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Preoperative neutrophil to lymphocyte
ratio as a predictor for pathologic sinus
fat invasion in renal cell carcinoma of
 ≤ 7 cm with presumed sinus fat invasion
on preoperative imaging

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Directed by Professor Won Sik Ham

The Master's Thesis
submitted to the Department of Medicine
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

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This certifies that the Master's Thesis of
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ABSTRACT

Preoperative NLR as a predictor for pathologic renal sinus invasion in renal cell carcinomas of ≤ 7 cm with presumed renal sinus fat invasion on preoperative imaging.

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Purpose: To evaluate whether preoperative neutrophil to lymphocyte ratio (NLR) could predict pathologic sinus fat invasion (SFI) in the patients with renal cell carcinoma (RCC) which is smaller than 7cm and presumed to invade renal sinus fat preoperative imaging.

Materials and methods: We reviewed the medical records of patients who underwent nephrectomy for non-metastatic RCC smaller than 7cm between November 2005 and May 2014. Among 1311 patients, patients without SFI in preoperative imaging, had unavailable preoperative data and had factors affect NLR were excluded, and 476 patients were involved in this study. We investigated age, gender, body mass index (BMI), hypertension, smoking and preoperative NLR. We used logistic regression analysis to assess whether these factors are associated with pathologic SFI.

Results: Cut off value of NLR was set as 1.98 by receiver operation

characteristic curve. 93 patients were confirmed to have pathologic SFI. Patients with SFI had larger tumor size in preoperative imaging and higher preoperative NLR. And in the SFI group, pathologic tumor size was larger, more frequent renal vein involvement and higher Fuhrman nuclear grade. In univariate analysis, age (OR 1.019, $p=0.05$), clinical tumor size (OR 1.645, $p<0.001$), collecting duct involvement (OR 4.052, $p=0.008$) and high NLR (OR 2.087, $p=0.002$) were associated with SFI. In multivariate analysis, high NLR (OR 2.032, $p=0.004$) was independent prognostic factor of SFI with clinical tumor size (OR 1.586, $p<0.001$) and collecting system involvement (OR 3.957, $p=0.011$).

Conclusions: Preoperative NLR is related with pathologic SFI in the patients with renal cell carcinomas of 7cm or less presumed SFI on preoperative imaging. However, the role of NLR to predict SFI seems to be limited.

Key words: renal cell carcinoma, renal sinus fat, nephrectomy, neutrophil, lymphocyte

**Preoperative NLR as a predictor for pathologic renal sinus invasion
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I. INTRODUCTION

Renal cell carcinoma (RCC) is the most common malignant tumor in the kidney, accounting for 85%. Incidence of renal cell carcinoma has increased gradually at the rate of 2% annually for last two decades.¹ Small renal cell carcinoma has been diagnosed more frequently because of widespread of ultrasonography and computed tomography (CT).² Renal tumors 7cm or less and confined to the kidney is stage T1 according to the 7th TNM stage published by American Joint Committed on Cancer(AJCC). Among clinical T1 stage renal cell carcinoma, some tumor invaded renal sinus fat up to 15.4%.³⁻⁶ The renal sinus fat is fatty area within the kidney that is not separated from the renal cortex by the capsule. It contains many vessel and lymphatic channels, sinus fat invasion of tumor may increase chance to spread cancer, and it is related with poor prognosis. So renal cell carcinoma with sinus fat invasion (SFI) is defined

as stage T3a according to 7th TNM system.

CT is one of the most widely used modality for characterizing and staging renal tumors. Multidetector computed tomography (MDCT) has allowed radiologists to overcome the limitations of single-detector helical CT by providing volume data that can be reformatted in various planes, which helps to determine complex renal tumors. However, it has limited role to predict SFI in renal tumor.⁷

Recently, C-reactive protein (CRP), a serum marker for systemic inflammation, was reported as a good prognostic marker in patients with RCC.⁸⁻¹¹ However, CRP is not readily available for all patients because it needs additional serum testing. Neutrophil-lymphocyte ratio (NLR) correlate well with serum CRP levels and easily calculated by dividing the absolute neutrophil count by the absolute lymphocyte count from a complete blood count with differential. And NLR has been reported to predict oncological outcomes in patients with RCC.^{12,13} We aimed to evaluate which NLR could predict pathologic SFI in 7cm or less renal cell carcinoma suspected SFI on preoperative imaging.

II. MATERIALS AND METHODS

1. Patients selection

We reviewed the medical record of 1311 patients who underwent partial or radical nephrectomy for renal tumors of ≤ 7 cm between November 2005 and December 2014. The patients with N1 or M1 disease at diagnosis were excluded. And the patients who had some factors which could affect NLR were excluded. Those factors include other malignancy diagnosed simultaneously, infectious disease, autoimmune or systemic inflammatory diseases, and using chemotherapeutic agent or immunosuppressants. And after excluded patients had unavailable preoperative data, finally 476 patients were enrolled in our study. We investigated age, gender, body mass index (BMI), hypertension, smoking status, preoperative NLR, radiologic information from preoperative CT and pathologic results. Preoperative NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count which were obtained from routine laboratory tests within one month before nephrectomy. Collection of retrospective data was approved by the Institutional Review Board.

2. CT data interpretation

We used CT images which were obtained using a 64-slice detector (Sensation 64, Siemens, Erlangen, Germany) for identifying renal tumors with SFI. One senior uro-radiologist and one senior urologist independently evaluated the CT images. They were informed that all patients included in the study were diagnosed with RCC, and no information was given about the size,

location, stage, or bone involvement of the tumor. Interobserver variation was evaluated by means of the Cohen κ statistical analysis, for which the value of κ was 0.98 ($P < 0.05$), which indicated that the estimated κ was not a result of chance. The final decision was made after reviewing the images together if there was inconsistent opinion. Tumors were categorized based on the Preoperative Aspects and Dimensions Used for an Anatomical (PADUA) classification which contains the information of SFI. The criteria used for the diagnosis of SFI included tumor extension into the renal sinus, proximity to the pelvi-calyceal system, or invasion of the pelvi-calyceal system.

3. Pathologic data analysis

Pathologic outcomes were obtained by reviewing medical records which were based on previous pathological reports which had been reported by a single genitourinary pathologist at our institute. SFI was defined as direct contact of cancer cells with the renal sinus stroma or fat cells. Tumors infiltrating the pelvi-calyceal system were classified as SFI. Tumors confined by a pseudocapsule bulging into renal sinus fat without clear evidence of infiltration were not classified as SFI.

4. Statistical analysis

Baseline characteristics of patients and tumors were compared between no SFI group and SFI group using descriptive statistics. The Mann–Whitney

Table 1. Clinical and preoperative characteristics of patients

Characteristics	No SFI	SFI	p-value
	383	93	
Gender (%)			0.538
Male	261 (68.1%)	60 (64.5%)	
Female	122 (31.9%)	33 (35.5%)	
Age (median)	54	58	0.049
IQR	45.0-63.0	48.5-64.0	
BMI (median)	24.1	24.4	0.567
IQR	22.50-26.23	21.75-26.20	
Hypertension (%)			0.41
No	233 (60.8%)	52 (55.9%)	
Yes	150 (38.2%)	41 (44.1%)	
DM (%)			0.253
No	331 (86.4%)	76 (81.7%)	
Yes	52 (13.6%)	17 (18.3%)	
Smoking (%)			0.081
Non-smoker	208 (54.3%)	60 (64.5%)	
Current or former smoker	175 (45.7%)	33 (35.5%)	
Clinical tumor size (median)	4.4	5.5	<0.001
IQR	3.50-5.40	4.35-6.35	
Collecting system involvement (%)			0.006
Not involved	59 (15.4%)	4 (4.3%)	
Involved	324 (84.6%)	89 (95.7%)	
NLR (continuous)	1.85	2.22	<0.001
IQR	1.38-2.38	1.46-3.35	
NLR (dichotomous) (%)			0.002
High NLR	222 (58.0%)	37 (39.8%)	
Low NLR	161 (42.0%)	56 (60.2%)	

SFI=sinus fat invasion; IQR=interquartile range; BMI=body mass index; DM=diabetes mellitus; NLR=neutrophil to lymphocyte ratio

U-test and Fisher's exact test were used to compare continuous and categorical variables, respectively. We used binomial logistic regression for identifying the factors associated with pathologic SFI. Statistical analysis was performed using SPSS version 18 (SPSS, Inc., Chicago, IL, USA).

III. RESULTS

There were 321 male and 155 female patients with a median age of 55 years (IQR 46.0-64.0). Median clinical tumor size was 4.6cm (IQR 3.6-5.6) and 172 patients (36.1%) were clinical T1a stage. The median value of NLR were 1.90 (IQR 1.39-2.53). Among 476 patients, SFI was observed in 93 patients. The cutoff value of NLR was determined as 1.98, which was calculated by the receiver operating curve (ROC) analysis. The areas under the curve (AUC) based on SFI was 0.615. NLR was evaluated as a dichotomized variable by dividing cases into 2 groups ($MLR < 1.98$ and $MLR \geq 1.98$).

Table 1 and table 2 shows the clinical and pathological characteristics of patients. Older patients were more likely involving renal sinus fat. And clinical tumor size was larger in SFI group. Collecting duct invasion on preoperative CT was more frequently observed in SFI group. Median preoperative NLR value was also higher in SFI group. On the pathologic results, SFI group has larger and high-grade renal cell carcinoma. And there were more patients renal vein involvement in SFI group.

Table 2. Pathologic characteristics of patients

Characteristics	No SFI	SFI	p-value
	383	93	
Pathologic tumor size (median)	4	5	<0.001
IQR	3.2-5.0	4.00-6.00	
Histologic subtype (%)			0.292
Clear cell	339 (88.5%)	78 (83.9%)	
Non-clear cell	44 (11.5%)	15 (16.1%)	
Fuhrman nuclear grade (%) **			<0.001
G1-2	200 (54.8%)	26 (31.0%)	
G3-4	165 (45.2%)	58 (69.0%)	
Perinephric fat invasion (%)			0.058
No	363 (94.8%)	83 (89.2%)	
Yes	20 (5.2%)	10 (10.8%)	
Renal vein or branch invasion (%)			<0.001
No	380 (99.2%)	82 (88.2%)	
Yes	3 (0.8%)	11 (11.8%)	
Sarcomatoid differentiation (%)			0.999
No	378 (98.7%)	91 (98.9%)	
Yes	5 (1.3%)	6 (1.3%)	

SFI=sinus fat invasion; IQR=interquartile range;

In univariate binary logistic regression for confirming preoperative factors associated with SFI, age (odds ratio (OR) 1.019, 95% confident interval (CI) 1.000-1.039, $p=0.05$), clinical tumor size (OR 1.645, 95% CI 1.360-1.990, $p<0.001$), collecting system involvement (OR 4.052, 95% CI 1.433-11.457, $p=0.008$) and NLR (OR 2.087, 95% CI 1.315-3.313, $p=0.002$) were associated

Table 3. Univariate and multivariate analysis of factors associated with sinus fat invasion

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Gender		0.503		
Male	1 (Ref)			
Female	1.177 (0.732-1.894)			
Age	1.019 (1.000-1.039)	0.05	1.014 (0.994-1.035)	0.168
BMI	1.021 (0.952-1.094)	0.566		
Hypertension		0.386		
No	1 (Ref)			
Yes	1.225 (0.775-1.936)			
Smoking		0.076		
Non-smoker	1 (Ref)			
Current or former smoker	0.654 (0.409-1.046)			
Clinical tumor size	1.645 (1.360-1.990)	<0.001	1.586 (1.305-1.926)	<0.001
Collecting system involvement		0.008		0.011
Not involved	1 (Ref)		1 (Ref)	
Involved	4.052 (1.433-11.457)		3.957 (1.371-11.417)	
NLR		0.002		0.004
Low	1 (Ref)		1 (Ref)	
High	2.087 (1.315-3.313)		2.032 (1.256-3.287)	

OR=odds ratio; CI=confidence interval; BMI=body mass index; NLR=neutrophil to lymphocyte ratio

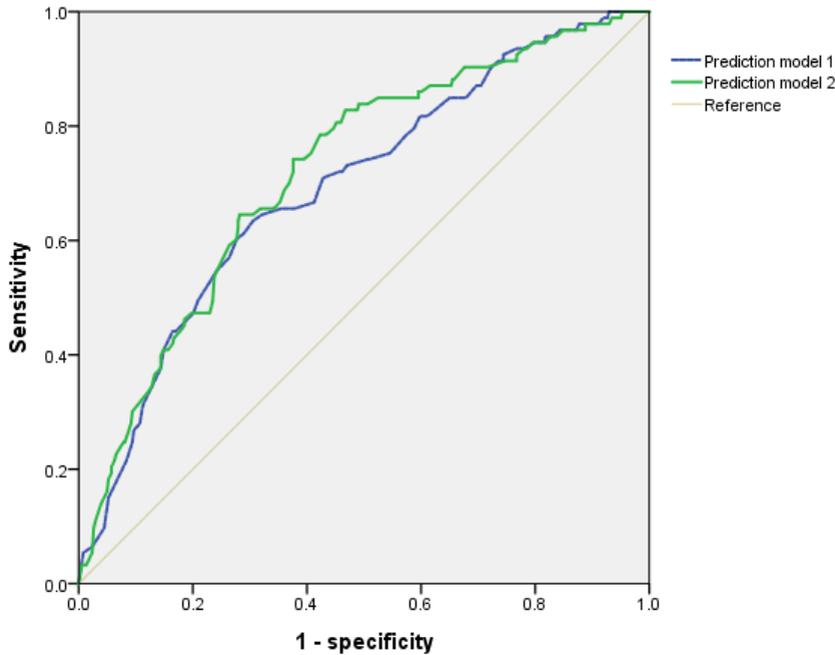


Figure 1. Receiver operating characteristic (ROC) curve of predictive models for sinus fat invasion
 Model 1 included clinical tumor size and clinical collecting system involvement. Model 2 included NLR with the factors of model 1. AUC of model 1 was 0.693 and model 2 was 0.720.

with SFI. In multivariate analysis, with increased clinical tumor size (OR 1.586, 95% CI 1.305-1.926, $p < 0.001$), collecting system involvement (OR 3.957, 95% CI 1.371-11.417, $p = 0.011$), high NLR (OR 2.032, 95% CI 1.256-3.287, $p = 0.004$) was independent predictor of SFI. (table 3)

To assess predictive power of NLR, we defined prediction model 1 as a model including clinical tumor size and collecting duct involvement. And

Table 4. Univariate and multivariate analysis of factors associated with sinus fat invasion in the patients with ≤ 4 cm renal cell carcinoma

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Gender		0.57		
Male	1 (Ref)			
Female	1.320 (0.506-3.441)			
Age	1.001 (0.963-1.040)	0.996		
BMI	1.113 (0.973-1.274)	0.119	1.093 (0.945-1.265)	0.231
Hypertension		0.934		
No	1 (Ref)			
Yes	1.041 (0.401-2.703)			
Smoking		0.224		
Non-smoker	1 (Ref)			
Current or former smoker	0.534 (0.194-1.467)			
Clinical tumor size	2.219 (1.013-5.412)	0.04	2.165 (1.007-5.300)	0.047
Collecting system involvement		0.15		0.126
Not involved	1 (Ref)		1 (Ref)	
Involved	4.508 (0.579-35.11)		5.153 (0.632-41.990)	
NLR*		0.113		0.193
Low	1 (Ref)		1 (Ref)	
High	2.145 (0.835-5.508)		1.930 (0.717-5.196)	

OR=odds ratio; CI=confidence interval; BMI=body mass index; NLR=neutrophil to lymphocyte ratio

Table 5. Univariate and multivariate analysis of factors associated with sinus fat invasion in the patients with 4cm to 7cm renal cell carcinoma

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Gender		0.57		
Male	1 (Ref)			
Female	1.170 (0.671-2.041)			
Age	1.023 (1.000-1.046)	0.049		
BMI	0.985 (0.907-1.071)	0.729	1.019 (0.995-1.044)	0.122
Hypertension		0.157		
No	1 (Ref)			
Yes	0.678 (0.395-1.162)			
Smoking		0.224		
Non-smoker	1 (Ref)			
Current or former smoker	0.534 (0.194-1.467)			
Clinical tumor size	1.994 (1.449-2.743)	<0.001	1.949 (1.412-2.691)	<0.001
Collecting system involvement		0.043		0.036
Not involved	1 (Ref)		1 (Ref)	
Involved	3.511 (1.041-11.843)		3.753 (1.088-12.943)	
NLR*		0.017		0.193
Low	1 (Ref)		1 (Ref)	
High	1.920 (1.123-3.283)		2.013 (1.150-3.522)	

OR=odds ratio; CI=confidence interval; BMI=body mass index; NLR=neutrophil to lymphocyte ratio

adding to model 1 is defined as model 2. After that we compared AUC of predictive model 1 and 2. (figure 1) AUC of model 1 and model 2 was 0.693 and 0.720. (figure 1)

Table 4 and table 5 shows the results of univariate and multivariate analysis of factors associated with SFI by dividing patients into subgroups according to tumor size. In the patients with 4cm or less RCC, NLR was not associated with SFI, and tumor size was the only predictor of SFI. However, in patients with renal cell carcinoma between 4 cm and 7 cm, NLR was still independent predictor of SFI with clinical tumor size and collecting system involvement.

IV. DISCUSSION

There are relatively many studies related to risk factor of upstaging in clinical T1 stage renal cell carcinoma. The occurrence of upstaging to T3a in clinical T1 renal cell carcinoma were observed at 4.8% to 31% according to some studies.^{3-6,14-17} Nayak et al ¹⁵ reported increasing age, Fuhrman nuclear grade and tumor size is independently associated with risk or renal sinus invasion. Other study reported tumor size, clear cell histologic feature and positive surgical margin is associated with upstaging.⁴ Population bases study also reported similar result. Ghanie et al ¹⁶ reported old age, male, large tumor size and higher Fuhrman grade were independent predictor of upstaging. Except

for the factors mentioned above, R.E.N.A.L. nephrometry score seemed one of the most important factors predicting upstaging. Many studies reported that higher R.E.N.A.L. nephrometry score is significant risk factors associated with upstaging.^{3,5,14}

The R.E.N.A.L. nephrometry score was introduced to quantify anatomical characteristics of renal tumors on CT or MRI.¹⁸ R.E.N.A.L. nephrometry score could be used for differential diagnosing of small renal masses or predicting perioperative outcome in renal cell carcinoma. Some studies showed that it is associated with malignancy and high-grade pathology in the patients with small renal mass.¹⁹⁻²¹ And higher RNS is associated with adverse perioperative outcome such as prolonged warm ischemic time and postoperative complications after partial nephrectomy. There is another scoring system for quantifying anatomical characteristics in CT or MRI, and perioperative aspects and dimensions used for anatomical (PADUA) classification is one of another scoring system. PADUA classification was introduced as standardized classification of renal tumors suitable for nephron-sparing surgery based on their anatomical features and size.²² PADUA classification is also an efficient tool to predicts the risk or postoperative complications. Tyrirtzis et al²³ reported PADUA score is an independent predictor for the risk of complications. They reported the proportion of patients with complications of Clavien score more than 3 was significantly higher in subjects with PADUA score ≥ 8 than in those with Padua score < 8 .

Unlike R.E.N.A.L. nephrometry, PADUA classification scored for a renal sinus invasion. The renal sinus is a cavity within the kidney formed by the extension of the perinephric space into the deep recess located at the medial border of the kidney. The major branches of the renal artery and vein along with the major and minor calices of the collecting system are located within the renal sinus. And with adipose tissue, nerve fibers and varying quantities of adipose tissue, lymphatic channels are one of the structures filling renal sinus.^{24,25} Unlike perirenal tissue, renal sinus is not separated from the renal cortex by a capsule. Therefore, invasion of renal sinus means tumor has more chance to spread. Actually, many studies showed that renal sinus invasion has poor prognosis. Thompson et al ²⁶ reported the cancer specific survival rate of patients with SFI was poorer than patients without SFI. Bertini et al ²⁷ assessed the impact of renal sinus fat sinus invasion on oncologic outcome in pT3a clear cell renal cell carcinoma. They found SFI was not associated with poorer cancer specific survival in the patients with distant metastasis. However, in patients without lymph node or distant metastasis, SFI was significantly associated with cancer specific survival.

Because renal sinus invasion is associated with oncologic outcome, predicting SFI became important to predict the prognosis of RCC patients. CT is gold standard for diagnosing renal cell carcinoma, and it provides many information about tumor such as size, location. And it also provides other information about anatomy of adjacent structures. CT may help to decide T

stage, but there is limitation to diagnosing renal sinus invasion. Some studies reported sensitivity is ranged from 71.0% to 81.8% and specificity is ranged from 71.0% to 91.7%.^{7,28}

Numerous serum inflammation markers, such as CRP, have proven to be good prognostic indicators in patients with a variety of malignancies.⁸⁻¹¹ However, CRP require separate laboratory testing, it is hard to apply to all patients. NLR was used as an alternative marker for systemic inflammation because it correlates with CRP and could be calculated easily with complete blood count.¹² Many studies demonstrated NLR was a simple biomarker with a prognostic value for RCC. de Martino et al¹³ reported high preoperative NLR is associated with poorer disease-free survival (DFS) in patients with localized RCC. Viers et al²⁹ showed preoperative NLR is significant prognostic factors for OS as well as DFS of localized RCC. In locally advanced or metastatic RCC, higher preoperative NLR was associated with poorer OS in many studies.³⁰⁻³²

There are few studies about predictive factors of SFI. In this study, preoperative NLR is associated with SFI in addition to clinical tumor size and collecting system involvement. Adding preoperative NLR to predictive model with tumor size in preoperative imaging and collecting duct involvement, AUC were increased from 0.693 to 0.720. In the study previously published by our institution, tumor size and collecting duct involvement were also associated with SFI.³³ And it reported there were equivalent oncologic outcome between partial nephrectomy and radical nephrectomy when clear surgical margins had

been obtained in the patients underwent partial nephrectomy. Therefore, if the NLR value is high and the suspicion of SFI is suspected, it is necessary to resect more deeply to obtain a clear surgical margin.

After patients were divided into 2 groups by the clinical tumor size of 4cm, subgroup analysis was performed. With clinical tumor size and collecting system involvement, NLR was still independent predictor of SFI in tumors 4cm to 7cm cm in size. However, NLR was not associated with SFI in the patients with 4cm or less RCC. When this result is considered, the predictive ability of NLR for SFI in the clinical T1 stage RCC seemed to have limitation.

The NLR has been known as the prognostic factor in numerous cancers including RCC, although the specific mechanism for this relationship is not understood completely. Several studies have reported that chronic inflammation is the key role in carcinogenesis.³⁴ Neutrophils play a major role in pro-tumoral activity by secreting substance such as reactive oxygen derivative or vascular endothelial growing factor.³⁵ Whereas lymphocytes reflect cell-mediated immunity which has antitumoral properties.³⁶ Therefore, a high NLR means a possible contribution to aggressive tumor biology and progression, and poor survival.

Other studies showed tumor-derived inflammation can increase myelopoiesis with defective myeloid cell differentiation and proliferation by regulating the bone marrow and spleen, leading to the accumulation of immature myeloid cells in the peripheral circulation.³⁷ Myeloid cells are known

to play a critical role in tumor pathogenesis by promoting cancer cell proliferation, tumor angiogenesis, cell invasion, and metastasis. In the context of cancer-mediated myelopoiesis, the neutrophil precursors myelocytes and promyelocytes proliferate and are released into the peripheral blood. Neutrophils are the most abundant granulocytes, which account for most peripheral white blood cells.³⁸ Thus, the prognostic and predictive value of peripheral neutrophils as an independent index or as part of the NLR in cancers is apparent, and enhanced neutrophil responses and/or lymphocyte suppression, leading to a high NLR, might promote tumor progression and inhibit the antitumor immune response.

In the context of locally advanced renal cell carcinoma, Sejima et al³⁹ reported the association between the NLR and local Fas ligand (FasL) expression. FasL is a surface receptor involved in cell apoptosis via the action of the cytotoxic T cell. A low NLR was correlated with a high level expression of FasL, and they are related with improved overall survival.

Our study has some limitations because its retrospective and non-randomized nature. We tried to overcome the drawback by leaving the presence of SFI judgment in pre-operative images to two doctors without information about SFI. Because our result was derived from data of single institution, it may not be generalizable. So further prospective and multicenter studies are needed to confirm our results.

V. CONCLUSION

With tumor size in preoperative CT and collecting system involvement, preoperative NLR is the independent prognostic factor of pathologic SFI in the patients with renal cell carcinomas of 7cm or less presumed SFI on preoperative imaging. It is recommended to resect more deeply to obtain a clear surgical margin if the NLR value is high and the suspicion of SFI is suspected. However, the role of NLR to predict SFI seems to be limited.

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\ABSTRACT(IN KOREAN)

수술 전 영상 검사에서 신동 침범이 의심되는 7cm 이하의
신세포암 환자에서 조직학적 신동 침범을 예측할 수 있는
인자로써의 호중구-림프구 비율

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목적: 수술 전 영상 검사에서 신동 침범이 의심되는 신종양이 조직학적으로는 신동을 침범하지 않는 경우가 많이 있다. 최근 신장암을 비롯한 다양한 암에서 예후와 연관이 있다고 알려진 호중구-림프구 비율(neutrophil-lymphocyte ratio, NLR)이 조직학적 신동 침범을 예측할 수 있는지 확인해보고자 한다.

대상 및 방법: 2005년 11월부터 2014년 12월까지 본원에서 7cm 이하의 신동 침범이 의심되는 신세포암으로 근치적 혹은 부분 신절제술을 받은 환자 중 NLR에 영향을 끼칠 수 있는 요인을 갖고 있는 환자들을 제외한 476명의 환자를 대상으로 연구를 진행하였다. 그리고 대상 환자들의 연령, 성별, 체질량지수, 과거력, 흡연 여부 및 술 전 NLR을 조사하였다. 이들 인자들과 조직학적 신동 침범 여부 사이에 연관성이 있는지 확인하기 위해 로지스틱 회귀분석을 이용하였다.

결과: NLR 값은 receiver operation characteristic(ROC) curve를 이용하여 1.98로 정하였다. 술 후에 조직학적으로 신동 침범이 확인된 환자는 총 93명(19.5%)이었다. 신동 침범이 있는 환자군에서 임상적 종양의 크기가 더 컸으며, 높은 NLR 값을 가지고 있었다. 또한 신동 침범이 있는 환자군에서 병리적 종양 크기가 더 컸고, Fuhrmann nuclear grade도 더 높은 것으로

나타났다. 단변량 분석에서 환자의 연령(Odds ratio (OR) 1.019, $p=0.05$), 임상적 종양 크기(OR 1.645, $p<0.001$), 집뇨계 침범 및 높은 NLR 값(OR 2.087, $p=0.002$)이 신동 침범과 연관이 있는 것으로 나타났다. 다변량 분석에서는 임상적 종양 크기(OR 1.586, $p<0.001$), 집뇨계 침범(OR 3.957, $p=0.011$)과 함께 높은 NLR 값(OR 2.032, $p=0.004$)이 신동 침범의 유의한 예측인자인 것으로 나타났다. 임상적 종양 크기와 집뇨계 침범 여부를 포함한 예측 모델을 모델 1로, 여기에 NLR을 추가한 것을 모델 2로 정하고 각 예측 모델의 신동 침범의 예측 능력을 확인하기 위해 ROC curve를 그렸을 때, area under curve는 모델 1과 모델 2에서 0.693과 0.720으로 확인되었다. 종양의 크기를 4cm을 기준으로 하여 두 그룹으로 나누어 하위 그룹 분석을 시행하였을 때, 4cm에서 7cm 사이의 신세포암에서는 NLR은 여전히 신동 침범의 독립적인 예측인자인 것으로 나타났다. 하지만 4cm 이하의 신세포암에서는 NLR이 신동 침범과 관련이 없는 것으로 나타났다.

결론: NLR은 임상적인 종양 크기와 집뇨계 침범 여부와 함께 실제 신동 침범과 통계적으로 유의한 관계가 있는 것으로 관찰되었지만 신동 침범 예측 능력은 제한적인 것으로 보인다.

핵심되는 말: 신세포암, 신동 침범, 신절제술, 림프구, 호중구