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Accuracy of Contrast-enhanced CT in Diagnosing Small-sized cT3a Renal Cell Carcinoma and Analysis of Factors Predicting Downstaging to pT1

KENSUKE BEKKU, KASUMI YOSHINAGA, SHOTA INOUE, YOSUKE MITSUI, TOMOAKI YAMANOI, TATSUSHI KAWADA, YUSUKE TOMINAGA, TAKUYA SADAHIRA, SATOSHI KATAYAMA, TAKEHIRO IWATA, SHINGO NISHIMURA, KOHEI EDAMURA, TOMOKO KOBAYASHI and MOTOO ARAKI

Department of Urology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan

Abstract

Background/Aim: This study assessed the accuracy of preoperative contrast-enhanced computed tomography (CECT) scans in staging small-sized, locally advanced (cT3a) renal cell carcinoma (RCC) and identified predictors of pathological downstaging following surgery.

Patients and Methods: Seventy-six patients who underwent radical nephrectomy for cT3aN0M0 RCC with tumors ≤7 cm were analyzed. Preoperative CECT evaluated features such as venous, peritumoral, or renal sinus fat, and urinary tract invasion, predictive values, and concordance index between radiological and pathological findings were calculated for these categories. The study also examined the impact of clinicopathologic factors on downstaging.

Results: Of 76 patients with cT3 RCC, 37% were down-staged to pT1. Down-staged cases had a higher proportion of male patients and non-clear cell carcinoma (86% *vs*. 58%, 32% *vs*. 6%; p=0.02, p=0.007, respectively). Multiple cT3a factors were less common in down-staged cases (4% *vs*. 23%, p=0.04). Non-clear cell carcinoma was significantly associated with downstaging compared to clear cell carcinoma (75% *vs*. 30%, p=0.006). Multivariate analysis confirmed non-clear cell carcinoma as an independent predictor (odds ratio=8.2, p=0.01). For venous invasion, CECT sensitivity and positive predictive value were high (73.5% and 83.3%, respectively) and the degree of agreement was substantial (κ=0.62).

Conclusion: The accuracy of preoperative CECT was acceptable for detecting venous invasion. The downstaging to pT1 occurred in 37% of cT3a RCC cases in the final pathology, with non-clear cell carcinoma being a significant predictor.

Keywords: Contrast-enhanced CT, renal cell carcinoma, staging, T3a, downstaging.

Kensuke Bekku, 2-5-1, Shikata-chou, Kita-ku, Okayama city, Okayama, Japan. Tel: +81 862357287, Fax: +81 862313986, e-mail: gmd421030@s.okayama-u.ac.jp

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Introduction

Renal cell carcinoma (RCC) is the most common renal malignant tumor in adults and the incidental detection of localized RCC has increased with the widespread use of imaging (1-3). Partial nephrectomy (PN) is recommended when technically feasible for small-sized RCCs, especially cT1 tumors (smaller than 7 cm), as it provides comparable oncological outcomes to radical nephrectomy while preserving kidney function more effectively (1, 4). The advent of novel technologies, such as robot-assisted surgery, has further enabled surgeons to perform nephron-sparing surgeries with greater precision. Consequently, more challenging tumors, such as hilar or large-sized tumors, are now being considered for PN. However, approximately 5-10% of patients who undergo PN experience upstaging from clinical T1 (cT1) to pathological T3a (pT3a) (2), which is associated with poorer prognoses compared to cases without upstaging (3). Thus, the accurate assessment of the clinical T stage is essential when deciding whether to proceed with nephron-sparing surgery.

Contrast-enhanced computed tomography (CECT) scans are commonly used for clinically staging localized renal cancers and are considered effective (5). Nevertheless, several studies have highlighted challenges in accurately diagnosing T3a disease (6-8).

This study aimed to evaluate the accuracy of CECT in diagnosing cT3a RCC smaller than 7cm and to identify factors associated with downstaging following radical nephrectomy for small-sized cT3a RCC.

Patients and Methods

Study's design. This study was approved by the Ethical Committee of Okayama University Hospital (Registration number: 2406-007). After approval, the data of patients who underwent radical nephrectomy for cT3a RCC were retrospectively collected from the medical records and assessed. The primary objective was to assess the accuracy of preoperative CTCE, including the sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), and concordance index of each cT3a category. The secondary objective was to identify the factors predicting downstaging from cT3a to pT1.

Inclusion and exclusion criteria. Patients with small-sized (tumor diameters <7 cm) but clinically advanced (cT3a) renal cancer who underwent radical nephrectomy at Okayama University Hospital between January 2015 and March 2024 were enrolled. All patients underwent CECT scans for clinical staging. Patients were excluded if they had distant metastases at the surgery, tumors measuring ≥7 cm in diameter on the axial plane, gross tumor thrombus in the main renal veins, or pathologically benign and malignant tumors other than RCC.

Data collection. The clinical stage was classified according to the TNM 2017 classification system (9). For the patients who underwent the surgery before the latest classification, the pathological stages were reclassified according to the latest classification. Clinicopathological data except for the cT3a factors, including age, sex, tumor size, tumor side, tumor location, the RENAL nephrometry score, the type and presence of multiple cT3a factors, pathological subtypes, pathological T stage, and nuclear grades, were collected.

Diagnoses of cT3a. Individual radiologists at our hospital suggested clinical staging based on CECT scans and the stages were confirmed in the conference of urologists. When necessary, a multidisciplinary conference involving radiologists and urologists was held to determine the clinical stage. Subsequently, two urologists reviewed the CT scans to confirm the following findings, which served as evidence of cT3a: *Peritumoral fat invasion:* Presence of one or more of the following: thickened perinephric fascia, increased perinephric vascularity, or perinephric stranding with high CT attenuation values (Figure 1A). i) *Sinus fat invasion:* Small hyperdense strands surrounding the lesion, indicating infiltration of the sinus fat (Figure 1B). ii) *Venous invasion:* Presence of one or more of the following: filling defects in the branches of the intrarenal veins adjacent to the tumor edge, venous dilation adjacent

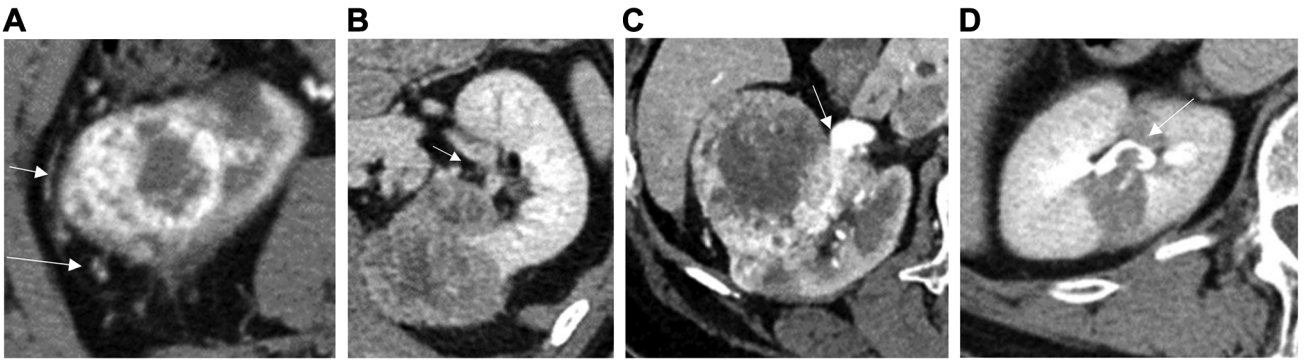

Figure 1. *Representative image of each factor on contrast-enhanced computed tomography A) Peritumoral fat invasion: The thickness of Gerota fascia (short arrow) and neo-vessels (long arrow) surrounding the tumor. B) Sinus fat invasion: small hyperdense strands surrounding the tumor (arrow). C) Venous invasion: a filling defect in the intrarenal vein, and the dilation of the vein adjacent to the tumor (arrow). D) Urinary tract invasion: a filling defect in the urinary tract (arrow).*

to the tumor, or venous tumor thrombus in the intrarenal veins with enhancement (Figure 1C). iii) *Urinary tract invasion:* Filling defects in the urinary tract (Figure 1D).

Additionally, irregular tumor types, characterized by multiple nodule formations and irregular edges, were identified as potential factors predicting local invasion (10) (Figure 2).

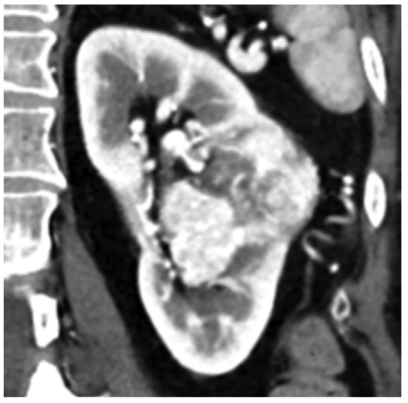

Figure 2. *Representative image of the irregular type of tumor shape: the multiple nodules with irregular edges.*

Statistical analysis. All statistical analyses were conducted using EZR ver. 1.52 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) (11). Continuous valuables were analyzed using the Mann-Whitney *U*-test, and categorized valuables were analyzed using Fisher's exact and chi-square tests. Uni- and Multivariate logistic regression models were used to detect the factors that predicted downstaging. *p*-Value <0.05 indicated significant difference. In addition, the sensitivity, specificity, PPV, and NPV of each cT3a factor were calculated. The concordance between radiological and pathological T stages was assessed utilizing κ statistics. The grade of concordance was defined as almost perfect for value of 0.8-1.0, substantial for 0.6-0.79, moderate for 0.4-0.59, and fair for <0.4 (6).

Results

A total of 90 patients with cT3a RCC underwent radical nephrectomy during the study period. Fourteen patients with distant metastases and/or 7 cm or larger tumor and/or gross tumor thrombus in the main renal veins were excluded. Finally, 76 patients were enrolled and pathological findings obtained following the surgery revealed that 30 (39%) tumors had venous invasion, 13 (17%) sinus fat invasions, five (7%) peritumoral fat invasions, and three (4%) urinary tract invasions. Sensitivity for identifying peritumoral fat, renal sinus fat, venous, and urinary tract invasion were 66.7%, 40.0%, 73.5%, and 60.0%, respectively. Specificity for the same categories were 91.8%, 86.4%, 88.1%, and 52.1%, respectively. The PPVs of preoperative CT for peritumoral fat, renal sinus fat, venous, and urinary tract invasion

Table I. *The number and rate of patients with downstaging and pathological findings for each cT3a factor.*

	Downstage	Ppf	Psf	Pv	Pu
Rpf: n=8	5 (62.5%)	2 (25.0%)	0 (0.0%)	2 (25.0%)	0 (0.0%)
Rsf: n=13	1 (7.7%)	1 (7.7%)	4 (30.8%)	6 (46.2%)	2 (15.4%)
Rv: n=30	3 (10.0%)	1 (3.3%)	1 (3.3%)	25 (83.3%)	0 (0.0%)
Ru: n=37	20 (54.1%)	1 (2.7%)	6 (16.2%)	9 (24.3%)	3 (8.1%)

Rpf: Radiological peritumoral fat invasion; Rsf: radiological sinus fat invasion; Rv: radiological venous invasion; Ru: radiological urinary tract invasion; Ppf: pathological peritumoral fat invasion; Psf: pathological sinus fat invasion; Pv: pathological venous invasion; Pu: pathological urinary tract invasion.

Table II. *Comparison of patient characteristics between downstaged and non-downstaged groups.*

	Downstaged N=28	Non-downstaged N=48	*p*-Value
Age	68 (IQR=58-74)	73 (IQR=62-78)	0.08
Sex (male *vs.* female)	24 *vs.* 4 (86% *vs.* 14%)	28 *vs.* 20 (58% *vs.* 42%)	0.02
Laterality (right *vs.* left)	14 *vs.* 14 (50% *vs.* 50%)	24 *vs.* 24 (50% *vs.* 50%)	1
Tumor size, mm	47 (IQR=33-54)	44 (IQR=34-52)	0.8
RENAL score >9	11 (39%)	27 (56%)	0.2
Clear cell subtype	19 (68%)	45 (94%)	<0.01
Location (a: p: x)	5 *vs.* 9 *vs.* 14 (18% *vs.* 32% *vs.* 50%)	16 *vs.* 16 *vs.* 16 (33% *vs.* 33% *vs.* 33%)	0.3
Multiple factors	1 (4%)	11 (23%)	0.047
Irregular type	15 (54%)	31 (65%)	0.15

IQR: Interquartile range.

were 25.0%, 30.8%, 83.3%, and 8.1%, respectively. The NPVs of the same categories were 98.5%, 90.5%, 80.4%, and 94.9%, respectively. Stratified by the cT3a features, the down-staged rate was 7.7% in patients radiographically suspected of having sinus fat invasion, 10.0% in those suspected of venous invasion, 62.5% in those suspected of peritumoral fat invasion, and 54.1% in those suspected of urinary tract invasion (Table I). Analysis of radiological and pathological agreement demonstrated substantial agreement in venous invasion (κ=0.62), while fair agreement was demonstrated in peritumoral fat, sinus fat, and urinary tract (κ=0.32, 0.23, and 0.03, respectively).

Out of 76 patients, 28 (37%) were down-staged to pT1. Compared to the non-down-staged group (n=48), the down-staged group had a higher proportion of male patients and non-clear cell carcinoma (86% *vs*. 58%; p=0.02, 32% *vs.* 6%; p=0.007, respectively), and a significantly lower proportion of patients with multiple cT3a factors (4% *vs.* 23%, p=0.04). No significant differences were observed in the proportion of high RENAL nephrometry score (≥10) and of irregular-type tumors between the two groups (39% *vs*. 56%, p=0.23, 54% *vs*. 65%, p=0.15, respectively). There was a significant difference in the occurrence of downstaging between clear cell carcinoma and non-clear cell subtype (30% *vs.* 75%, p=0.006) (Table II). Univariate analysis identified male sex and non-clear cell carcinoma as significant predictors of downstaging [odds ratio (OR)=4.29, 95% confidence interval (CI)=1.29-14.3, p=0.02; and OR=7.11, 95%CI=1.73-29.3, p=0.007, respectively]. Multivariate analysis identified non-clear cell carcinoma as a significant

Table III. *The results of uni- and multivariate logistic regression models to predict downstaging.*

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% confidence interval)	*p*-Value	Odds ratio (95% confidence interval)	*p*-Value
Age	0.62 (0.93-1.01)	0.3		
Male sex	4.29 (1.29-14.3)	0.02		
Size >4 cm	1.01 (0.39-2.63)	1	2.37 (0.7-8.03)	0.16
RENAL score <9	1.99 (0.77-5.13)	0.16	2.82 (0.87-9.17)	0.09
Non-clear cell	7.11 (1.73-29.2)	<0.01	8.21 (1.67-40.3)	0.01
Multiple factors	0.13 (0.02-1.02)	0.05	0.19 (0.02-1.61)	0.13
Irregular type	0.48 (0.18-1.23)	0.13		

predictor of downstaging (OR=8.2, 95%CI=1.7-40.3, *p*=0.01) (Table III). Among 12 patients with non-clear cell subtypes, chromophobe RCC was the most common subtype (n=4), followed by papillary RCC (n=3), acquired cystic disease-associated RCC (n=3), unclassified RCC (n=1), and transcription factor E3 (TFE3) rearranged RCC (n=1). Eleven out of 12 were suspected of urinary tract invasions on the preoperative CT scans, however, only one patient with papillary RCC revealed invasion to the urinary tract and the other one with TFE3 rearranged RCC had a venous invasion.

Discussion

The advent of novel surgical technologies, such as robotic surgical systems, has enabled surgeons to perform more challenging procedures, including PN (3). According to the EAU guidelines, PN for pT3a RCC is reasonable when technically feasible, as it could provide comparable oncological outcomes and better kidney function preservation than radical nephrectomy for pT3a cases (4, 12, 13). Clinical stages T1 and T2 are defined based on tumor size, with larger tumors indicating more advanced stages. For renal tumors measuring 7 cm or larger, the feasibility and safety of PN are still under debate (4). Therefore, this study focused on tumors smaller than 7 cm. Although the PPVs of the factors evaluated in this study may be low, the observed rate of mis-staging (37%) is comparable to previous studies. Renard *et al.* reported a 27% downstaging rate in 62 renal cancers with a median tumor size of 43 mm (range=10-150 mm) (14). Similarly, Ucer *et al.* analyzed 3,309 renal cancers and investigated the accuracy of imaging modalities, including CT and magnetic resonance imaging (MRI), revealing sensitivity values for stage III, perinephric fat invasion, and renal vein invasion of 27.7%, 15.4%, and 11.3%, respectively (15). These findings underscore that accurate staging remains a challenge across all stages of renal cancer.

cT3a renal cancers exhibit heterogeneous clinical features as they encompass four distinct characteristics: peritumoral fat invasion, sinus fat invasion, renal vein invasion, and urinary tract invasion. Among these, venous invasion was the most common cT3a factor observed in this study. A previous study indicated that venous invasion is associated with a worse prognosis compared to other factors, such as peritumoral fat invasion (16). Consequently, detecting venous invasion preoperatively is critical for determining the optimal surgical strategy. In this study, the sensitivity, PPV, and concordance index for venous invasion were relatively high. Additionally, radiological findings of venous invasion and sinus fat invasion were associated with low downstaging rates (10.0% and 7.7%, respectively). One potential reason includes that the tumors exhibiting radiological signs of venous or sinus fat invasion tended to be located in the central of the kidney, which correlated with lower downstaging rates compared to tumors with radiological peritumoral fat invasion or urinary tract invasion.

Although CECT scans are widely used to determine the clinical stage of localized renal cancers, the degree of agreement among radiologists varies depending on the specific cT3a factors. Sokhi *et al.* reported strong inter-radiologist agreement in diagnosing renal vein invasion but noted lower agreement for peritumoral fat invasion (17). In this study, the κ value and PPV for features other than venous invasion, particularly urinary tract invasion, were significantly lower. The 2017 revision of the TNM classification introduced urinary tract invasion as a cT3a factor, which has led to limited studies exploring this feature and its imaging characteristics. Fateh *et al.* reported high sensitivity and PPV (88.23% for both) in diagnosing urinary tract invasion, but their study included more advanced cancers, such as cT3b, cT3c, and T4 cases (7). In this study, pathological urinary tract invasion was identified in only three patients, with a PPV of 8.1%. This discrepancy may reflect that smaller renal cancers are less likely to infiltrate the urinary tract.

Studies assessing the accuracy of staging in non-clear cell RCC are limited due to their rarity (18). In this study, the non-clear cell subtype emerged as the sole independent predictor of downstaging. This finding suggests that non-clear cell subtypes, such as papillary RCC or chromophobe RCC, may lack the subcapsular structures that clearly delineate the tumor from normal renal tissue. Further research is needed to explore the relationship between non-clear cell subtypes and the possibility of downstaging.

Study limitations. First, it is a retrospective study with a small sample size. Second, its generalizability is limited as it was conducted at a single institution, and radiological and pathological evaluations may vary across institutions. Third, not all patients underwent thin-slice, four-phase CECT scans, nor were alternative imaging modalities such as MRI used, potentially leading to less accurate evaluations. A previous study demonstrated that 1-mm thin-slice CECT with four phases (plain, arterial, nephrographic, and excretory) achieves 95% accuracy (5). However, some patients in this study did not receive thin-slice CT with these phases, which might have influenced the results.

Conclusion

This study revealed that CECT is a reliable tool for detecting intrarenal vein invasion, while urinary tract invasion was found to be less common in small-sized renal cancers. Furthermore, downstaging following PN occurred in 37% of cT3a RCC, with non-clear cell subtypes identified as the sole independent predictor of downstaging.

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

Conceptualization, K.B. and K.Y.; methodology, K.B.; software, K.B.; validation, K.B., K.Y. and M.A.; formal analysis, K.B.; investigation, K.B.; resources, K.B.; data curation, K.B.; writing – original draft preparation, K.B.; writing – review and editing, K.Y., S.I, Y.M, T.Y., T.K., T.S., Y.T., T.I., S.K., S.N., K.E., and T.K.; visualization, K.B.; supervision, M.A.; project administration, M.A. All Authors have read and agreed to the published version of the manuscript.

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Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (Grammarly) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual

data were generated or modified using generative AI or machine learning–based image enhancement tools.

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