minutes), mean ± SD	162.5 ± 19.2
Estimated blood loss (mL), mean ± SD	279.0 ± 67.7
Warm ischemia time (minutes), mean ± SD	18.7 ± 4.8
Histological subtype	
Clear cell RCC	263 (75.1%)
Papillary RCC	52 (14.9%)
Chromophobe RCC	35 (10.0%)
ISUP grade*	
Grade 1	60 (19.0%)
Grade 2	161 (51.1%)
Grade 3	60 (19.0%)
Grade 4	34 (10.8%)
Final pathological stage	
pT1	299 (85.4%)
pT3a (upstaged)	51 (14.6%)
Upstaging by surgical procedure	
Partial nephrectomy	6/258 (2.3%)
Radical nephrectomy	45/92 (48.9%)
Surgical margin status	
Negative margins	337 (96.3%)
Positive margins	13 (3.7%)

TABLE 2: Surgical management and pathological outcomes (N = 350).

Data are presented as n (%) unless otherwise specified.

SD: standard deviation; RCC: renal cell carcinoma; ISUP: International Society of Urological Pathology; pT1: pathological stage T1; pT3a: pathological stage T3a.

* ISUP grade was available for 315 graded tumors.

Univariate Analysis and Secondary Outcomes

Maximum tumor diameter >4 cm showed a trend toward association with pathological upstaging but did not reach statistical significance (49.0% vs. 35.1%, p = 0.06). In contrast, several anatomical variables were strongly associated with pT3a disease. Hilar proximity was observed in 84.3% of upstaged tumors compared

with 13.7% of non-upstaged tumors ($p < 0.001$). Similarly, main renal vessel contact was more frequent in pT3a tumors than in pT1 tumors (60.8% vs. 6.0%, $p < 0.001$). Endophytic growth pattern was also significantly associated with pathological upstaging (74.5% vs. 24.7%, $p < 0.001$).

High-complexity R.E.N.A.L. nephrometry scores were more common among pT3a tumors (17.6% vs. 7.0%, $p = 0.039$). Clinical presentation ($p = 0.17$), ISUP grade distribution ($p = 0.79$), and surgical margin status ($p = 1.00$) did not differ significantly between groups (Table *3*).

Variable	pT1 (n = 299)	pT3a (n = 51)	p-value
Maximum tumor diameter			
≤4 cm (cT1a)	194 (64.9%)	26 (51.0%)	0.06
>4 cm (cT1b)	105 (35.1%)	25 (49.0%)	0.06
Hilar proximity			
Yes	41 (13.7%)	43 (84.3%)	<0.001
No	258 (86.3%)	8 (15.7%)	<0.001
Contact with main renal vessels			
Yes	18 (6.0%)	31 (60.8%)	<0.001
No	281 (94.0%)	20 (39.2%)	<0.001
Tumor growth pattern			
Endophytic (<50% exophytic)	74 (24.7%)	38 (74.5%)	<0.001
Exophytic (≥50% exophytic)	225 (75.3%)	13 (25.5%)	<0.001
Clinical presentation			
Asymptomatic (incidental)	219 (73.2%)	42 (82.4%)	0.17
Symptomatic (hematuria/pain)	80 (26.8%)	9 (17.6%)	0.17
R.E.N.A.L. nephrometry complexity			
Low complexity (4-6)	110 (36.8%)	15 (29.4%)	0.039
Moderate complexity (7-9)	168 (56.2%)	27 (52.9%)	0.039
High complexity (10-12)	21 (7.0%)	9 (17.6%)	0.039
Histopathological subtype			
Clear cell RCC	220 (73.6%)	43 (84.3%)	0.036
Papillary RCC	44 (14.7%)	8 (15.7%)	0.036
Chromophobe RCC	35 (11.7%)	0 (0.0%)	0.036
ISUP grade*			
Grade I-II	186 (70.5%)	35 (68.6%)	0.79
Grade III-IV	78 (29.5%)	16 (31.4%)	0.79
Surgical margin status			
Negative margins	288 (96.3%)	49 (96.1%)	1
Positive margins	11 (3.7%)	2 (3.9%)	1

TABLE 3: Univariate analysis of clinical, anatomical, and secondary outcomes by pathological stage.

* ISUP grade was assigned to 264 pT1 and 51 pT3a clear cell and papillary tumors; the 35 chromophobe RCCs (all pT1) were not graded.

Values are column percentages. Pearson's chi-square test was used for tumor diameter, hilar proximity, main renal vessel contact, growth pattern, clinical presentation, R.E.N.A.L. complexity (3 × 2), histopathological subtype (3 × 2), and ISUP grade. Fisher's exact test was used for surgical margin status. P-values are overall tests for each variable and are repeated across its categories for readability.

cT1a: clinical stage T1a; cT1b: clinical stage T1b; R.E.N.A.L.: Radius, Exophytic/endophytic, Nearness to collecting system or sinus, Anterior/posterior, and Location; RCC: renal cell carcinoma; ISUP: International Society of Urological Pathology; pT1: pathological stage T1; pT3a: pathological stage T3a.

Univariable Logistic Regression Analysis

On univariable logistic regression, maximum tumor diameter >4 cm demonstrated a non-significant increase in the odds of pT3a upstaging (OR: 1.78, 95% CI: 0.98-3.23, p = 0.060). Hilar proximity showed the strongest unadjusted association with pathological upstaging (OR: 33.82, 95% CI: 14.85-77.06, p < 0.001). Main renal vessel contact was similarly associated with a marked increase in risk (OR: 24.20, 95% CI: 11.58-50.56, p < 0.001). Endophytic tumors demonstrated significantly higher odds of pT3a disease than predominantly exophytic tumors (OR: 8.89, 95% CI: 4.49-17.58, p < 0.001); Wald χ^2 statistics for each variable are given in Table 4.

Variable	Crude OR	95% CI	Wald χ^2	p-value
Maximum tumor diameter >4 cm (cT1b vs. cT1a)	1.78	0.98-3.23	3.55	0.060
Hilar proximity (yes vs. no)	33.82	14.85-77.06	70.24	<0.001
Contact with main renal vessels (yes vs. no)	24.20	11.58-50.56	71.81	<0.001
Endophytic growth pattern (<50% vs. ≥50% exophytic)	8.89	4.49-17.58	39.38	<0.001

TABLE 4: Univariable logistic regression analysis for predictors of occult pT3a upstaging.

Wald χ^2 has 1 degree of freedom (univariable logistic regression, n = 350).

OR = odds ratio; CI = confidence interval; cT1a: clinical stage T1a; cT1b: clinical stage T1b; pT3a: pathological stage T3a.

Multivariable Logistic Regression Analysis

In the forced-entry multivariable model (350 patients, 51 events), all four preoperative variables remained independent predictors of pathological upstaging after mutual adjustment (Table 5). Hilar proximity was the strongest independent predictor (aOR: 21.84, 95% CI: 8.94-53.32, Wald χ^2 = 45.82, p < 0.001), followed by main renal vessel contact (aOR: 12.96, 95% CI: 5.31-31.64, Wald χ^2 = 31.66, p < 0.001) and endophytic growth pattern (aOR: 6.88, 95% CI: 2.93-16.14, Wald χ^2 = 19.63, p < 0.001). Maximum tumor diameter >4 cm, which was not significant on univariable analysis, also emerged as an independent predictor after adjustment (aOR: 2.42, 95% CI: 1.12-5.21, Wald χ^2 = 5.08, p = 0.024).

Variable	Adjusted OR	95% CI	Wald χ^2	p-value
Maximum tumor diameter >4 cm (cT1b vs. cT1a)	2.42	1.12-5.21	5.08	0.024
Hilar proximity (yes vs. no)	21.84	8.94-53.32	45.82	<0.001
Contact with main renal vessels (yes vs. no)	12.96	5.31-31.64	31.66	<0.001
Endophytic growth pattern (<50% vs. ≥50% exophytic)	6.88	2.93-16.14	19.63	<0.001

TABLE 5: Multivariable logistic regression analysis for independent predictors of occult pT3a upstaging.

Model performance: AUC = 0.93; bootstrap optimism = 0.005; optimism-corrected AUC = 0.93; Hosmer-Lemeshow χ^2 = 6.12, p = 0.19.

Wald χ^2 has 1 degree of freedom. The model included all four listed variables (forced entry; n = 350, 51 pT3a events).

AUC: area under the curve; OR = odds ratio; CI = confidence interval; cT1a: clinical stage T1a; cT1b: clinical stage T1b; pT3a: pathological stage T3a.

ROC Curve Analysis and Internal Validation

Maximum tumor diameter alone demonstrated limited discriminatory ability for predicting occult pathological upstaging (AUC: 0.61, 95% CI: 0.52-0.70). In contrast, the multivariable model incorporating tumor size, hilar proximity, main renal vessel contact, and tumor growth pattern demonstrated excellent discrimination (AUC: 0.93, 95% CI: 0.88-0.97). Bootstrap internal validation revealed minimal optimism (0.005), with an optimism-corrected AUC of 0.93, indicating good model stability. Calibration analysis

demonstrated acceptable agreement between observed and predicted outcomes (Hosmer-Lemeshow χ^2 = 6.12, p = 0.19). The multivariable model demonstrated significantly superior discrimination compared with tumor size alone (DeLong p < 0.001).

Discussion

In this retrospective cohort of surgically treated clinical T1 RCC, occult pathological upstaging to pT3a occurred in 14.6% of patients. This finding is consistent with previously published institutional series and meta-analyses demonstrating that a clinically meaningful proportion of apparently localized renal tumors harbor adverse pathological features at final histology [3,4,8]. Given the association between pT3a disease and inferior oncological outcomes, accurate preoperative identification of patients at increased risk of occult upstaging remains clinically relevant.

In this cohort, the evaluated anatomical imaging characteristics were more strongly associated with observed pathological upstaging than tumor size alone. Although maximum tumor diameter >4 cm showed borderline significance on univariable analysis, hilar proximity, main renal vessel contact, and endophytic growth pattern retained associations with pT3a status after mutual adjustment. Hilar proximity showed the largest adjusted association. These findings should be interpreted in the context of possible clinical understaging and differences in outcome ascertainment between surgical procedures.

Combining the imaging variables yielded a higher apparent AUC in the development cohort (0.93) than tumor size alone (0.61). The results suggest that anatomical location and growth pattern are associated with the pathological stage assigned after surgery. They do not, however, establish that the model identifies genuinely occult invasion independently of subtle radiological signs of extension or differences in pathological sampling.

Tumor size and anatomical predictors of occult pT3a upstaging

Tumor size has traditionally been considered an important determinant of pathological aggressiveness in localized RCC, and several previous studies have identified increasing tumor diameter as a predictor of occult pT3a upstaging [8,9,16,17]. In the present study, maximum tumor diameter >4 cm demonstrated limited discriminatory ability on standalone analysis but emerged as an independent predictor after multivariable adjustment. This pattern suggests that the relationship between tumor size and occult upstaging may be influenced by coexisting anatomical tumor characteristics.

The strongest findings of our study are related to anatomical imaging variables. Hilar proximity emerged as the most powerful independent predictor of occult pT3a disease. This observation is biologically plausible, given the anatomical properties of the renal sinus, which contains abundant vascular, lymphatic, and adipose tissue pathways that may facilitate early microscopic extension beyond the renal parenchyma [12]. Tumors located adjacent to the hilum or renal sinus may therefore possess a greater propensity for sinus fat or vascular invasion despite appearing clinically confined on imaging. Similar observations regarding tumor location and anatomical complexity have been reported in previous predictive models for pathological upstaging [9,17].

Contact with the main renal vessels also demonstrated a strong independent association with pathological upstaging. Although less extensively studied as an isolated imaging marker, direct tumor abutment against hilar vasculature likely reflects increased tumor centrality and closer anatomical relationships with structures implicated in pT3a disease. Endophytic growth pattern represented another important predictor, with endophytic tumors showing substantially higher odds of occult pT3a disease than predominantly exophytic lesions. This observation is consistent with the conceptual framework of the R.E.N.A.L. nephrometry system, in which tumor depth and centrality contribute to anatomical complexity [10,11].

Collectively, these findings warrant further investigation of anatomy-oriented approaches to preoperative risk assessment in cT1 renal masses, alongside conventional tumor-size assessment and standardized staging and pathological ascertainment.

Model performance and clinical implications

The combined model demonstrated high apparent discrimination for pT3a status in the development cohort (AUC: 0.93, 95% CI: 0.88-0.97), and bootstrap resampling suggested limited statistical optimism. Nevertheless, internal validation cannot address potential bias arising from radiological understaging, selection of more complex tumors for radical nephrectomy, or differences in the detection of microscopic invasion between specimen types. Accordingly, this AUC should not be interpreted as established performance in independent clinical populations. Previous studies have also explored clinical and imaging-based prediction of pathological upstaging [16,17].

The clinical implications of accurately identifying occult pT3a disease extend beyond pathological classification alone. Previous studies and systematic reviews have shown that pathological upstaging in clinically localized RCC may be associated with adverse oncological outcomes, including increased

recurrence risk and inferior survival compared with organ-confined disease [4-7]. Consequently, improved preoperative recognition of high-risk patients may influence surgical planning and patient counseling.

Recognition of high-risk anatomical features may be particularly useful in patients with central, hilar, or highly endophytic tumors, where awareness of increased upstaging risk may inform discussions regarding operative complexity, surgical approach, and the balance between nephron preservation and oncological safety. Importantly, our findings do not argue against partial nephrectomy in appropriately selected cT1 tumors; rather, they support a more individualized, anatomy-informed approach to preoperative risk stratification using routinely available imaging data. Further external validation across diverse populations will be necessary before broader clinical implementation.

Implications for preoperative counseling and surgical planning

The observed associations may alert clinicians to the possibility of pT3a disease in patients with anatomically central tumors, but the model should not yet be used to generate individual risk estimates. In this cohort, the observed frequency of pT3a upstaging was 51.2% (43/84) in tumors with hilar proximity versus 3.0% (8/266) in those without, 63.3% (31/49) with versus 6.6% (20/301) without main renal vessel contact, and 33.9% (38/112) in endophytic versus 5.5% (13/238) in exophytic tumors, compared with 19.2% (25/130) in tumors >4 cm versus 11.8% (26/220) in tumors ⩽4 cm. These crude rates reflect a single-center surgical cohort and may be influenced by patient selection and differential pathological ascertainment. Closer postoperative follow-up may be appropriate when pT3a disease is confirmed, consistent with established oncological considerations [4-7].

For surgical planning, awareness of these features may prompt careful review of the preoperative imaging, including the relationship of the tumor to the renal sinus fat and hilar vessels, and additional dedicated imaging when sinus or vascular involvement is uncertain. It may also support attention to the completeness of resection at the sinus interface and thorough pathological assessment of sinus and perinephric fat. Because upstaging was observed in 6/258 partial and 45/92 radical nephrectomies, and the operative approach was not randomly assigned, our data should not be taken to indicate that nephron-sparing surgery is unsafe or that radical nephrectomy is preferable; the choice of procedure should remain individualized, balancing tumor complexity, renal function, and oncological risk [2].

Strengths and limitations

This study evaluated a surgical cohort of patients with preoperatively classified cT1 RCC and incorporated clearly defined, clinically interpretable imaging features alongside tumor diameter. Its pathology-based outcome and comparison of a multivariable model with tumor size alone provide an exploratory assessment of associations between central renal anatomy and observed pathological upstaging.

Several limitations warrant consideration. First, the retrospective, single-center design introduces the possibility of selection bias and limits generalizability. Patients were treated between January 2014 and December 2025, during which imaging technology, interpretation, surgical practice, and pathological assessment may have changed. No period-stratified comparison was performed. Imaging characteristics were assessed retrospectively, and although disagreements were resolved by consensus, quantitative interobserver agreement estimates are not reported; the reproducibility of individual measurements therefore remains uncertain. Only a limited range of imaging variables was evaluated, and additional features, such as perinephric fat stranding and tumor margin characteristics, were not included. Isolated pelvicalyceal system invasion was not separately categorized in the pathological outcome assessment.

An important limitation concerns the distinction between anatomical proximity and radiological evidence of invasion. Although tumors were classified as cT1 because preoperative imaging did not show definite perinephric or renal sinus fat invasion or venous tumor thrombus, loss of the perivascular fat plane was included in the definition of main renal vessel contact. This finding may sometimes represent subtle invasive disease rather than a purely anatomical relationship. Consequently, some tumors may have been radiologically understaged rather than exhibiting genuinely occult pathological upstaging. Hilar proximity and vessel contact also involve structures related to the pathological definition of pT3a, potentially strengthening their associations with the outcome. Sensitivity analyses omitting main renal vessel contact from the model or excluding patients with this finding were not performed. Therefore, the contribution of potential clinical understaging to the reported discrimination (AUC: 0.93) cannot be quantified.

Pathological ascertainment may also have differed according to the type of surgery. Upstaging was identified in six of 258 patients (2.3%) undergoing partial nephrectomy and 45 of 92 (48.9%) patients undergoing radical nephrectomy. More anatomically complex or suspicious tumors may have been preferentially selected for radical nephrectomy. In addition, partial nephrectomy specimens may contain less renal sinus or perinephric fat, potentially reducing the detection of microscopic pT3a invasion compared with radical nephrectomy specimens. Neither surgery-stratified nor surgery-adjusted multivariable analyses were performed. The relative contributions of selection effects and differences in pathological detection to the observed associations therefore remain uncertain. The findings must not be used to infer that one surgical procedure is oncologically superior to the other.

Finally, the number of pT3a events was modest, and predictor selection was informed in part by observed associations; the regression coefficients and apparent AUC may therefore be unstable or optimistic. Although bootstrap validation was reported, it cannot correct for systematic bias, and no independent external validation was undertaken. Long-term outcomes, including recurrence-free and cancer-specific survival, were not evaluated. Accordingly, these findings should be regarded as exploratory and hypothesis-generating. Future investigations should use standardized imaging and pathology assessment, appropriate sensitivity and procedure-adjusted analyses, and external validation before the model is considered for clinical use.

Conclusions

In this retrospective cohort of patients with clinical T1 RCC, hilar proximity, main renal vessel contact, and endophytic growth pattern were associated with pathological upstaging to pT3a. A model combining these imaging features with tumor size demonstrated higher apparent discrimination than tumor size alone in the development cohort. However, potential radiological understaging, surgical selection, and differences in pathological ascertainment between partial and radical nephrectomy specimens may have influenced the observed associations and model performance. These findings remain exploratory. Sensitivity analyses, standardized pathological assessment, and external validation are needed before clinical application.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Vishwajeet Singh, Amit K. Patel, Archit Garg, Sandesh G. Nair

Critical review of the manuscript for important intellectual content: Vishwajeet Singh, Amit K. Patel, Archit Garg

Supervision: Vishwajeet Singh

Concept and design: Amit K. Patel, Archit Garg, Sandesh G. Nair

Drafting of the manuscript: Amit K. Patel, Archit Garg, Sandesh G. Nair

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. King George's Medical University issued approval 275/Ethics/2026. The study was reviewed and approved by the Institutional Ethics Committee (IEC) of King George's Medical University, Lucknow, at its meeting held on May 13, 2026, following review of the clarification submitted on April 21, 2026. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Capitanio U, Montorsi F: Renal cancer. Lancet. 2016, 387:894-906. 10.1016/S0140-6736(15)00046-X
2. Campbell S, Uzzo RG, Allaf ME, et al.: Renal mass and localized renal cancer: AUA guideline . J Urol. 2017, 198:520-9. 10.1016/j.juro.2017.04.100
3. Nayak JG, Patel P, Saarela O, et al.: Pathological upstaging of clinical T1 to pathological T3a renal cell carcinoma: a multi-institutional analysis of short-term outcomes. Urology. 2016, 94:154-60. 10.1016/j.urology.2016.03.029
4. Veccia A, Falagario U, Martini A, et al.: Upstaging to pT3a in patients undergoing partial or radical nephrectomy for cT1 renal tumors: a systematic review and meta-analysis of outcomes and predictive factors. Eur Urol Focus. 2021, 7:574-81. 10.1016/j.euf.2020.05.013
5. Chen L, Deng W, Liu X, Wang G, Fu B: Impact of pathological T3a upstaging on oncological outcomes of clinical T1 renal cell carcinoma: a meta-analysis. J Cancer. 2019, 10:4998-5006. 10.7150/jca.32859
6. Ramaswamy K, Kheterpal E, Pham H, Mohan S, Stifelman M, Taneja S, Huang WC: Significance of pathologic T3a upstaging in clinical T1 renal masses undergoing nephrectomy. Clin Genitourin Cancer. 2015, 13:344-9. 10.1016/j.clgc.2015.01.001
7. Weight CJ, Lythgoe C, Unnikrishnan R, Lane BR, Campbell SC, Fergany AF: Partial nephrectomy does not compromise survival in patients with pathologic upstaging to pT2/pT3 or high-grade renal tumors

compared with radical nephrectomy. Urology. 2011, 77:1142-6. 10.1016/j.urology.2010.11.058
8. Jeong SH, Kim JK, Park J, et al.: Pathological T3a upstaging of clinical T1 renal cell carcinoma: outcomes according to surgical technique and predictors of upstaging. PLoS One. 2016, 11:e0166183. 10.1371/journal.pone.0166183
9. Fukui S, Miyake M, Iida K, et al.: The preoperative predictive factors for pathological T3a upstaging of clinical T1 renal cell carcinoma. Diagnostics (Basel). 2019, 9:76. 10.3390/diagnostics9030076
10. Kutikov A, Uzzo RG: The R.E.N.A.L. nephrometry score: a comprehensive standardized system for quantitating renal tumor size, location and depth. J Urol. 2009, 182:844-53. 10.1016/j.juro.2009.05.035
11. Canter D, Kutikov A, Manley B, et al.: Utility of the R.E.N.A.L. nephrometry scoring system in objectifying treatment decision-making of the enhancing renal mass. Urology. 2011, 78:1089-94. 10.1016/j.urology.2011.04.035
12. Zhang Z, Yu C, Velet L, Li Y, Jiang L, Zhou F: The difference in prognosis between renal sinus fat and perinephric fat invasion for pT3a renal cell carcinoma: a meta-analysis. PLoS One. 2016, 11:e0149420. 10.1371/journal.pone.0149420
13. Kawaljit S, Janak SR, Ashok G, Vishwajeet S: Decadal experience of renal cell carcinoma from a tertiary care teaching institute in North India. Indian J Surg Oncol. 2018, 9:558-64. 10.1007/s13193-018-0812-0
14. DiBianco JM, Gomella PT, Ball MW: Pathologic T3a renal cell carcinoma: a classification in need of further refinement. Ann Transl Med. 2018, 6:S133. 10.21037/atm.2018.12.51
15. Delahunt B, Cheville JC, Martignoni G, et al.: The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. Am J Surg Pathol. 2013, 37:1490-504. 10.1097/PAS.0b013e318299f0fb
16. Cao C, Kang X, Shang B, et al.: A novel nomogram can predict pathological T3a upstaged from clinical T1a in localized renal cell carcinoma. Int Braz J Urol. 2022, 48:784-94. 10.1590/S1677-5538.IBJU.2021.0859
17. de la Barra CC, González PG, Baeza MÁ, Pérez OP, Cruzat JD: A preoperative model to predict pT3 upstaging in clinically localized renal cell carcinoma. Cent European J Urol. 2020, 73:173-7. 10.5173/ceju.2020.0005