Distinguishing endophytic renal cell carcinoma from urothelial carcinoma

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PURPOSE
We aimed to characterize the clinical and multiphase computed tomography (CT) features of the distinguishing endophytic clear cell renal cell carcinoma (ECCRCC) from endophytic renal urothelial carcinoma (ERUC).

METHODS
Data from 44 patients (35 men and 9 women) with ECCRCC and 21 patients (17 men and 4 women) with ERUC were retrospectively assessed. The mean patient age was 55 years (48.25-59.50 years) and 68 years (63.00-73.00 years), respectively. Univariate and multivariate logistic regression analyses were performed to determine independent predictors for ECCRCC and to construct a predictive model that comprised clinical and CT characteristics for the differential diagnosis of ECCRCC and ERUC. Differential diagnostic performance was assessed using the area under the receiver operating characteristic curve (AUC).

RESULTS
The independent predictors of ECCRCC were heterogeneous enhancement (odds ratio [OR] = 0.027, P = .005), hematuria (OR for gross hematuria = 53.995, P = .003; OR for microscopic hematuria = 31.126, P = .027), and an infiltrative growth pattern (OR = 24.301, P = .022). The AUC of the predictive model was 0.938 (P < .001, sensitivity = 84.10%, specificity = 95.20%), which had a better diagnostic performance than heterogeneous enhancement (AUC = 0.766, P = .001, sensitivity = 81.82%, specificity = 71.43%), hematuria (AUC = 0.786, P < .001, sensitivity = 81.82%, specificity = 66.67%), and infiltrative growth pattern (AUC = 0.748, P = .001, sensitivity = 90.48%, specificity = 59.09%).

CONCLUSION
The independent predictors, as well as the predictive model of CT and clinical characteristics, may assist in the differential diagnosis of ECCRCC and ERUC and provide useful information for clinical decision-making.
of CSI. Takamatsu et al.15 explored the correlation between the CT signs of CSI and the survival rate. However, to the best of our knowledge, there are no published studies specifically on CT-based diagnosis to differentiate between ECCRCC and ERUC.

The clinical history and the patient’s symptoms are important in the diagnosis of RCC and upper urinary tract UC. Smoking is a risk factor for both RCC and upper urinary tract UC.16,17 Further, kidney stones may be associated with upper urinary tract UC.18,19 Flank pain and hematuria are considered typical symptoms of both ccRCC20 and upper urinary tract UC.21,22 Neither Raza et al.9 nor Bata et al.10 determined the correlation between clinical data and CT for the differential diagnosis of ECCRCC and ERUC.

Therefore, we aimed to retrospectively assess and adequately describe the CT characteristics of ECCRCC and ERUC and to determine their correlations with clinical data.

**Methods**

This study was approved by our institutional research ethics committee (protocol number: 2021 [KY-E-214]), who waived the need for informed patient consent.

**Patients**

Patients with UC or ccRCC, who had undergone surgery or biopsy in our hospital from August 2008 to December 2020, were involved, and their data were retrospectively analyzed. All the patients underwent a multiphase CT scan within 1 week before surgery or biopsy. Patients with ERUC or ECCRCC who also had other tumor components and patients with tuberculous or a purulent infection were excluded. Patients with exophytic solid ccRCCs and cystic-dominant ccRCCs were also excluded.23 Patients with combined masses of the ureter or bladder were excluded. Finally, patients with diffuse UCs with hydronephrosis and exophytic renal UC were excluded (Figure 1).

**Clinical and pathological data**

Clinical data of included patients were collected using the hospital information system (DHC Software Co), which included age, sex, smoking history, flank pain, kidney stone history, and hematuria. Patients with a smoking history of more than 20 years and no less than a pack of cigarettes per day were considered as having a positive smoking history.16,17 Patients who had had kidney stones for more than 5 years were considered to have a positive history of kidney stones. Cases with asymptomatic small calculi or microcalculi were not considered positive.18,19 A patient was considered positive for microscopic hematuria if the result for occult blood in routine urine tests was positive, without visible blood. Pathology reports were obtained from the picture archiving and communication system (PACS) (Shenzhen Annet Information System Co. Ltd). Histological slides from all included patients were reviewed for this study. The final pathological diagnosis was established by 2 pathologists (each with 10 years of experience in diagnosing renal diseases) via combined microscopic and immunohistochemical examination (ccRCC: vimentin [+], CD10 [+], RCC Ma [+], PAX-8 [+]; UC: CK7 [+], P63 [+], CK20 [+/-]), and any differences were arbitrated by another senior pathologist who was blinded to the study information.

**Computed tomography scanning**

Patients underwent multiphase CT scanning, including an unenhanced phase (UP) scan, and contrast enhancement scanning of the corticomedullary phase (CP), nephrographic phase (NP), and excretory phase (EP). Patients were scanned using 16-slice, 64-slice, 128-slice, and 256-slice spiral CT (Light Speed VCT and Revolution, GE Healthcare; SOMATOM sensation 16, SOMATOM Definition Flash, and SOMATOM Force, Siemens Healthcare). The scanning area was from the top of the diaphragm to the level of the iliac wing. The scanning parameters were as follows: tube voltage, 120 kV; tube current, 250-300 mA; and

**Main points**

- Endophytic clear cell renal cell carcinoma (ECCRCC) and endophytic renal urothelial carcinoma (ERUC) have different computed tomographic (CT) characteristics and clinical features.
- ECCRCC can be distinguished from ERUC by using CT characteristics and clinical data.
- A predictive model may improve the differential diagnosis of ECCRCC and ERUC.

![Figure 1. Flowchart for inclusion and exclusion of patients. ccRCC, clear cell renal cell carcinoma; CT, computed tomography; RCC, renal cell carcinoma; RUC, renal urothelial carcinoma; UC, urothelial carcinoma.](image-url)
slice thickness, 5 mm. After the abdominal plain scan, a contrast agent (Iopamiro, 300 mgI/mL; Shanghai Bracco Sine Pharmaceutical Corp. Ltd.) was injected using a high-pressure syringe around the median cubital vein, with an injection flow rate of 3 mL/s. Contrast-enhanced CT scans were performed at 25-30 seconds (renal cortex phase), 75-85 seconds (NP), and 210-280 seconds (EP).

**Imaging analysis**

All CT images were obtained from the PACS of our hospital (Shenzhen Annet Information System Co. Ltd). The maximum tumor diameter was measured only in the axial direction. The CT features analyzed included the location, size, infiltrative growth pattern, renal calculi, hydronephrosis, necrosis, and enhancement pattern. ccRCC with CSI was defined as follows according to Karlo et al.\(^2\): a tumor causing a filling defect in the EP, a tumor in contact with the collecting system on the CT image, and/or a tumor separated from the collecting system. Renal urothelial carcinoma (RUC) mimicking RCC was defined as a UC that was difficult to diagnose as a renal pelvic carcinoma via CT urography, which is the method of choice for imaging-based diagnosis of upper urinary tract UC according to the European Association of Urology Guidelines.\(^3\)

As described by Gervais et al.,\(^2\) we defined endophytic renal tumors as the tumors centrally located in the renal pelvis. Necrosis was defined as areas of low attenuation or non-enhancement in the tumor that was not sharply demarcated and lacked apparent walls, according to Shinagare et al.\(^24\)

As described by Dyer et al.,\(^25\) we defined solid renal mass infiltrative growth patterns as bean-shaped (tumor infiltrative growth using renal parenchyma as scaffold) and ball-shaped (dominant tumor expansion growth). Hyperenhancement and hypoenhancement were defined as ≥70 Hounsfield units (HU) or 20-40 HU of absolute enhancement, respectively, in the CP.\(^21\)

We used the definition of Pano et al.\(^26\) for heterogeneous/homogeneous enhancement, that is, tumors with non-enhancing or low-attenuation areas were described as heterogeneous, and tumors that enhanced uniformly were described as homogeneous, throughout the visual assessment in the soft-tissue window. Referring to the report by Jung et al.,\(^27\) we set the window width to 300 and the window level to 40. Heterogeneous/homogeneous enhancement was visually assessed with the same window settings (Figure 2). In every patient, as per Bata et al.,\(^10\) we defined endophytic renal tumors as the tumors centrally located in the renal pelvis. Necrosis was defined as areas of low attenuation or non-enhancement in the tumor that was not sharply demarcated and lacked apparent walls, according to Shinagare et al.\(^24\)

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Clinical data and CT features of ECCRCC and ERUC are summarized in Supplementary Tables 3 and 4, respectively. Subsequently, variables with statistically significant differences were evaluated using the receiver operating characteristic (ROC) curve analysis. The cutoff value was determined by calculating the maximum Youden index. Variables in the ROC curve analysis with an area under the curve (AUC) < 0.7 (low accuracy) were excluded, according to Swets.28 Next, the variables with statistically significant differences were analyzed using univariate logistic regression for associations with ERUC or ECCRCC. We assigned values for variables before we commenced logistic regression analysis (Supplementary Table 5). Then, we attempted to avoid over-fitting the ROC curve of the predictive model by excluding variables with odds ratios close to 1 (reflecting a weak association) from the multivariate logistic regression analysis.29–31 The rest of the variables were analyzed using multivariate logistic regression. Statistically significant variables (independent predictors) were used in the multivariate logistic regression analysis to construct the predictive model (Supplementary Equation 1).22 A Hosmer–Lemeshow test was used to assess the statistical significance of the model. Ultimately, ROC curves were drawn based on the independent predictors and the predictive model to evaluate and compare the diagnostic performance of CT characteristics and clinical features for ERUC and ECCRCC. Statistical significance was set at $P < .05$.

Results

All kappa and intraclass correlation coefficient values were >0.8 (Supplementary Tables 1 and 2; hence, there was excellent agreement between the 2 readers. All continuous variables were non-normally distributed, except for the UP.

Results of the clinical characteristics are summarized in Supplementary Table 3. This study included 44 patients with ECCRCC (with CSI) (35 men and 9 women) and 21 patients with ERUC (mimicking RCC) (17 men and 4 women). No significant difference was found between sex, smoking history, and history of kidney stones among the groups ($P = .193$, and $P = .214$, respectively). The median patient age was 55 years (48.25–59.50 years) and 68 years (63.00–73.00 years) in the ECCRCC and ERUC groups, respectively ($P < .001$). The frequency of flank pain differed ($P = .034$) between the ECCRCC (17 patients, 38.64%) and ERUC (14 patients, 66.67%) groups.

The distribution of hematuria classification also differed ($P < .001$) between ECCRCC (8 [18.18%] with gross hematuria and 9 [20.45%] with microscopic hematuria) and ERUC (14 [66.67%] with gross hematuria and 4 [19.05%] with microscopic hematuria) groups.

Results of CT features are summarized in Supplementary Table 4. No differences were observed among the side, preserving reniform contour, perinephric stranding, calcification, renal vein invasion, lymphatic node metastasis, and distant metastasis between the groups ($P = .386$, $P = .993$, $P = .095$, $P = .133$, $P = .180$, $P = .200$, and $P = .200$, respectively). The median tumor size was 43.20 cm (32.70–68.70 cm) and 44.37 cm (33.32–59.20 cm) between the groups, respectively ($P = .768$). The mean UP CT values were $36.67 \pm 6.02$ HU and $36.25 \pm 3.68$ HU in ERCCCs and ERUCs, respectively ($P = .063$). The infiltrative growth pattern differed ($P < .001$) between the ECCRCC (18 tumors [40.91%] with a bean shape and 26 [59.09%] with a ball shape) and ERUC (19 tumors [90.48%] with a bean shape and 2 [9.52%] with a ball shape) groups. The pseudo-capsule sign was more common ($P = .002$) in the ECCRCC group (22 patients, 50.00%) than in the ERUC group (2 patients, 9.52%). Hydronephrosis was less common ($P = .003$) in the ECCRCC group (9 patients, 20.45%) than in the ERUC group (12, 57.14%). The extent of necrosis differed ($P = .015$) between ECCRCC (17 patients [38.64%] with extensive necrosis and 17 [38.64%] with local necrosis) and ERUC (1 patient [4.76%] with extensive necrosis and 14 [66.67%] with local necrosis) groups. Renal calculi ($P = .019$) were less common in the ECCRCC group (n = 5, 11.36%) than in the ERUC group (n = 8, 38.10%). Heterogeneous enhancement ($P < .001$) was more common in the ECCRCC group (n = 36, 81.82%) than in the ERUC group (n = 6, 28.57%; CP [P < .001], NP [P < .001], and EP [P = .002]). The median CT value of ECCRCC in each phase of enhancement...
(103.07 HU [82.6-126.08 HU], 94.76 HU [79-110.76 HU], and 73.70 HU [66.74-87.54 HU]) was significantly higher (P < .001, P < .001, and P = .002) than that of ERUC group (62.59 [54.64-66.7], 77.94 [65.76-79.68], and 64.75 [58.43-73.49]). The ECCRCC group was prone to exhibit hyperenhancement in the CP (Figures 2a and 6). The ERUC group was prone to hypoenhancement in the CP (Figures 2b, 3, and 5), while the ERUC group was more prone to infiltrative growth in the renal parenchyma as well as hydronephrosis and renal calculus. On the other hand, the ECCRC group more commonly exhibited heterogeneous enhancement, the pseudo-capsule sign, and necrosis (Figures 2b, 3, and 5).

In the multivariate logistic regression analysis, we did not include necrosis (P = .54), flank pain (P = .069), or renal calculi (P = .083) as they did not exhibit statistically significant differences upon ROC curve analysis. Next, hydronephrosis (AUC = 0.683, P = .017) was also excluded because its AUC < 0.7 (Table 1). Then, age (OR = 0.894, 95% CI: 0.839-0.953, P = .001), CP (OR = 1.142, 95% CI: 1.062-1.229, P < .001), NP (OR = 1.095, 95% CI: 1.039-1.155, P = 0.001), and EP (OR = 1.098, 95% CI: 1.028-1.173, P = .005) were excluded since their OR values being close to 1. The logistic regression results are presented in Table 2. Ultimately, heterogeneous enhancement, hematuria, infiltrative growth pattern, and the pseudo-capsule sign were included in the multivariate logistic regression analysis (Table 2). The independent predictors of ECCRC including heterogeneous enhancement (OR = 0.027, 95% CI: 0.002-0.342, P = .005), hematuria (for gross hematuria, OR = 53.995, 95% CI: 3.987-731.168, P = .003; for microscopic hematuria, OR = 31.126, 95% CI: 1.490-650.085, P = .027), and infiltrative growth pattern (OR = 24.301, 95% CI: 1.586-372.402, P = .022) (Table 2) were used to construct the predictive model (model-1). According to Supplementary Table 6, the probabilistic predictive value is 

\[ P = 1/(1 + e^{- (3.831 \text{ gross hematuria} + 3.206 \text{ microscopic hematuria} + 2.783 \text{ infiltrative growth pattern} - 3.416 \text{ heterogeneous enhancement})}). \]

The Hosmer–Lemeshow test revealed that the fitting equation of the model did not differ (P = .940) from the real equation. The ROC curves of heterogeneous enhancement (AUC = 0.766, sensitivity = 81.82%, specificity = 71.43%, P = .001), hematuria (AUC = 0.786, sensitivity = 81.82%, specificity = 66.67%, P < .001), the infiltrative growth pattern (AUC = 0.748, sensitivity = 90.48%, specificity = 59.09%, P = .001), and model-1

**Table 1. ROC analysis results of clinical and CT features for diagnosis of ECCRC**

| Variables             | Cutoff | AUC   | SE    | P      | Sensitivity | Specificity | 95% CI   |
|-----------------------|--------|-------|-------|--------|-------------|-------------|---------|
| Hematuria             | 1.500  | 0.786 | 0.062 | <.001  | 66.67       | 81.82       | 0.665-0.907 |
| Heterogeneous enhancen | 0.500  | 0.766 | 0.069 | .001   | 81.82       | 71.43       | 0.635-0.898 |
| Infiltrative growth pattern | 0.500  | 0.748 | 0.063 | .001   | 90.48       | 59.09       | 0.626-0.869 |
| Pseudo-capsule        | 0.500  | 0.702 | 0.067 | .009   | 50.00       | 90.48       | 0.574-0.831 |
| Hydronephrosis        | 0.500  | 0.683 | 0.076 | .017   | 57.14       | 79.55       | 0.538-0.829 |
| Necrosis              | 1.500  | 0.649 | 0.068 | .054   | 38.64       | 95.24       | 0.516-0.782 |
| Flank pain            | 0.500  | 0.640 | 0.080 | .069   | 66.67       | 61.36       | 0.496-0.785 |
| Calculus              | 0.500  | 0.634 | 0.075 | .083   | 38.10       | 88.64       | 0.481-0.787 |
| CP                    | 74.950 | 0.936 | 0.030 | <.001  | 86.36       | 95.24       | 0.876-0.995 |
| NP                    | 80.150 | 0.813 | 0.053 | <.001  | 72.73       | 80.95       | 0.711-0.915 |
| EP                    | 66.350 | 0.742 | 0.064 | .002   | 79.55       | 60.00       | 0.617-0.867 |
| Age                   | 62.500 | 0.793 | 0.067 | <.001  | 81.00       | 84.10       | 0.666-0.922 |
| Model-1               | 0.878  | 0.938 | 0.031 | <.001  | 84.10       | 95.20       | 0.877-0.999 |

ROC, receiver operating characteristic; CT, computed tomography; ECCRC, endophytic clear cell renal cell carcinoma; AUC, area under the receiver operating characteristic curve; SE, standard error; CI, confidence interval; CP, corticomedullary phase; NP, nephrogenic phase; EP, excretory phase; model-1 = 1/(1 + e^(- (3.831 \text{ gross hematuria} + 3.206 \text{ microscopic hematuria} + 2.783 \text{ infiltrative growth pattern} - 3.416 \text{ heterogeneous enhancement})).
(AUC = 0.938, sensitivity = 84.10%, specificity = 95.20%, P < .001) were presented (Table 1) (Figure 4).

**Discussion**

The reported incidence of CSI in RCC is 3%-14%. To the best of our knowledge, the incidence of CSI has not been reported specifically in ccRCC. In our study, the incidence of CSI in ccRCC was approximately 46.54% (289/621) and that of ECCRCC among ccRCCs was approximately 15.22% (44/289). Endophytic renal neoplasms are different from those present in CSI. ECCRCC is one of the ccRCCs included with CSI, although most CSIs are exophytic tumors. Tumors that are centrally located in the renal pelvis are usually urothelial neoplasms, especially UC. In this study, the incidence of RUC among all the cases of UC was approximately 14.08% (165/1172), while the incidence of ERUC among all cases of RUC was approximately 12.73% (21/165). Previous reports of the CT features of RUC did not include flowcharts depicting the selection of the patients.

The description and characteristics of ERUC cases in the present study differed in certain ways from those in previous studies. In the present ERUC cases, renal calculi and hydronephrosis were recorded, which were not mentioned in 3 previous reports and were reported only as unusual imaging manifestations by Prando et al. Zhu et al. reported a few RUCs with necrosis, whereas Raza et al. did not mention the number of necrosis. Moreover, we
observed higher incidence of flank pain and hematuria in the present cases of ERUC as compared to that of previous reports. These differences may be attributable to the study populations, including the difference in lifestyle factors. Another reason may be the larger size of UC cases in our study compared to others.

In our study, heterogeneous enhancement, hematuria, and the infiltrative growth pattern were independent predictors of ECCRCC vs. ERUC. The predictive model was able to distinguish ECCRCC from ERUC; a diagnosis of ERUC was more likely with homogeneous enhancement, hematuria, and an infiltrative growth pattern (Table 2) (Figure 4). In this study, ECCRCC (Figures 2b, 5) was more susceptible to a distinct heterogeneous enhancement than ERUC (Figures 2a, 6), which was consistent with previous reports. This may be caused by the rich blood supply and susceptibility to hemorrhage and necrosis in ECCRCCs. A larger cRCC is reportedly prone to necrosis and heterogeneous enhancement. Furthermore, our clinical data revealed that patients with ERUC were more susceptible to hematuria (both gross and microscopic) than those with ECCRCC. Intermittent microscopic hematuria may be missed upon clinical examination. Additionally, a bean shape and a ball shape corresponded to the patterns of mass infiltrative growth and expansive growth in the renal parenchyma, respectively. ERUC tended to invade the renal parenchyma with an infiltrative growth pattern (Figure 6), whereas ECCRCC tended to expand in an expansive growth pattern in the renal parenchyma (Figure 5), similar to previous findings.

Although age, CP, NP, EP, and the pseudo-capsule sign were excluded from the predictive model, they may be of some assistance in the differentiation of ECCRCC from ERUC during a clinical examination. Similar to previous reports, patients with ECCRCC in this study were younger than those with ERUC. Shariat et al. reported a peak incidence of upper urinary tract UC in individuals aged 70-90 years. In the study by Bata et al., the attenuation of cRCC was significantly higher than that of RUC in CP and NP. However, in our study, the attenuation of ECCRCC was significantly higher than that of ERUC for each phase of CT dynamic contrast-enhanced scanning. The hyperenhancement of ECCRCC and the hypoenhancement of ERUC in the CP may be attributed to the hypervascular nature of ECCRCC and the hypovascular nature of ERUC. In addition, 2 patients with ERUC in our study exhibited pseudo-capsule signs (Figure 7), which has not been reported before. However, the pseudo-capsule sign in patients with ERUC differed from that in patients with ECCRCC (Figure 5a and c). The former was the compression of renal pelvis fat, while the latter was the separation of fibrous tissue after compression, leading to ischemic necrosis.

Our study has certain limitations. First, we analyzed and compared the clinical and CT characteristics of patients with ERUC and ECCRCC only, without investigating other RCC subtypes. Second, although this study included a larger sample of patients with ECCRCC and ERUC than that in previous studies, the sample size remains small, which would inevitably lead to statistical bias. Further studies with larger samples are required to validate the results of our study. Third, our study considered the diagnosis only, not the prognosis.

In brief, our predictive model, which incorporates CT and clinical characteristics, may assist in the differential diagnosis of ECCRCC and ERUC. Endophytic renal tumors with an expansive growth pattern, distinct heterogeneous enhancement, and no hematuria may be considered ECCRCC. Moreover, cases in which patients are younger and exhibit hyperenhancement and the pseudo-capsule sign should be more supported for consideration as ECCRCC.

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Conflict of interest disclosure
The authors declared no conflicts of interest.

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### Supplementary Table 1. Inter-rater agreement of the 2 readers as measured by intraclass correlation coefficient

| Characteristics | ICC     | 95% CI       | P        |
|-----------------|---------|--------------|----------|
| Size            | 0.935   | 0.910-0.966  | .009     |
| UP              | 0.834   | 0.776-0.878  | <.001    |
| CP              | 0.851   | 0.801-0.892  | <.001    |
| NP              | 0.881   | 0.593-0.969  | <.001    |
| EP              | 0.927   | 0.883-0.955  | <.001    |

ICC, intraclass correlation coefficient; UP, unenhanced phase; CP, corticomedullary phase; NP, nephrographic phase; EP, excretory phase.

### Supplementary Table 2. Inter-rater agreement of the 2 readers as measured by kappa statistics

| Characteristics               | Kappa | 95% CI       | P        |
|-------------------------------|-------|--------------|----------|
| Infiltrative growth pattern   | 0.844 | 0.713-0.975  | <.001    |
| Pseudo-capsule sign           | 0.863 | 0.734-0.992  | <.001    |
| Preserving reniform contour   | 0.815 | 0.674-0.956  | <.001    |
| Perinephric stranding         | 0.851 | 0.710-0.992  | <.001    |
| Hydronephrosis                | 0.930 | 0.834-1.000  | <.001    |
| Necrosis                      | 0.928 | 0.848-1.000  | <.001    |
| Heterogeneous enhancement     | 0.833 | 0.694-0.972  | <.001    |
| Calcification                 | 0.920 | 0.812-1.000  | <.001    |
| Renal calculus                | 0.909 | 0.786-1.000  | <.001    |
| Renal vein invasion           | 0.860 | 0.707-1.000  | <.001    |
| Lymphatic metastasis          | 0.858 | 0.666-1.000  | <.001    |
| Distant metastasis            | 0.840 | 0.622-1.000  | <.001    |

### Supplementary Table 3. Clinical characteristics of patients with ECCRC and ERUC

| Characteristics                  | ECCRC (n = 44) | ERUC (n = 21) | P     |
|----------------------------------|----------------|---------------|-------|
| **Median (range)/n (%)**         |                |               |       |
| Sex                              |                |               |       |
| Male                             | 35 (79.55)     | 17 (80.95)    | 1.000 |
| Female                           | 9 (20.45)      | 4 (19.05)     |       |
| Age (years)                      | 55 (48.25-59.50) | 68 (63.00-73.00) | <.001 |
| Smoking history                  | 12 (27.27)     | 6 (28.57)     | .913  |
| Flank pain                       | 17 (38.64)     | 14 (66.67)    | .034  |
| History of kidney stones         | 8 (18.18)      | 7 (33.33)     | .214  |
| Hematuria                        |                |               |       |
| Gross hematuria                  | 8 (18.18)      | 14 (66.67)    | <.001 |
| Microscopic hematuria            | 9 (20.45)      | 4 (19.05)     |       |

ECCRC, endophytic clear cell renal cell carcinoma; ERUC, endophytic renal urothelial carcinoma.
Supplementary Equation 1. Equation of the prediction model.

\[
\text{Logit}(p) = \ln\left(\frac{p}{1-p}\right)
\]

\(p\), the probabilistic predictive value

**Supplementary Table 4.** CT characteristics of patients with ECCRCC and ERUC

| Characteristics                        | ECCRCC (n = 44) | ERUC (n = 21) | \(P\) |
|----------------------------------------|-----------------|---------------|-------|
| **Side, n (%)**                        |                 |               |       |
| Left                                   | 28 (63.64)      | 11 (52.38)    | .386  |
| Right                                  | 16 (36.36)      | 10 (47.62)    |       |
| **Size (cm)**                          | 43.20 (32.70-68.70) | 44.37 (33.32-59.20) | .768  |
| Preserving reniform contour            | 21 (47.73)      | 10 (47.62)    | .993  |
| Perinephric stranding                  | 10 (22.73)      | 9 (42.86)     | .095  |
| **Infiltrative growth pattern**        |                 |               |       |
| Bean shape                             | 18 (40.91)      | 19 (90.48)    | <.001 |
| Ball shape                             | 26 (59.09)      | 2 (9.52)      |       |
| **Pseudo-capsule sign**                | 22 (50.00)      | 2 (9.52)      | .002  |
| Hydronephrosis                         | 9 (20.45)       | 12 (57.14)    | .003  |
| **Necrosis**                           |                 |               |       |
| Extensive (\(\geq 50\%\))             | 17 (38.64)      | 1 (4.76)      | .009  |
| Local (\(< 50\%\))                    | 17 (38.64)      | 14 (66.67)    |       |
| **Heterogeneous enhancement**          | 36 (81.82)      | 6 (28.57)     | <.001 |
| Calcification                          | 14 (31.82)      | 3 (14.29)     | .133  |
| Renal calculus                         | 5 (11.36)       | 8 (38.10)     | .019  |
| Renal vein invasion                    | 6 (13.64)       | 6 (28.57)     | .180  |
| Lymphatic node metastasis              | 3 (6.82)        | 4 (19.05)     | .200  |
| **Distant metastasis**                 | 3 (6.82)        | 4 (19.05)     | .200  |
| **UP (HU)**                            | 36.67 ± 6.02    | 36.25 ± 3.68  | .063  |
| **CP (HU)**                            | 103.07 (82.6-126.08) | 62.59 (54.64-66.7) | <.001 |
| **NP (HU)**                            | 94.76 (79-110.76) | 77.94 (65.76-79.68) | <.001 |
| **EP (HU)**                            | 73.70 (66.74-87.54) | 64.75 (58.43-73.49) | .002  |

CT, computed tomography; ECCRCC, endophytic clear cell renal carcinoma; ERUC, endophytic renal urothelial carcinoma; SD, standard deviation; UP, unenhanced phase; HU, Hounsfield units; CP, corticomedullary phase; NP, nephrogenic phase; EP, excretory phase.

**Supplementary Table 5.** Variable assignments before logistic regression analysis

| Assignment | Tumor   | HE     | Hematuria | IGP     | PcS     | Hydronephrosis | Necrosis | RC | FP |
|------------|---------|--------|-----------|---------|---------|----------------|----------|----|----|
| 2          | GH      |        | EN        |         |         |                |          |    |    |
| 1          | ECCRCC  | Yes    | MH        | Bean shape | Yes    | Yes            | LN       | Yes| Yes|
| 0          | ERUC    | No     | No        | Ball shape | No     | No             | No       | No | No |

HE, heterogeneous enhancement; IGP, infiltrative growth pattern; PcS, pseudo-capsule sign; RC, renal calculus; FP, flank pain; ECCRCC, endophytic clear cell renal cell carcinoma; GH, gross hematuria; EN, extensive necrosis; MH, microscopic hematuria; LN, local necrosis; ERUC, endophytic renal urothelial carcinoma.

**Supplementary Table 6.** Multivariable logistic regression analyses (construction of the prediction model) of CT findings and clinical data for differentiation of ECCRCC and ERUC

|                      | \(\beta\) | \(P\)  | OR        | 95% CI     |
|----------------------|-----------|--------|-----------|------------|
| Heterogeneous        | -3.416    | .004   | 0.033     | 0.003-0.330|
| growth pattern       | 2.783     | .008   | 16.171    | 2.083-125.527|
| Gross hematuria      | 3.831     | .002   | 46.120    | 3.959-537.244|
| Microscopic hematuria| 3.206     | .023   | 24.671    | 1.553-391.852|
| Constant             | -0.698    | .334   | 0.498     |            |

CT, computed tomography; ECCRCC, endophytic clear cell renal cell carcinoma; ERUC, endophytic renal urothelial carcinoma.