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Preoperative Lung Immune Prognostic Index (LIPI) Predicts Postoperative Outcomes in Clear Cell Renal Cell Carcinoma: A Multicenter Study

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Abstract

Background: Lactate dehydrogenase (LDH) and derived neutrophil-to-lymphocyte ratio (dNLR) are key prognostic factors for renal cancer. However, the association between the Lung Immune Prognostic Index (LIPI), based on dNLR and LDH, and renal cancer prognosis remains unclear. This study evaluates the prognostic value of LIPI for recurrence and survival in clear cell renal cell carcinoma (ccRCC) after nephrectomy.

Methods: This retrospective study included 687 ccRCC patients who underwent radical or partial nephrectomy at three medical centers. Patients were stratified into good and intermediate/poor (int./poor) LIPI groups based on dNLR and LDH. Propensity score matching (PSM) was performed. Recurrence-free survival (RFS) and overall survival (OS) were analyzed using Kaplan–Meier curves and Cox models. Model discrimination was evaluated using C-indices, and subgroup and center-stratified analyses tested robustness.

Results: A total of 687 patients were included, with 491 classified into the good LIPI group and 196 into the int./poor group. After 1:1 PSM, each group comprised 196 patients. In the Kaplan-Meier survival analysis, the int./poor LIPI group exhibited significantly worse RFS

and OS both before (RFS: P < 0.001; OS: P < 0.001) and after PSM (RFS: P < 0.001; OS: P < 0.001). In the multivariate Cox regression analysis post-PSM, int./poor LIPI remained independently associated with increased risk of recurrence (HR = 2.156, 95% CI: 1.349–3.449, P = 0.001) and mortality (HR = 3.238, 95% CI: 1.437 - 7.298, P = 0.005).

Conclusion: Preoperative LIPI predicts ccRCC prognosis after nephrectomy. Patients in the good LIPI group exhibit significantly better RFS and OS.

Trial registration: The study was registered at ClinicalTrials.gov (NCT06775574).

Keywords clear cell renal cell carcinoma, lung immune prognostic index, partial nephrectomy, radical nephrectomy, neutrophil-to-lymphocyte ratio

Background

Clear cell renal carcinoma (ccRCC) accounts for approximately 80% of malignant renal tumors and is characterized by an aggressive phenotype, making it the most common histological subtype of renal cell carcinoma (RCC)(1). Surgical resection remains the most effective treatment for RCC and significantly improves survival outcomes in patients with RCC(2). However, approximately 20%-30% of patients will experience recurrence following nephrectomy(3, 4). Therefore, identifying potential biomarkers to select RCC patients who are likely to benefit from surgical treatment and to guide subsequent therapeutic decisions is crucial.

The two main isoforms of lactate dehydrogenase (LDH), LDHA and LDHB, are thought to be associated with immune infiltration in ccRCC. Upregulation of LDHA has been shown to predict poor prognosis in ccRCC patients(5, 6). In recent years, numerous studies have

demonstrated that LDH levels are correlated with prognosis in RCC(7, 8). Additionally, a meta-analysis incorporating 76 studies found that elevated serum LDH levels (LDH > 245 U/L) can serve as a prognostic biomarker in various solid tumors, particularly melanoma, prostate cancer, and RCC. Increasing evidence supports the critical role of systemic inflammatory responses in the formation and progression of malignant tumors(9). Among these, the neutrophil-to-lymphocyte ratio (NLR) and higher derived neutrophil-to-lymphocyte ratio (dNLR) levels have been shown to be negatively associated with overall survival (OS), cancer-specific survival (CSS), disease-free survival (DFS), and progression-free survival (PFS) in urological cancers. These markers may serve as independent prognostic predictors for urological tumors(10).

The lung immune prognostic index (LIPI), derived from dNLR and LDH, is associated with resistance to immune checkpoint inhibitors and serves as a biomarker for predicting the prognosis of advanced non-small cell lung cancer patients(11). Subsequent studies have increasingly demonstrated that LIPI not only holds predictive value for the efficacy of immunotherapy in solid tumors such as renal cell carcinoma, melanoma, and breast cancer(12, 13), but is also associated with prognosis in conditions like metastasis in osteosarcoma(14), postoperative survival in esophageal squamous cell carcinoma(15), postoperative outcomes following radical treatment of urothelial bladder cancer(16), and survival after pancreatic cancer resection(17). These previous studies underscore the potential value of LIPI in predicting outcomes across a variety of treatment settings, including both surgical and non-surgical interventions.

However, the prognostic value of LIPI in postoperative ccRCC patients remains unclear.

Therefore, this study aims to investigate the predictive role of preoperative LIPI in the postoperative recurrence of ccRCC and further explore whether LIPI impacts postoperative survival.

Methods

Study Design and Patient Cohort

This multicenter, retrospective study included patients with ccRCC who underwent radical or partial nephrectomy at three medical centers in China. The study was approved by the Institutional Review Boards of all participating institutions, which granted waivers for informed consent due to its retrospective nature. The research adhered to the ethical principles of the Declaration of Helsinki (2013 revision). The study was registered at ClinicalTrials.gov (NCT06775574).

Inclusion and Exclusion Criteria

The inclusion criteria for patients were: (a) Pathologically diagnosed with ccRCC; (b) Underwent radical or partial nephrectomy (without neoadjuvant or other perioperative systemic therapy). Patients were excluded based on the following criteria: (a) presence of concurrent malignancies; (b) missing data or failure to follow-up; (c) presence of distant metastasis (M1) **(Figure 1)**.

Data Collection and Study Variables

For all eligible patients, demographic, clinical, and pathological data were collected from electronic medical records. The most recent preoperative complete blood count and biochemical tests within one week prior to surgery were used to calculate study variables. The

dNLR was calculated as: absolute neutrophil count / (white blood cell count – absolute neutrophil count). LDH levels were recorded in U/L(18). The estimated glomerular filtration rate (eGFR) was calculated using the modified MDRD equation for the Chinese population: 175 × (Scr)^−1.234 × (age)^−0.179 × 0.79 (if female), with serum creatinine converted to mg/dL when necessary. Pathological staging was performed according to the latest European Association of Urology (EAU) guidelines for ccRCC(19).

Patients were stratified according to the original Lung Immune Prognostic Index (LIPI) proposed by Mezquita et al.(11), which combines the derived neutrophil-to-lymphocyte ratio (dNLR) and serum lactate dehydrogenase (LDH). Consistent with prior immuno-oncology studies, the dNLR cutoff was set at 3(20). Patients with dNLR < 3 and LDH < 245 U/L were classified as the good LIPI group, those with one adverse factor (dNLR ≥ 3 or LDH ≥ 245 U/L) as the intermediate group, and those with both adverse factors as the poor group. Given the limited number of patients in the poor group, the intermediate and poor groups were combined into a single intermediate/poor (int./poor) group for the primary analyses.

Study Endpoints

The primary endpoints were recurrence-free survival (RFS) and OS. RFS was defined as the time from nephrectomy to the first documented evidence of local recurrence or distant metastasis. OS was defined as the time from nephrectomy to death from any cause. Patients alive at last follow-up were censored at their most recent contact date.

Follow-up Protocol and Study Timeframe

Patients underwent nephrectomy between April 7, 2016 and July 10, 2024. The final follow-up date was December 31, 2024. Follow-up was conducted through scheduled

outpatient visits and structured telephone interviews. Clinical assessments included physical examination, routine blood tests, and imaging to detect local recurrence or distant metastasis, in accordance with institutional surveillance protocols.

Statistical Analysis

Continuous variables were expressed as mean ± SD for normally distributed data or median (IQR) for non-normally distributed data, and were compared using Student's t-test or the Mann–Whitney U test, as appropriate. Categorical variables were compared using the chi-square test. To reduce baseline confounding, 1:1 propensity score matching (PSM) was performed using the optimal matching method without replacement. The matching model included clinically relevant covariates. Balance between the matched groups was assessed using standardized mean differences (SMD), with SMD ≤ 0.1 indicating adequate balance(21). Survival outcomes (RFS and OS) were estimated using the Kaplan-Meier method and compared with the log-rank test. To identify potential confounders for multivariable adjustment, we constructed a directed acyclic graph (DAG) based on prior knowledge and clinical plausibility **(Figure S1)**. Univariate and multivariate Cox proportional hazards regression models were used to identify independent prognostic factors. Multicollinearity among covariates was assessed using variance inflation factors (VIFs). VIF > 10 is considered indicative of severe multicollinearity in the regression model. Variables with $P < 0.1$ in univariate analysis were considered for inclusion in the multivariate model. The discriminative ability of the models was evaluated using Harrell's concordance index (C-index). A bootstrap-corrected C-index was calculated using 1,000 bootstrap resamples to reduce overfitting bias. Sensitivity analyses included subgroup analyses stratified by

individual medical center to assess the robustness and generalizability of the findings. All statistical analyses were performed using R software (version 4.0.2). A two-sided P-value of less than 0.05 was considered statistically significant.

Results

Patient baseline characteristics

This retrospective study included 687 ccRCC patients who underwent partial or radical nephrectomy (The flowchart can be found in **Figure 1**). The clinical characteristics of the patients are summarized in **Table 1**. Among the cohort, 442 were male and 245 were female, with a median age of 57 years, and the majority of patients (72.6%) were under 65 years of age. In our study, 329 patients underwent radical nephrectomy, while 358 patients underwent partial nephrectomy.

Most patients were classified as having pT1 disease, accounting for 528 patients (76.9%), while 14.3%, 7.6%, and 1.3% of patients were staged as pT2, pT3, and pT4, respectively. Pathologically, 95 patients (13.8%) had tumor hemorrhage, 87 patients (12.6%) had cystic changes, and 54 patients (7.9%) had tumor necrosis. The surgical margin status of 28 patients (4.1%) was positive. Regarding dNLR, 552 patients (80.3%) were classified as having a low dNLR (< 3), while 135 patients (19.7%) had a high dNLR (≥ 3). For LDH levels, 607 patients (88.4%) had low LDH (< 245 U/L), while 80 patients (11.6%) had high LDH (≥ 245 U/L). The distribution of LIPI scores was as follows: 71.5% of patients were classified as having a good LIPI, 26.1% as int., and 2.5% as poor. We combined the int. and poor groups into a single category, referred to as the int./poor group.

Before PSM, there were statistically significant differences between the two groups in terms of WHO/ISUP classification, histological necrosis, tumor size, hemoglobin levels, eGFR, pT stage, eastern cooperative oncology group performance status (ECOG) performance status, and Surgical margin status (all $P < 0.05$). Covariate balance before and after PSM was assessed using SMDs and visualized with a Love plot **(Figure S2)**. Although histological necrosis did not reach the predefined SMD threshold of ≤ 0.1, their imbalances were substantially reduced, indicating mild residual imbalance. **(Table 1)**.

Survival Analysis

During the follow-up period, 101 patients (14.7%) experienced postoperative recurrence, and 35 patients (5.1%) died. Because fewer than 50% of patients experienced the event during follow-up, the median survival time was not reached. Before PSM, the RFS and OS of the int./poor LIPI group were significantly lower than those of the good LIPI group, with statistical significance ($P < 0.001$ for both RFS and OS) **(Figure 2A, B)**. Similarly, after PSM, the RFS and OS of the int./poor LIPI group remained significantly lower than those of the good LIPI group ($P < 0.001$ for both RFS and OS) **(Figure 2C, D)**. Additionally, we have also generated Kaplan-Meier survival curves using the original three-category LIPI classification **(Figure 3).**

Univariate and multivariate survival analysis of RFS and OS

Prior to performing the univariate and multivariate analyses, the VIF for each variable was calculated to assess multicollinearity, we found that the VIF was less than 5 for all variables **(Table S1)**. In univariate and multivariate survival analysis, we included the following variables: age, gender, BMI, WHO/ISUP classification, bleeding, cystic tumor, histological

necrosis, eGFR, pT stage, ECOG performance status, surgical margin status, and LIPI groups. Before PSM analysis, in univariate analysis, WHO/ISUP classification 3 or 4, histological necrosis, eGFR, pT stage 4, ECOG performance status ≥ 1, positive surgical margin, and LIPI groups were identified as potential predictors of RFS. However, multivariate analysis demonstrated that only eGFR (HR: 0.981, 95% CI: 0.970 - 0.992, P < 0.001), pT stage 4 (ref. Stage 1, HR: 4.909, 95% CI: 2.103 - 11.460, P < 0.001), ECOG performance status ≥ 1 (ref. < 1, HR: 4.430, 95% CI: 2.921 - 6.717, P < 0.001), positive surgical margin (HR: 3.010, 95% CI: 1.624 - 5.579, P < 0.001), and the int./poor LIPI group (ref. good group, HR: 2.262, 95% CI: 1.485 - 3.446, P < 0.001) were significantly associated with shorter RFS (**Table S2**). In univariate regression analysis, histological necrosis, pT stage, ECOG performance status, positive surgical margin, and LIPI groups were identified as potential predictors of OS. Multivariate regression analysis revealed that ECOG performance status ≥ 1 (ref. < 1, HR: 2.339, 95% CI: 1.079 - 5.072, P = 0.031), positive surgical margin (HR: 6.859, 95% CI: 3.038 - 15.484, P < 0.001), and the int./poor LIPI group (ref. good group, HR: 4.820, 95% CI: 2.185 - 10.630, P < 0.001) were significantly associated with shorter OS (**Table S3**).

In the univariate regression analysis of RFS after PSM, histological necrosis, eGFR, pT stage, ECOG performance status, surgical margin status, dNLR, LDH, and the int./poor group were identified as potential predictors of shorter RFS. In the multivariate regression analysis, eGFR (HR: 0.983, 95% CI: 0.972 - 0.995, P = 0.004), pT stage 4 (ref. Stage 1, HR: 4.893, 95% CI: 2.035 - 11.764, P < 0.001), ECOG performance status ≥ 1 (ref. < 1, HR: 4.351, 95% CI: 2.746 - 6.893, P < 0.001), positive surgical margin (HR: 3.054, 95% CI: 1.631 - 5.717, P <

0.001), and the int./poor LIPI group (ref. good group, HR: 2.156, 95% CI: 1.349 - 3.449, P < 0.001) were identified as independent predictors of shorter RFS **(Table 2)**.

In the univariate regression analysis of OS after PSM, tumor pT stage, ECOG performance status, positive surgical margin, and the int./poor group were identified as potential predictors of shorter OS. In the multivariate regression analysis, ECOG performance status ≥ 1 (ref. < 1, HR: 2.505, 95% CI: 1.165 - 5.387, P = 0.019), positive surgical margin (HR: 7.249, 95% CI: 3.368 - 15.602, P < 0.001), and the int./poor group (ref. good group, HR: 3.238, 95% CI: 1.437 - 7.298, P = 0.005) were identified as independent predictors of shorter OS **(Table 3)**. Given the low number of death events, we repeated Cox regression for OS with fewer variables. The LIPI groups remained independently significant (int./poor ref. good, HR: 3.238, 95% CI: 1.437 - 7.298, P = 0.005) **(Table S4)**.

Subgroup Analysis

To further evaluate the prognostic value of LIPI across different patient populations, we performed subgroup analyses based on baseline clinical characteristics. Consistent results for both RFS and OS were observed across LIPI groups before and after PSM. HRs and corresponding confidence intervals for each subgroup were estimated using univariate Cox regression models.

Before PSM, consistent prognostic trends favoring the good LIPI group were observed across most subgroups for both RFS and OS. Although numerically stronger associations were observed in several subgroups, no statistically significant interactions between LIPI and survival outcomes were detected (all interaction P-values > 0.05) **(Figure S3)**.

After PSM, subgroup analysis for RFS revealed a potential interaction between LIPI grouping and history of cardiovascular disease, whereas no such interactions were found in other subgroups. For OS, the good LIPI group was consistently associated with a lower risk of death across all subgroups, although some comparisons did not reach statistical significance **(Figure S4)**.

In addition, we conducted stratified survival analyses by medical center and plotted institution-specific survival curves. The prognostic trends of LIPI remained consistent across the three participating hospitals **(Figure S5)**.

Incremental prognostic value of combined clinical variables

To assess discriminative ability, we constructed Cox models and calculated C-indices with 95% CIs for individual and combined variables in predicting RFS and OS **(Figure 4 and Figure 5; Table S5 and Table S6)**. We observed consistent patterns between the apparent C-index and bootstrap-corrected C-index **(Figure S6 and Figure S7)**. Single variables showed limited predictive value (e.g., ECOG, pT stage, eGFR, surgical margin status, and LIPI classification), whereas their combinations yielded stepwise improvement. The full model achieved the highest bootstrap-corrected C-index (RFS: 0.775 [0.727–0.830]; OS: 0.777 [0.706–0.854]). Among individual predictors for OS, LIPI classification performed best (bootstrap-corrected C-index: 0.662 [0.594–0.734]).

Discussion

Surgical resection remains the cornerstone of treatment for localized and locally advanced RCC, offering the highest potential for cure(2). However, not all patients derive equal benefit

from nephrectomy, and recurrence remains a concern for a significant subset(3, 4). Therefore, accurate postoperative risk stratification is essential for guiding surveillance and therapeutic decisions. Existing models such as UISS, SSIGN, and the Leibovich score offer some prognostic value(22-24), yet they rely heavily on pathological features and lack integration of systemic biomarkers that reflect the host's inflammatory or immune status(25-27).

In our cohort, conventional pathological variables, including pT stage and WHO/ISUP classification, showed limited independent prognostic significance in multivariable analyses. Furthermore, our analysis of the prognostic impact of positive surgical margins revealed that patients with positive surgical margins had nearly four-fold higher risk of recurrence and almost six-fold higher risk of death compared to those with negative margins, consistent with the 2025 update of the European Association of Urology (EAU) Guidelines on Renal Cell Carcinoma, which report a positive surgical margins incidence of 2-8% and a markedly increased local recurrence rate (16% vs. 3% for negative margins)(28). However, positive surgical margins is an invasive, postoperative pathological finding that cannot be assessed preoperatively and offers limited utility for early risk stratification or treatment planning. The attenuated prognostic impact of pT stage and tumor grade in our cohort likely reflects the predominance of early-stage, organ-confined disease, low metastatic burden, and high-quality surgical resection, all of which are characteristic of contemporary renal cancer series(29). The LIPI, combining dNLR and LDH, has emerged as a useful prognostic marker in multiple malignancies, particularly in the setting of immunotherapy(12, 13, 25). Our study is the first to demonstrate its independent prognostic value in surgically treated ccRCC patients. After adjustment for multiple clinicopathologic factors, an int./poor LIPI was significantly

associated with higher risks of recurrence and mortality. This suggests that preoperative systemic inflammation and metabolic stress, reflected by dNLR and LDH respectively, may play a critical role in tumor progression even after curative-intent surgery(10, 30, 31). Preoperative LIPI may reflect not only tumor burden itself, but also a persistent host-related systemic inflammatory and metabolic status that is not completely eliminated after tumor resection (32). Previous studies have shown that inflammation-based biomarkers remain associated with recurrence and survival even in surgically treated malignancies, potentially reflecting occult micrometastatic disease, impaired antitumor immunity, and underlying tumor aggressiveness(15, 33, 34). Therefore, the prognostic value of preoperative LIPI may extend beyond the presence of the primary tumor alone. Mechanistically, an elevated dNLR reflects a shift toward neutrophil-mediated immunosuppression and lymphopenia, conditions that facilitate immune evasion by tumors. Meanwhile, elevated LDH indicates increased glycolytic activity and tumor hypoxia, both of which promote angiogenesis and metastasis. These processes together contribute to a more aggressive tumor microenvironment.

Compared with individual markers, the LIPI offers a composite measure that may better capture the complexity of tumor-host interactions. Given its accessibility and ease of calculation from routine blood tests, LIPI could be readily integrated into postoperative workflows. It may help clinicians identify patients who require closer surveillance, consider early adjuvant therapy, or enroll in clinical trials. In particular, patients with an unfavorable LIPI may represent a subgroup at higher risk of postoperative recurrence and mortality who could potentially benefit from intensified surveillance imaging and follow-up strategies. Furthermore, in selected borderline or equivocal clinical scenarios, LIPI may provide

additional information to support decisions regarding closer monitoring or consideration for adjuvant therapy. In line with previous findings in metastatic RCC and other solid tumors, our results suggest that elevated LIPI identifies a biologically aggressive phenotype, potentially resistant to conventional treatments(35, 36). The consistent prognostic effect across subgroups further supports its robustness.

In addition, we constructed simplified models incorporating clinical variables and observed that multivariable models offered superior discriminative performance in predicting postoperative outcomes. Future research should investigate the integration of LIPI with other prognostic tools, such as radiomic signatures or genomic classifiers, to establish a more comprehensive and individualized risk stratification system. Furthermore, longitudinal monitoring of LIPI may provide insights into treatment response and support clinical decision-making regarding systemic therapy. Prospective studies are needed to validate the prognostic and predictive utility of LIPI across diverse RCC populations.

Nevertheless, this study has several limitations. First, its retrospective design may introduce inherent selection bias and residual confounding despite the use of propensity score matching and multivariable adjustment. In addition, mild residual imbalance remained for certain variables after PSM, which should be considered when interpreting the findings. Second, several potentially relevant clinicopathological and inflammatory variables, including sarcomatoid, rhabdoid differentiation and C-reactive protein, were unavailable(36-38). Third, the relatively short follow-up duration limited the assessment of long-term survival outcomes and precluded reliable estimation of median survival times. In addition, the relatively small number of OS events may have reduced the stability of multivariable estimates, although a

reduced-variable Cox model yielded consistent results. Fourth, LIPI was assessed only at a single preoperative time point, and longitudinal changes in LIPI after surgery were not evaluated. Fifth, although bootstrap correction was performed to reduce optimism in model performance estimation, the prognostic models were not externally validated, and the reported predictive performance may therefore remain optimistic. Finally, because this was a multicenter retrospective study, variations in clinical management and follow-up strategies across institutions may have introduced additional heterogeneity. Future prospective multicenter studies with longer follow-up durations, external validation cohorts, longitudinal biomarker assessment, and incorporation of molecular and inflammatory biomarkers are warranted to further validate and extend our findings.

In conclusion, the LIPI is a readily accessible, non-invasive biomarker that can aid in identifying ccRCC patients at higher risk for recurrence and mortality after nephrectomy. Incorporating LIPI into existing prognostic frameworks could enhance personalized management strategies in RCC.

Ethics approval and consent to participate

The ethical approvals for this study were provided by the Institutional Review Board of Wuhan Union Hospital, the Institutional Review Board of the Second Affiliated Hospital of Fujian Medical University, and the Institutional Review Board of Jiangsu Provincial People's Hospital. The ethics committees of all three institutions independently reviewed the study protocol and granted waivers for informed consent due to its retrospective nature.

Consent for publication

This retrospective study utilized de-identified patient data, and the requirement for informed consent was waived by three institutional review boards.

Availability of data and materials

The raw data used in the study can be further requested; for specific inquiries, please contact the corresponding author.

Competing interests

All authors declare no conflict of interest.

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Authors' contributions

Z.P. (Zhenliang Pan): Writing - original draft, Visualization, Methodology; Y.L. (Yi Li): Writing - original draft, Methodology; J.L. (Jie Lou): Data curation, Formal analysis, Methodology; Y.G. (Yusheng Guo): Writing - original draft, Formal analysis; S.S. (Shuai Shan): Data curation; S.J. (Shanshan Jiang): Data curation; Q.H. (Qingliu He): Resources, Supervision, Writing - original draft; G.Z. (Guofeng Zhou): Writing - review & editing, Validation; L.Y. (Lian Yang): Writing - review & editing, Validation, Funding acquisition. All authors have read and approved the final version of the manuscript.

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List of abbreviations

Cancer-specific survival (CSS)

Clear cell renal cell carcinoma (ccRCC)

Derived neutrophil-to-lymphocyte ratio (dNLR)

Disease-free survival (DFS)

Eastern cooperative oncology group performance status (ECOG)

European Association of Urology (EAU)

Estimated Glomerular filtration rate (eGFR)

Hazard ratios (HRs)

Institutional review board (IRB)

Interquartile range (IQR)

Lactate dehydrogenase (LDH)

Lung Immune Prognostic Index (LIPI)

Metastasis-free survival (MFS)

Neutrophil-to-lymphocyte ratio (NLR)

Overall survival (OS)

Propensity score matching (PSM)

Reactive oxygen species (ROS)

Recurrence-free survival (RFS)

Renal cell carcinoma (RCC)

Standardized mean difference (SMD)

Figure legends

Figure 1. The flowchart of patients inclusion.

Figure 2. Kaplan-Meier curve of RFS (A) and OS (B) in the LIPI int./poor group (blue) and LIPI good group (red) before PSM analysis; Kaplan-Meier curve of RFS (C) and OS (D) in two groups after PSM analysis. Analyses were conducted using LogRank tests.

Figure 3. Kaplan-Meier curves for three-category LIPI classification (Good / Intermediate / Poor). (A) Recurrence-free survival and (B) overall survival .

Figure 4. **Bootstrap-corrected concordance indices (C-indices) with 95% confidence intervals for recurrence-free survival (RFS) prediction across Cox proportional hazards models.** RFS, recurrence-free survival; eGFR, estimated glomerular filtration rate; pT stage, pathological tumor stage; ECOG, Eastern Cooperative Oncology Group; LIPI, Lung Immune Prognostic Index; SMS, surgical margin status.

Figure 5. Bootstrap-corrected concordance indices (C-indices) with 95% confidence intervals for overall survival (OS) prediction across Cox proportional hazards models. OS, overall survival; ECOG, Eastern Cooperative Oncology Group; LIPI, Lung Immune Prognostic Index; SMS, surgical margin status.

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Table 1. Baseline Characteristics of Patients Before and After PSM

	Before PSM				After PSM		
	Good N = 491	**Int./Poor N = 196**	**SMD**	**p-value**	**Good N = 196**	**Int./Poor N = 196**	**SMD**
± SD	57 ± 11	58 ± 11	0.148	0.084	59 ± 11	58 ± 11	-0.022
				0.711			
	173 (35%)	72 (37%)	0.031		74 (38%)	72 (37%)	-0.021
	318 (65%)	124 (63%)	-0.031		122 (62%)	124 (63%)	0.021
				0.418			
	351 (71%)	134 (68%)	-0.067		125 (64%)	134 (68%)	0.099
	140 (29%)	62 (32%)	0.067		71 (36%)	62 (32%)	-0.099
fication, n (%)				**0.002**			
	56 (11%)	11 (5.6%)	-0.252		15 (7.7%)	11 (5.6%)	-0.089
	307 (63%)	107 (55%)	-0.159		113 (58%)	107 (55%)	-0.061
	110 (22%)	67 (34%)	0.248		58 (30%)	67 (34%)	0.097
	18 (3.7%)	11 (5.6%)	0.085		10 (5.1%)	11 (5.6%)	0.022
	66 (13%)	29 (15%)	0.038	0.642	33 (17%)	29 (15%)	-0.057

	Before PSM				After PSM		
	Good N = 491	**Int./Poor N = 196**	**SMD**	**p-value**	**Good N = 196**	**Int./Poor N = 196**	**SMD**
%)	63 (13%)	24 (12%)	-0.018	0.835	28 (14%)	24 (12%)	-0.062
sis, n (%)	26 (5.3%)	28 (14%)	0.257	**<0.001**	19 (9.7%)	28 (14%)	0.131
(%)				0.227			
	263 (54%)	95 (48%)	-0.102		97 (49%)	95 (48%)	-0.020
	228 (46%)	101 (52%)	0.102		99 (51%)	101 (52%)	0.020
	42 (8.6%)	23 (12%)	0.099	0.198	23 (12%)	23 (12%)	0.000
%)	174 (35%)	70 (36%)	0.006	0.946	72 (37%)	70 (36%)	-0.021
g, n (%)	69 (14%)	32 (16%)	0.062	0.447	34 (17%)	32 (16%)	-0.028
, mean ± SD	134 ± 24	122 ± 20	-0.617	**<0.001**	123 ± 19	122 ± 20	-0.024
), mean ± SD	227 ± 71	227 ± 80	-0.004	0.963	228 ± 78	227 ± 80	-0.014
73 m²), mean ± SD	91 ± 14	83 ± 20	-0.358	**<0.001**	85 ± 16	83 ± 20	-0.097
				0.004			
	393 (80%)	135 (69%)	-0.241		133 (68%)	135 (69%)	0.022
	65 (13%)	33 (17%)	0.096		37 (19%)	33 (17%)	-0.055
	29 (5.9%)	23 (12%)	0.181		23 (12%)	23 (12%)	0.000
	4 (0.8%)	5 (2.6%)	0.110		3 (1.5%)	5 (2.6%)	0.065
				<0.001			
	431 (88%)	152 (78%)	-0.245		156 (80%)	152 (78%)	-0.049
	60 (12%)	44 (22%)	0.245		40 (20%)	44 (22%)	0.049
tatus, n (%)				**0.032**			
	476 (97%)	183 (93%)	-0.144		185 (94%)	183 (93%)	-0.041
	15 (3.1%)	13 (6.6%)	0.144		11 (5.6%)	13 (6.6%)	0.041

Abbreviations: PSM, propensity score matching; SMD, Standardized Mean Difference; Int., intermediate; SD, standard deviation; BMI, body mass index; PN, partial nephrectomy; RN, radical nephrectomy; eGFR, estimated glomerular filtration rate; ECOG, Eastern Cooperative Oncology Group.

Table 2. Univariate and Multivariate Cox Proportional Hazards Analyses for RFS After PSM

Parameter	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Age	1.011 (0.991 - 1.031)	0.294		

Gender				
Female	Reference			
Male	1.280 (0.808 - 2.030)	0.293		
BMI				
< 25 kg/m^2	Reference			
≥ 25 kg/m^2	0.713 (0.434 - 1.171)	0.181		
WHO/ISUP classification				
I	Reference		Reference	
II	1.959 (0.469 - 8.176)	0.356	1.212 (0.285 - 5.145)	0.795
III	4.358 (1.051 - 18.066)	**0.043**	1.767 (0.417 - 7.498)	0.440
IV	8.452 (1.850 - 38.616)	**0.006**	3.792 (0.805 - 17.870)	0.092
Bleeding				
No	Reference			
Yes	0.954 (0.517 - 1.761)	0.880		
Cystic tumour				
No	Reference			
Yes	0.574 (0.265 - 1.247)	0.161		
Histological necrosis				
No	Reference		Reference	
Yes	2.136 (1.236 - 3.693)	**0.007**	1.495 (0.832 - 2.687)	0.178
eGFR	0.982 (0.970 - 0.993)	**0.002**	0.983 (0.972 - 0.995)	**0.004**
pT				
1	Reference		Reference	
2	1.011 (0.556 - 1.838)	0.971	0.829 (0.450 - 1.528)	0.548
3	1.428 (0.759 - 2.686)	0.269	1.042 (0.536 - 2.027)	0.903
4	7.794 (3.517 - 17.273)	**< 0.001**	4.893 (2.035 - 11.764)	**< 0.001**
ECOG				
0	Reference		Reference	
≥1	4.957 (3.203 - 7.671)	**< 0.001**	4.351 (2.746 - 6.893)	**< 0.001**
Surgical margin status				
Negative	Reference		Reference	
Positive	3.118 (1.723 - 5.644)	**< 0.001**	3.054 (1.631 - 5.717)	**< 0.001**
LIPI group				
Good	Reference		Reference	
Int./Poor	2.283 (1.445 - 3.606)	**< 0.001**	2.156 (1.349 - 3.449)	**0.001**

Abbreviations: RFS, recurrence-free survival; PSM, propensity score matching; CI, confidence interval; BMI, body mass index; eGFR, estimated glomerular filtration rate; ECOG, Eastern Cooperative Oncology Group; Int., intermediate.

Table 3. Univariate and Multivariate Cox Proportional Hazards Analyses for OS After

PSM

Parameter	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Age	1.015 (0.984 - 1.047)	0.353		
Gender				
Female	Reference			
Male	1.073 (0.528 - 2.181)	0.847		
BMI				
< 25 kg/m^2	Reference			
≥ 25 kg/m^2	0.724 (0.326 - 1.607)	0.427		
WHO/ISUP classification				
I	Reference			
II	0.708 (0.158 - 3.162)	0.651		
III	1.751 (0.402 - 7.622)	0.455		
IV	1.806 (0.301 - 10.818)	0.518		
Bleeding				
No	Reference			
Yes	0.761 (0.267 - 2.165)	0.608		
Cystic tumour				
No	Reference			
Yes	0.396 (0.095 - 1.654)	0.204		
Histological necrosis				
No	Reference			
Yes	1.783 (0.736 - 4.320)	0.200		
eGFR	1.000 (0.978 - 1.022)	0.971		
pT				
1	Reference		Reference	
2	0.662 (0.226 - 1.944)	0.453	0.648 (0.219 - 1.912)	0.432
3	1.375 (0.516 - 3.666)	0.524	0.839 (0.301 - 2.337)	0.737
4	6.772 (2.307 - 19.874)	**< 0.001**	2.796 (0.838 - 9.328)	0.094
ECOG				
0	Reference		Reference	
≥1	2.986 (1.484 - 6.011)	**0.002**	2.505 (1.165 - 5.387)	**0.019**
Surgical margin status				
Negative	Reference		Reference	
Positive	7.897 (3.821 - 16.323)	**< 0.001**	7.249 (3.368 - 15.602)	**< 0.001**
LIPI group				
Good	Reference		Reference	
Int./Poor	3.699 (1.667 - 8.204)	**0.001**	3.238 (1.437 - 7.298)	**0.005**

Abbreviations: OS, overall survival; PSM, propensity score matching; CI, confidence interval; BMI, body mass index; eGFR, estimated glomerular filtration rate; ECOG, Eastern Cooperative Oncology Group; Int., intermediate.