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Efficacy of Pre-operative ^{18}F-FDG PET/CT in Prognostic Prediction in Patients With Renal Cell Carcinoma

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Abstract. *Background/Aim: This study analyzed the parameters provided by preoperative ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) for prognostic prediction of renal cell carcinoma (RCC). Patients and Methods: FDG-PET/CT data from 66 clear cell RCC and 19 non-clear cell RCC cases between January 2015 and October 2018 were reviewed retrospectively. We compared the two groups according to recurrence/metastasis to determine prognosis-influencing factors. Multivariate Cox hazard regression models were constructed to evaluate factors potentially predicting disease-free survival (DFS) after adjustment for confounders. DFS was then compared between groups. Results: Standardized uptake values (SUV) of the PET/CT scan were independent predictors of prognosis after adjusting for confounders. RCC cases were divided into two groups by optimal cut-off values. Differences between DFS percentages in high and low SUV groups were significant. Similar results were obtained in clear cell RCC groups. Conclusion: Increased SUV of the PET/CT scan are significant predictors of worse prognoses in patients with surgically resected RCC.*

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^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) is used for the assessment of tumor glucose metabolism, and is widely accepted as a pre-operative tumor staging, postoperative follow up, and monitoring treatment response imaging modality in many patients with malignancy. However, since renal cell carcinoma (RCC) displays limited FDG accumulation due to physiological excretion of FDG by the tumor (1), FDG-PET/CT is not always appropriate for preoperative evaluation of patients with RCC. In clinical practice, the histological diagnosis of RCC, tumor spread, lymph nodes, and distant metastases can be evaluated by dynamic contrast-enhanced CT and MRI in the majority of cases.

Contrary to current practice, some recent studies have demonstrated that pathological nuclear grade and histological subtypes of RCC can be predicted by the maximum standardized uptake value (SUV max) on preoperative FDG-PET/CT (2-4). There is limited research on the power of FDG-PET/CT analysis for prognosis parameter evaluation, such as disease-free survival (DFS), progression-free survival, and overall survival in patients with RCC (5-9). Furthermore, no studies have performed prognostic analysis of cases with surgically resected RCC while accounting for confounding factors. Therefore, if preoperative FDG-PET/CT can be used to evaluate the risk of recurrence or metastasis after surgery, aid tumor staging, and provide pathological information, the clinical relevance of FDG-PET/CT in renal neoplasm diagnosis and prognosis would be increased. Moreover, FDG-PET/CT can provide several metabolic parameters, such as SUV peak, SUV mean, and metabolic tumor volume (MTV) in addition to SUV max. SUV peak represents the average SUV over a small volume of interest centered on the SUV max and its neighboring voxels and is less affected by image noise than SUV max. MTV and SUV mean can evaluate not only metabolic activity but also total tumor burden.

Therefore, we examined whether several functional parameters provided by preoperative FDG-PET/CT were useful for predicting recurrence or metastasis before surgery.

Patients and Methods

Subjects and study protocol. The current study was approved by the ethical review board of our institute (approval number: 1499). All patients provided written informed consent before each radiological examination and surgery. Data was retrospectively collected from a database of RCC cases between January 2015 and October 2018. A total of 96 patients who underwent FDG-PET/CT for preoperative assessment of RCC were included. Of these patients, nine who underwent surgery at another institute and two whose pathological diagnosis was angiomyolipoma were excluded. Finally, 66 patients with clear cell RCC and 19 with non-clear cell RCC were enrolled. Patient characteristics and preoperative imaging (CT, MRI and FDG PET/CT) findings, including age, sex, tumor size, T score of the TNM classification, SUV max, SUV peak, SUV mean, MTV, pathological diagnosis, Fuhrman grade, recurrence or metastasis, and follow up period, were obtained from reviewing medical records.

Imaging studies, techniques and data acquisition. After fasting for at least 6 h, the patients were injected intravenously with 3.5 MBq/kg FDG and then allowed to rest for approximately 70 min (range=66-75 min). Then, PET/CT scans of the skull to upper thighs were obtained using an integrated Biograph mCT PET/CT scanner (Siemens Healthcare, Erlangen, Germany). Prior to PET image acquisition, low-dose CT (tube voltage, 120 kV; tube current, auto mA) was performed for attenuation correction and precise anatomical localization. Time-of-flight PET imaging was performed in three-dimensional mode and reconstructed on a 200×200 image matrix using the iterative reconstruction algorithm provided. Section thickness was 2.0 mm. Attenuation-corrected FDG-PET images were reconstructed using the CT data and an ordered subset expectation maximization algorithm. A Gaussian filter, set at full width at half maximum, and scatter correction were applied for smoothing. CT and PET images were co-registered using dedicated software (syngo. via VA30A; Siemens Healthcare, Erlangen, Germany). Each metabolic parameter of each tumor, such as SUV max, SUV peak, SUV mean, and MTV, was obtained by placing a volume of interest (VOI) including the entire tumor volume and largest FDG uptake lesion on a PET/CT fusion image.

Statistical analysis. R software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses (10). Continuous variables are expressed as means and standard deviations or medians with corresponding interquartile ranges (IQR), and categorical values are expressed as numbers and frequencies.

We determined the significant predictors that influence prognosis by comparing the two groups according to the presence or absence of recurrence in patients with all RCC and clear cell RCC. Considering the obtained predictor as a confounding factor, multivariate Cox proportional hazard regression models were conducted to evaluate the factors potentially predicting DFS and estimate hazard ratios with 95% confidence intervals, after adjustment for confounding factors.

Finally, we established the optimal cut-off value of SUV parameters by the Youden index, which predicts recurrence in patients with all RCC and clear cell RCC using receiver operating characteristic (ROC) analysis. For each parameter, sensitivity, specificity, and diagnostic accuracy were also calculated. Kaplan–Meier analysis was used to estimate the probability of DFS based on the obtained cut-off value. The DFS was defined as local recurrence, lymph node metastasis, or distant metastasis. The log-rank test was used to assess the resulting DFS curves. A p-value <0.05 was considered statistically significant.

Results

In all RCC patients, mean age was 61±11 (47 male, 38 female). Fifteen patients had diabetes mellitus, 3 of which used insulin. Median tumor size was 4.1 (IQR=2.6-5.7) cm. T-stage (T1a, T1b, T2a, T2b) was 39, 33, 10, and 3 in all cases, respectively. Median value of SUV max, SUV peak, SUV mean, and MTV were 3.76 (IQR=3.09-5.16), 3.21 (IQR=2.69-4.24), 2.42 (IQR=2.08-3.34), and 11.03 (IQR=4.60-33.6), respectively. Median observation time was 385 (IQR=189-675) days. There were nineteen cases of non-clear cell RCC, including four chromophobe RCC cases, three type 2 papillary RCC, five acquired cystic disease-related RCC, one 6p21translocated RCC, one collecting duct carcinoma, and two unclassified RCC.

Table I and Table II present the differences between the two groups according to the presence or absence of recurrence in patients with all RCC and clear cell RCC, respectively. The metabolic parameters SUV max, SUV peak, and SUV mean were significantly different between the two groups in measures in addition to size parameters of tumor size and T stage. Among both all RCC and clear cell RCC groups, multivariate Cox proportional hazard regression analysis revealed that the SUV max, SUV peak and SUV mean parameters were independent factors predicting DFS; regarding the all RCC group, the statistics are as follows: hazard ratio (HR)=1.189, 95%CI=1.069-1.323, p<0.01, c-index=0.897, HR=1.252, 95%CI=1.099-1.426, p<0.01, c-index=0.897, HR=1.400, 95%CI=1.145-1.711, p<0.01, c-index=0.892. As for the clear cell RCC only group, the statistics are: HR=1.155, 95%CI=1.024-1.304, p<0.05, c-index=0.878, HR=1.212, 95%CI=1.035-1.419, p<0.05, c-index=0.885, HR=1.330, 95%CI=1.047-1.691, p<0.05, c-index=0.882. Adjustment for T stage as a confounding factor was performed in the above analyses (Table III).

Among all RCC cases groups, ROC analysis demonstrated that the optimal cut-off value, sensitivity, specificity, and accuracy in each SUV parameter for predicting DFS were 10.54, 63.6%, 94.6%, and 90.6% for SUV max, 8.90, 54.5%, 97.3%, and 91.8% for SUV peak, 5.70, 63.6%, 93.2%, and 89.4% for SUV mean, respectively.

Among the clear cell RCC cases, the optimal cut-off value, sensitivity, specificity and accuracy in each SUV

Table I. *Clinical characteristics of all RCCs.*

	No recurrence (n=74)	Recurrence (n=11)	*p*-Value
Age (mean±SD)	62.1±10.8	62.6±12.1	0.743
Gender (M:F)	42:32	5:6	0.489
Tumor size (median)	3.9 (2.5-5.6) cm	5.5 (4.7-7.7) cm	0.006*
T stage (T1a: T1b: T2a: T2b)	38:28:6:2	1:5:4:1	0.002*
SUV max (median)	3.47 (2.98-4.71)	10.63 (6.28-14.63)	<0.001*
SUV peak (median)	3.00 (2.67-3.96)	8.90 (5.39-11.35)	<0.001*
SUV mean (median)	2.35 (1.96-3.06)	6.01 (3.48-7.60)	<0.001*
MTV (median)	8.91 (2.89-31.52)	25.13 (18.95-38.92)	0.063
Fuhrman grade (G1:G2:G3:G4)	22:35:13:4	1:7:1:2	0.821
Observation time (median)	368 (190-669) days	547 (184-907) days	0.475

RCC: Renal cell carcinoma; SUV: standardized uptake value; MTV: metabolic tumor volume; M: male; F: female. *p<0.05.

Table II. *Clinical characteristics of clear cell RCC.*

	No recurrence (n=57)	Recurrence (n=9)	*p*-Value
Age (mean±SD)	62.4±10.9	60.9±12.5	0.888
Gender (M:F)	30:27	4:5	0.658
Tumor size (median)	4.0 (2.5-5.7) cm	7.2 (5.0-7.8) cm	0.010*
T stage (T1a: T1b: T2a: T2b)	28:21:6:2	1:3:3:1	0.006*
SUV max (median)	3.37 (2.93-4.30)	10.54 (3.82-12.64)	0.001*
SUV peak (median)	2.91 (2.67-3.53)	8.73 (3.50-9.93)	<0.001*
SUV mean (median)	2.26 (1.95-2.81)	5.70 (2.50-6.52)	0.004*
MTV (median)	10.85 (4.51-30.46)	25.13 (17.72-34.37)	0.158
Fuhrman grade (G1:G2:G3:G4)	21:28:5:3	1:6:1:1	0.147
Observation time (median)	436 (196-675) days	547 (159-979) days	0.751

RCC: Renal cell carcinoma; SUV: standardized uptake value; MTV: metabolic tumor volume; M: male; F: female. *p<0.05.

parameter for predicting DFS were 10.54, 55.6%, 98.2%, and 92.4% for SUV max, 8.73, 55.6%, 98.2%, and 92.4% for SUV peak, 5.70, 55.6%, 98.2%, and 92.4% for SUV mean, respectively. For all indicators, accuracy rate was as high as approximately 90%.

Kaplan–Meier curves between two groups divided by the obtained each cut-off value are shown in Figure 1. There was a significant (p<0.01) difference in DFS between the two groups in all parameters according to the log-rank test. In the groups of all RCC patients with low and high SUV max, SUV peak, and SUV mean, the 1-year DFS rates were 96.9% and 60.0%, 95.2% and 66.7 %, and 96.9% and 64.8%, respectively. Similarly, the 2-year DFS rates were 98.4% and 46.9%, 95.2% and 33.3%, and 96.9% and 38.9%, respectively. The 3-year DFS rates were 80.0% and 15.0%, 78.5% and 16.7%, and 79.9% and 19.4%, respectively. In the groups of clear cell RCC patients with low and high SUV max, SUV peak, and SUV mean, the 1-year DFS rates were 96.3% and 60.0%, 96.3% and 60.0 %, and 96.3% and 60.0%, respectively. Similarly, the 2-year DFS rates were 96.3% and 20.0%, 96.3% and 20.0%, and 96.3% and 20.0%, respectively. The 3-year DFS rates were 74.8% and 20.0%, 75.8% and 20.0%, and 75.8% and 20.0%, respectively.

Table III. *Multivariable Cox regression analysis of disease-free survival.*

	Parameter	*p*-Value	Hazard ratio (95%CI)
All RCC	SUV max	0.001*	1.189 (1.069-1.323)
	T stage	0.066	2.252 (0.948-5.352)
	SUV peak	<0.001*	1.252 (1.099-1.426)
	T stage	0.048*	2.353 (1.006-5.503)
	SUV mean	0.001*	1.400 (1.145-1.711)
	T stage	0.036*	2.449 (1.058-5.668)
Clear cell RCC	SUV max	0.019*	1.155 (1.024-1.304)
	T stage	0.084	2.285 (0.894-5.835)
	SUV peak	0.017*	1.212 (1.035-1.419)
	T stage	0.087	2.268 (0.867-5.801)
	SUV mean	0.020*	1.330 (1.047-1.691)
	T stage	0.067	2.363 (0.942-5.925)

RCC: Renal cell carcinoma; SUV: standardized uptake value; CI: confidence interval. *p<0.05.

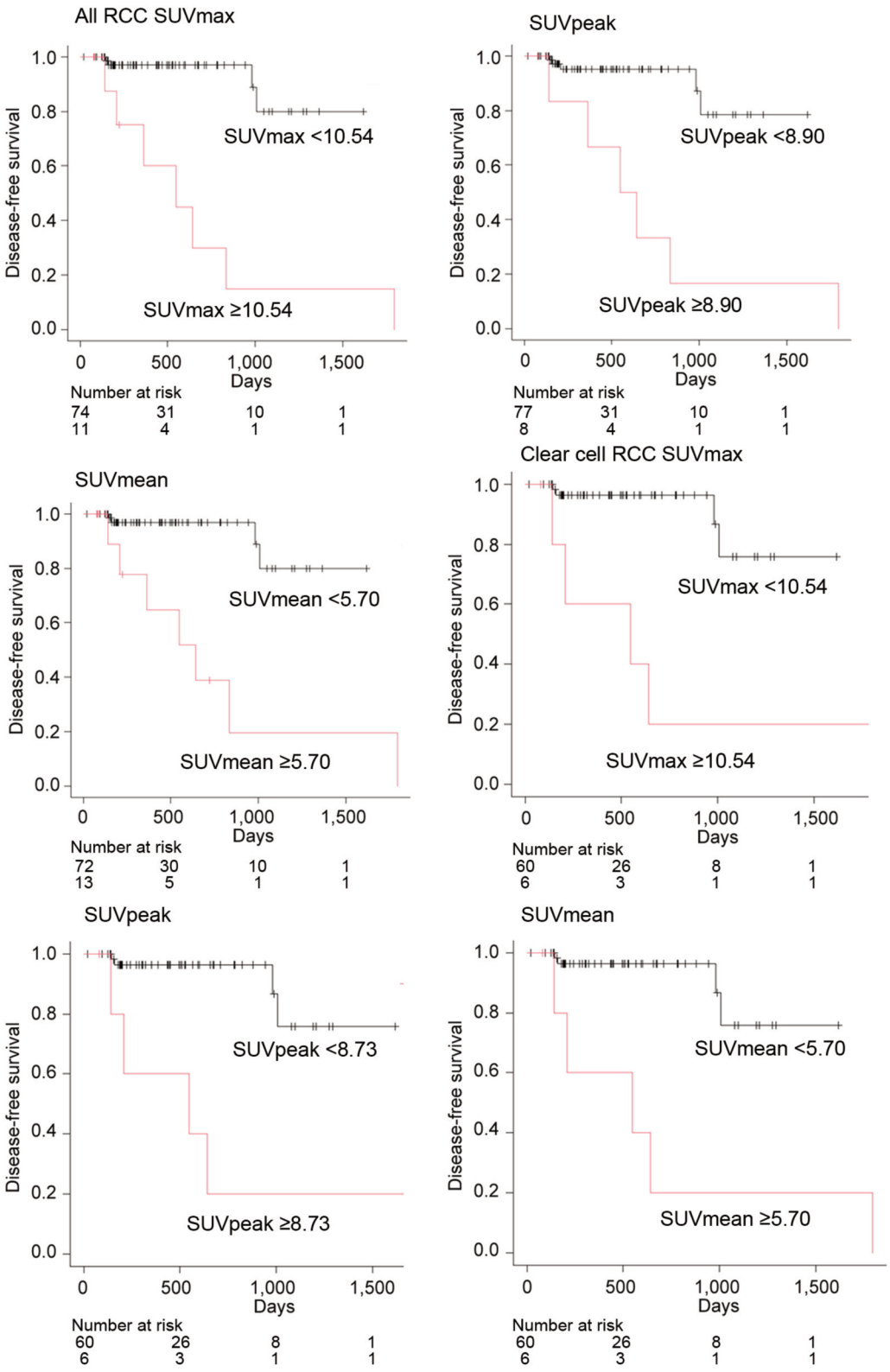

Figure 1. *Kaplan–Meier curves demonstrating the disease-free survival (DFS) of patients with renal cell carcinoma (RCC) divided in two groups by the respective optimal cut-off value (upper row: all RCC, lower row: clear cell RCC). There were significant ($p<0.05$) differences in DFS percentages between the two groups, according to the log-rank test.*

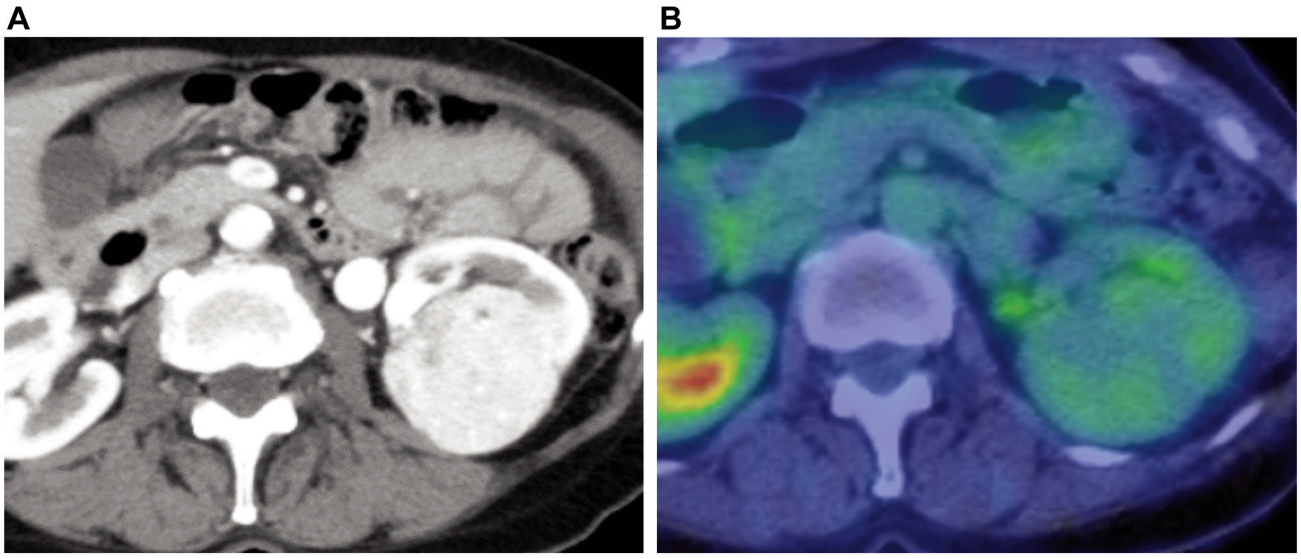

Figure 2. *Representative clear cell renal cell carcinoma images in groups of low standardized uptake value (SUV) max. A 67-year-old female had a left renal mass noted during annual health check-up. A: Dynamic contrast-enhanced computed tomography image demonstrated a hypervascular mass, suggesting a clear cell renal carcinoma. B: On ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography, the SUV max of the lesion was 3.11. Postoperative pathological diagnosis was Fuhrman grade 1. The patient was disease-free at 2 years after surgery and later.*

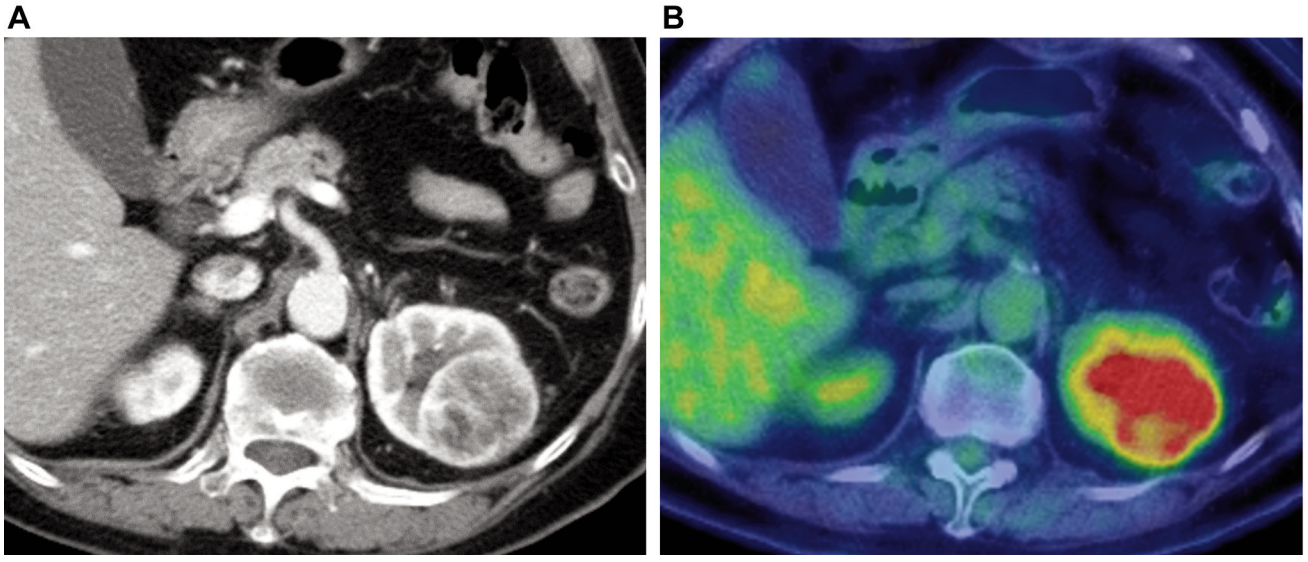

Figure 3. *Representative clear cell renal cell carcinoma cases in groups of high standardized uptake value (SUV) max. An 81-year-old female complained of gross hematuria. A: Dynamic contrast-enhanced computed tomography image demonstrated a hypervascular mass, suggesting a clear cell renal carcinoma. B: On ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography, the SUV max of the lesion was 10.74. Postoperative pathological diagnosis was Fuhrman grade 2. Lung metastases occurred at 6 months after surgery.*

In the two groups, the HR of SUV max, SUV peak, SUV mean by each cut-off value was 12.6 (95%CI=3.523-44.7), 9.62 (95%CI=2.754-33.6), and 11.0 (95%CI=3.059-39.24) among the all RCC group, and 10.2 (95%CI=2.528-40.98), 10.2 (95%CI=2.528-40.98), and 10.2 (95%CI=2.528-40.98) among the clear cell RCC group.

Representative cases of clear cell RCC with high SUV max (Figure 2) and low SUV max (Figure 3) are shown.

Discussion

In the current study, FDG-PET/CT was found to be a useful modality for assessing the risk of recurrence. Specifically, the parameters of SUV max, SUV peak, and SUV mean were independent prognostic predictors of local recurrence/metastasis, regardless of the histologic RCC subtype. Furthermore, the optimal cut-off value, by which it is possible to detect cases of high-risk of recurrence/metastasis, was also demonstrated, with accuracy rate of approximately 90% and a hazard ratio of approximately 10.

Among previous studies that used PET to discriminate tumours based on the Fuhrman grades, Nakajima *et al*. used a cut-off SUV max of 4.63 to predict higher Fuhrman grades and distinguish clear cell from non-clear cell RCC (3). In another study, authors used a cut-off SUV max of 4.18 to discriminate histological subtypes (4). Regarding survival outcome, some researchers demonstrated that SUV max values were predictive of overall survival or progression-free survival in patients with advanced RCC treated with various molecular target therapies (5-9). Only a few studies have performed recurrence risk assessment based on imaging prior to surgery, and some have suggested that higher SUV max indicates a worse prognosis, but the number of cases analysed was as small as 30 (11-13). Moreover, no previous study performed multivariate analyses with tumor size accounted for as a confounding factor.

Regarding FDG accumulation, past reports demonstrate the correlation between glucose transporter 1 (GLUT1) expression and FDG uptake in tumours derived from organs other than kidney (14, 15). In renal cancer, no correlation between FDG uptake and GLUT1 expression has been demonstrated (1, 16). In contrast, Chen *et al*. demonstrated the correlation (17). Moreover, Ambrosetti *et al*. demonstrated correlations between expression of monocarboxylate transporter1 (MCT1), in addition to GLUT1 and Fuhrman grade, and concluded that both glycolytic markers were strong prognostic markers (18). More interestingly, Chen *et al*. have also demonstrated that fructose-1,6-bisphosphatase 1 (FBP1) suppressed FDG accumulation (17), and Li *et al*. demonstrated that FBP1 suppresses progression of RCC (19).

In general, patients with RCC have a relatively good prognosis, especially cases where surgery is indicated, with a 5-year survival rate of approximately 70%. Although many patients do not experience recurrence or metastasis for a long period after surgery, recurrence or metastasis sometimes occurs soon after surgery even when pre-operative CT or MRI shows image findings typical of early-stage clear cell carcinoma.

The cut-off values in FDG-PET/CT parameters made it possible to classify those cases preoperatively. Thereby, we were able to estimate a 10 times higher risk of recurrence/metastasis with high accuracy rate of approximately 90% if a SUV parameter was set at an appropriate threshold. For patients whose risk of recurrence/metastasis is high, careful follow-up after surgery facilitates the speed in implementation of adjuvant therapies, such as molecular-targeted drugs and immune checkpoint inhibitors, immediately after recurrence, resulting in improved prognosis. Furthermore, the cost will be decreased by precluding the need for unnecessary sequential image screenings in patients with low recurrence/metastasis risk. The current study demonstrates that preoperative FDG-PET/CT is useful for evaluating the risk of recurrence/metastasis, clarifying the role of preoperative imaging modalities. In other words, dynamic CT and MRI can be used to assess the histological subtype, local tumor progression, lymph node metastasis, and distant metastasis. FDG-PET/CT can be used to assess prognosis (*i.e*., DFS) regardless of tumor size and RCC subtype.

The limitations of the current study are its retrospective nature and the small sample size, especially in the non-clear cell RCC cohort. The reason of sample size was because FDG-PET/CT was introduced at our institute and it applied to urological malignancies only recently. In addition, postoperative follow up was performed at the initial hospital.

In conclusion, preoperative FDG-PET/CT is a useful modality for prognostic assessment of RCC after surgery.

Conflicts of Interest

The Authors have no relevant financial or non-financial interests to disclose regarding this study.

Authors' Contributions

All Authors contributed to the study conception and design. Masafumi Toguchi prepared the first draft of the manuscript, performed data collection and analysis. Kousei Ishigami provided critical revision. Masato Goya and Seiichi Saito provided intellectual clinical advises and contributed to the interpretation of data. Sadayuki Murayama and Akihiro Nishie commented on previous versions. All Authors read and approved the final manuscript.

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References

1 Miyakita H, Tokunaga M, Onda H, Usui Y, Kinoshita H, Kawamura N and Yasuda S: Significance of ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) for detection of renal cell carcinoma and immunohistochemical glucose transporter 1 (GLUT-1) expression in the cancer. Int J Urol *9(1)*: 15-18, 2002. PMID: 11972644. DOI: 10.1046/j.1442-2042.2002.00416.x

2 Noda Y, Kanematsu M, Goshima S, Suzui N, Hirose Y, Matsunaga K, Nishibori H, Kondo H, Watanabe H, Kawada H,

Kawai N, Tanahashi Y and Bae KT: 18-F fluorodeoxyglucose uptake in positron emission tomography as a pathological grade predictor for renal clear cell carcinomas. Eur Radiol *25(10)*: 3009-3016, 2015. PMID: 25854217. DOI: 10.1007/s00330-015-3687-2

3 Nakajima R, Abe K, Kondo T, Tanabe K and Sakai S: Clinical role of early dynamic FDG-PET/CT for the evaluation of renal cell carcinoma. Eur Radiol *26(6)*: 1852-1862, 2016. PMID: 26403580. DOI: 10.1007/s00330-015-4026-3

4 Nakajima R, Nozaki S, Kondo T, Nagashima Y, Abe K and Sakai S: Evaluation of renal cell carcinoma histological subtype and fuhrman grade using ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography. Eur Radiol *27(11)*: 4866-4873, 2017. PMID: 28523353. DOI: 10.1007/s00330-017-4875-z

5 Chen JL, Appelbaum DE, Kocherginsky M, Cowey CL, Rathmell WK, McDermott DF and Stadler WM: FDG-PET as a predictive biomarker for therapy with everolimus in metastatic renal cell cancer. Cancer Med *2(4)*: 545-552, 2013. PMID: 24156027. DOI: 10.1002/cam4.102

6 Nakaigawa N, Kondo K, Tateishi U, Minamimoto R, Kaneta T, Namura K, Ueno D, Kobayashi K, Kishida T, Ikeda I, Hasumi H, Makiyama K, Kubota Y, Inoue T and Yao M: FDG PET/CT as a prognostic biomarker in the era of molecular-targeting therapies: max SUVmax predicts survival of patients with advanced renal cell carcinoma. BMC Cancer *16*: 67, 2016. PMID: 26857818. DOI: 10.1186/s12885-016-2097-4

7 Ito H, Kondo K, Kawahara T, Kaneta T, Tateishi U, Ueno D, Namura K, Kobayashi K, Miyoshi Y, Yumura Y, Makiyama K, Hayashi N, Hasumi H, Osaka K, Yokomizo Y, Teranishi JI, Hattori Y, Inoue T, Uemura H, Yao M and Nakaigawa N: One-month assessment of renal cell carcinoma treated by everolimus using FDG PET/CT predicts progression-free and overall survival. Cancer Chemother Pharmacol *79(5)*: 855-861, 2017. PMID: 28331985. DOI: 10.1007/s00280-017-3275-z

8 Nakaigawa N, Kondo K, Kaneta T, Tateishi U, Minamimoto R, Namura K, Ueno D, Kobayashi K, Kishida T, Ikeda I, Hasumi H, Makiyama K, Hayashi N, Osaka K, Muraoka K, Izumi K, Kawahara T, Teranishi JI, Miyoshi Y, Yumura Y, Uemura H, Inoue T and Yao M: FDG PET/CT after first molecular targeted therapy predicts survival of patients with renal cell carcinoma. Cancer Chemother Pharmacol *81(4)*: 739-744, 2018. PMID: 29464355. DOI: 10.1007/s00280-018-3542-7

9 Pankowska V, Malkowski B, Wedrowski M, Wedrowska E and Roszkowski K: FDG PET/CT as a survival prognostic factor in patients with advanced renal cell carcinoma. Clin Exp Med *19(1)*: 143-148, 2019. PMID: 30488140. DOI: 10.1007/s10238-018-0539-9

10 R Development Core Team: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria, 2007. Available at: http://www.R-project.org/ [Last accessed on March 20, 2019]

11 Namura K, Minamimoto R, Yao M, Makiyama K, Murakami T, Sano F, Hayashi N, Tateishi U, Ishigaki H, Kishida T, Miura T, Kobayashi K, Noguchi S, Inoue T, Kubota Y and Nakaigawa N: Impact of maximum standardized uptake value (SUVmax) evaluated by 18-Fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (^{18}F-FDG-PET/CT) on survival for patients with advanced renal cell carcinoma: a preliminary report. BMC Cancer *10*: 667, 2010. PMID: 21129184. DOI: 10.1186/1471-2407-10-667

12 Ferda J, Ferdova E, Hora M, Hes O, Finek J, Topolcan O and Kreuzberg B: ^{18}F-FDG-PET/CT in potentially advanced renal cell carcinoma: a role in treatment decisions and prognosis estimation. Anticancer Res *33(6)*: 2665-2672, 2013. PMID: 23749925.

13 Lee H, Hwang KH, Kim SG, Koh G and Kim JH: Can initial (18)F-FDG PET-CT imaging give information on metastasis in patients with primary renal cell carcinoma? Nucl Med Mol Imaging *48(2)*: 144-152, 2014. PMID: 24900155. DOI: 10.1007/s13139-013-0245-1

14 Horiuchi C, Tsukuda M, Taguchi T, Ishiguro Y, Okudera K and Inoue T: Correlation between FDG-PET findings and GLUT1 expression in salivary gland pleomorphic adenomas. Ann Nucl Med *22(8)*: 693-698, 2008. PMID: 18982472. DOI: 10.1007/s12149-008-0162-z

15 Meziou S, Ringuette Goulet C, Hovington H, Lefebvre V, Lavallée É, Bergeron M, Brisson H, Champagne A, Neveu B, Lacombe D, Beauregard JM, Buteau FA, Riopel J and Pouliot F: GLUT1 expression in high-risk prostate cancer: correlation with ^{18}F-FDG-PET/CT and clinical outcome. Prostate Cancer Prostatic Dis *23(3)*: 441-448, 2020. PMID: 31932660. DOI: 10.1038/s41391-020-0202-x

16 Betsunoh H, Sakamoto S, Kaji Y, Nukui A, Kobayashi M, Yashi M, Hayashi K, Anzai N and Kamai T: Clinical significance of ^{18}F-fluorodeoxyglucose and glucose transporter 1 mRNA in clear cell renal cell carcinoma. Anticancer Res *41(10)*: 5179-5188, 2021. PMID: 34593470. DOI: 10.21873/anticanres.15336

17 Chen R, Zhou X, Huang G and Liu J: Fructose 1,6-bisphosphatase 1 expression reduces ^{18}F-FDG uptake in clear cell renal cell carcinoma. Contrast Media Mol Imaging *2019*: 9463926, 2019. PMID: 30723389. DOI: 10.1155/2019/9463926

18 Ambrosetti D, Dufies M, Dadone B, Durand M, Borchiellini D, Amiel J, Pouyssegur J, Rioux-Leclercq N, Pages G, Burel-Vandenbos F and Mazure NM: The two glycolytic markers GLUT1 and MCT1 correlate with tumor grade and survival in clear-cell renal cell carcinoma. PLoS One *13(2)*: e0193477, 2018. PMID: 29481555. DOI: 10.1371/journal.pone.0193477

19 Li B, Qiu B, Lee DS, Walton ZE, Ochocki JD, Mathew LK, Mancuso A, Gade TP, Keith B, Nissim I and Simon MC: Fructose-1,6-bisphosphatase opposes renal carcinoma progression. Nature *513(7517)*: 251-255, 2014. PMID: 25043030. DOI: 10.1038/nature13557

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