Clinical significance of prognostic nutritional index in renal cell carcinomas

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Abstract

Prognostic nutritional index (PNI) could reflect the nutrition and inflammation status in cancer patients. This study aims to identify the prognostic significance of PNI in patients with renal cell carcinoma (RCC).

A total of 694 RCC patients from our institution were included in this study. The prognostic correlation between PNI and overall survival (OS) and recurrence-free survival (RFS) was analyzed respectively using Kaplan–Meier method and univariate and multivariate Cox model. Studies about the association between pretreatment or preoperative PNI and prognosis of RCC were systemically reviewed and a meta-analysis method was performed to further evaluate the pooled prognostic value of PNI in RCC.

267 (38.47%) RCC patients had low PNI according to the cut off value (49.08). Low PNI was associated with poor OS ($P < .001$) and RFS ($P < .001$), respectively. In the multivariate Cox analysis, PNI was identified to be an independent prognostic factor for OS (hazard ratio [HR] = 2.13, 95%CI: 1.25–3.62, $P = .005$). Compared to other nutritional indexes, this risk correlation of PNI is better than that of geriatric nutritional risk index (GNRI; HR = 1.19; $P = .531$), while is no better than that of neutrophil–lymphocyte ratio (NLR; 1/HR = 2.56; $P < .001$) and platelet–lymphocyte ratio (PLR; 1/HR = 2.85; $P < .001$) respectively. Meanwhile, additional 4785 patients from 6 studies were included into pooled analysis. For RCC patients who underwent surgery, low preoperative PNI was significantly associated with worse OS (pooled HR = 1.57, 95%CI: 1.37–1.80, $P < .001$) and worse RFS (pooled HR = 1.69, 95%CI: 1.45–1.96, $P < .001$). Furthermore, low PNI (<41–51) was also significantly associated with poor OS (HR = 1.78, 95%CI: 1.26–2.53 $P < .05$) and poor RFS (HR = 2.03, 95%CI: 1.40–2.95, $P < .05$) in advanced cases treated with targeted therapies.

The present evidences show that PNI is an independent prognostic factor in RCC. Low PNI is significant associated with poor prognosis of RCC patients.

Abbreviations: CI = confidence intervals, GNRI = geriatric nutritional risk index, HR = hazard ratio, NLR = neutrophil–lymphocyte ratio, OS = overall survival, PNI = prognostic nutritional index, RCC = renal cell carcinoma, RFS = recurrence-free survival, ROC = receiver operating characteristic.

Keywords: overall survival, prognostic nutritional index, recurrence-free survival, renal cell carcinoma

1. Introduction

Renal cell carcinoma (RCC) is one of the most common malignancies worldwide. A total of 66,000 new RCC cases were estimated occurred in China per year between 2000 to 2011.[1] Clinically, 20% to 30% of patients who diagnosed as localized RCC and underwent surgical resection will develop local recurrence or metastasis.[2] The prognostic assessment of RCC is pivotal towards both physicians and patients during

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postoperative management. For patients underwent nephrectomy, current parameters, such as tumor stage, nuclear grade, tumor size are insufficient to evaluate the host status that largely affecting their oncologic outcome. Therefore, identification of the host-related prognostic factors is still needed to assist clinical decision-making.

Serum albumin level is a crucial marker reflecting the nutritional status and immune status of cancer patients.[3] Accordingly, it is reported to correlated with prognosis of RCC.[4] In addition, by combining serum albumin level and total lymphocyte count, Buzby et al[5] first put forward the concept of prognostic nutritional index (PNI). Following studies reported the correlation between PNI and short-term prognosis, postoperative infection and wound healing.[6–9] Takushima and colleagues[10] further found an association between PNI and cancer patients, and they also suggested the calculation formula of PNI.

In 2015, Hofbauer et al[11] reported that low preoperative PNI was an independent poor prognostic factor for long-term survival of localized RCC. Although several related studies from different countries also reported a potential prognostic impact of PNI in RCC in the following years, its role is still controversial and remains to be verified with stronger evidence. In this study, aim to comprehensively assess the prognostic effect of preoperative PNI in RCC, we retrospectively analyzed RCC cases from our hospital. Moreover, the prognostic correlation of PNI was further validated in a meta-analysis of pooled patient cohorts.

2. Materials and methods

We retrospectively reviewed the medical records of RCC patients who underwent curative surgery in our department from January 2009 to May 2014. RCC cases meet the following criteria were included: age >18 years, pathological diagnosed as renal cell carcinoma and negative surgical margins. Patients with history of other life-threatening diseases within 5 years, and those who have received preoperative chemotherapy or radiotherapy were excluded. Finally, 694 patients were included in this study. Clinicopathological data including demographic characteristics, date and type of surgery, tumor size, Fuhrman grade, clinical-pathologic TNM stage, coagulation necrosis, smoking history, and laboratory results. TNM stage were evaluated according to the 2018 NCCN guidelines for kidney cancer.[12] The study conformed to the Declaration of Helsinki and was approved by the Ethics Committee of West China Hospital.

The PNI were calculated according to preoperative laboratory examination results: $10 \times$ serum albumin level (g/dl) $+0.005 \times$ total lymphocyte count (per mm^3). Patients were categorized into 2 groups (normal or low PNI group). A receiver operating characteristic (ROC) curve method was used to determine the best cut off value. Patients were followed-up every 3 to 6 months for the first 2 years, then regularly evaluated based on standard protocol at our institution. Overall survival (OS) was defined as time from primary resection of RCC to death due to any cause. Recurrence-free survival (RFS) was defined as time from primary resection of RCC to first recurrence based on clinical, radiographic, and laboratory evidence. Progression-free survival (PFS) was defined as the time from initial treatment to the earliest timepoint of disease progression or death from any cause.

Survival analyses were analyzed by Kaplan–Meier method and log-rank test. 95% confidence intervals (CI) and median survival time were estimated in Kaplan–Meier analyses. Univariate and multivariate Cox regression analyses were performed to identify the significant risk factors. Gender, age, pathological T stage, pathological N stage, Fuhrman grade, tumor size, surgical type, pathological type, coagulation necrosis, tumor thrombus, smoking history, and PNI were included in the univariate Cox proportional hazards regression. Next, variables with a P value <.05 were included in the multivariate Cox regression. Statistical analyses were performed using the R system (version 3.4.4). Besides, several other nutritional indexes were employed for compare with PNI as prognostic factors, including geriatric nutritional risk index (GNRI), neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR).

In the meta-analysis, prognostic nutrition/nutritional index (PNI), renal cell carcinoma (RCC), renal cancer, and kidney cancer were used as key words. We systemically searched related records in PubMed, web of Science, Embase, and Cochrane Library before January 1, 2019. The systematic literature review and data extraction were performed following the PRISMA guidelines for meta-analysis. Publication bias was evaluated by Begg funnel plots and Begg examination using Stata 14.0 (Stata Corp, College Station, Texas). The data heterogeneity was examined by Cochran Q test. When the studies contained no or weak heterogeneity on the basis of Q test ($P > .10$ and $I^2 < 50\%$), the fixed-effect model was adopted using the Mantel–Haenszel method. Otherwise, the random-effect model would be used when $P < .10$ and/or $I^2 > 50\%$. A P value <.05 was considered statistically significant.

3. Results

A total of 694 patients were included in our final cohort (Table 1): 632 (91.07%) cases were clear-cell carcinoma and 62 (8.93%) cases were non-clear cell carcinoma. Patients at early stage (pT1/2) accounted for 85.73%. All patients underwent surgical

Table 1

Clinicopathologic features of the study cohort.

| Characteristics	Number of cases (%)	Characteristics	Number of cases (%)
Gender		Tumor thrombus	
Female	252 (36.31)	No	662 (95.39)
Male	442 (63.69)	Yes	32 (4.61)
Age		Smoking history	
≤60	449 (64.70)	No	455 (67.00)
>60	245 (35.30)	Yes	229 (33.00)
Pathological T stage		Surgery type	
T1+T2	595 (85.73)	radical nephrectomy	467 (67.29)
T3+T4	99 (14.27)	partial nephrectomy	227 (32.71)
Pathological N stage		PNI	
N0/Nx	666 (95.97)	Normal	427 (50.00)
N1	28 (4.03)	Low	267 (50.00)
Tumor size		GNRI	
≤5 cm	451 (64.99)	Normal	535 (61.53)
>5 cm	243 (35.01)	Low	129 (38.47)
Fuhrman grade		NLR	
I-II	411 (59.22)	High	159 (22.91)
III-IV	283 (40.78)	Normal	535 (77.09)
Pathological type		PLR	
clear cell	632 (91.07)	High	204 (29.39)
Non-clear cell	62 (8.93)	Normal	493 (70.61)
Necrosis			
No	588 (84.73)		
Yes	106 (15.27)		
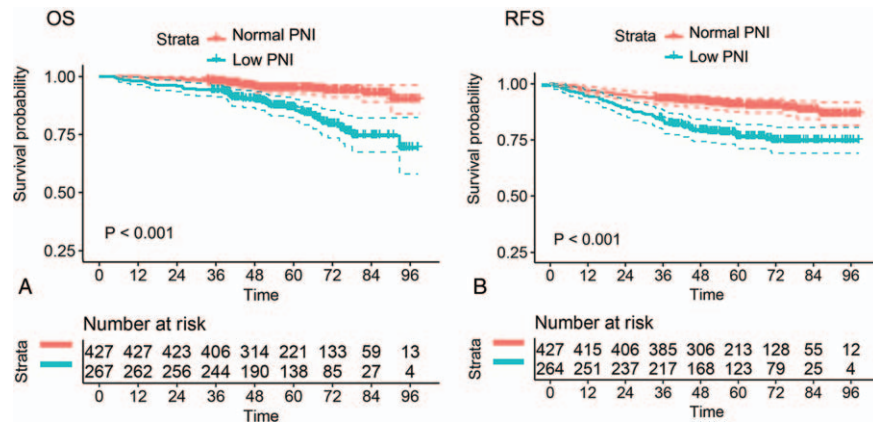
Figure 1. Kaplan–Meier curve and risk table of overall survival and recurrence-free survival in normal/Low PNI group. Time: time after surgery.

tumor resection, which includes laparoscopic radical nephrectomy (n=101), laparoscopic partial nephrectomy (n=99), open radical nephrectomy (n=366) and open partial nephrectomy (n=128). Median follow-up time is 60.9 (IQR:46.9–76.1) months. Based on the ROC curve result, the cut off of PNI was set as 49.075 in our current patient cohort. Accordingly,

patients were divided into 2 groups: low PNI group and normal PNI group. As a result, patients with low PNI were found more likely to have worse OS (log rank $P<.001$) and RFS (log rank $P<.001$), respectively (Fig. 1).

To further identify the prognostic factors in RCC, we included multiple parameters in the Cox regression analysis (Table 2).

Table 2

Univariate and multivariate cox analyses of overall survival and recurrence-free survival in the study cohort.

	Univariate analysis			Multivariate analysis		
Variables	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
OS						
Gender	1.06	0.65–1.72	.811	–	–	–
Age	2.1	1.32–3.35	.002	1.8	1.08–3.01	.024
Pathological T stage	5.28	3.25–8.56	<.001	2.9	1.58–5.32	.001
Pathological N stage	5.44	2.34–12.66	<.001	1.52	0.56–4.14	.415
Fuhrman grade	2.31	1.44–3.72	.001	1.26	0.75–2.1	.384
Tumor size	4.78	2.87–7.95	<.001	2.82	1.61–4.94	<.001
Surgical type	1.15	0.88–1.5	.321	–	–	–
Pathological type	1.32	1.02–1.7	.032	1.33	1.04–1.7	.022
Necrosis	3.02	1.85–4.92	<.001	2.08	1.21–3.56	.008
Tumor thrombus	6.23	3.47–11.19	<.001	1.17	0.55–2.47	.681
Smoking history	0.65	0.37–1.14	.135	–	–	–
PNI	3.26	2.00–5.34	<.001	2.13	1.25–3.63	.005
GNRI	2.17	1.32–3.57	.002	1.19	0.69–2.04	.531
NLR	0.23	0.14–0.36	<.001	0.39	0.24–0.64	<.001
PLR	0.23	0.14–0.37	<.001	0.35	0.21–0.58	<.001
RFS						
Gender	1.2	0.8–1.81	.386	–	–	–
Age	2.14	1.45–3.15	<.001	2.31	1.5–3.56	<.001
Pathological T stage	4.53	3.03–6.77	<.001	2.11	1.27–3.51	.004
Pathological N stage	7.86	4.18–14.77	.001	2.94	1.31–6.62	.009
Fuhrman grade	2.53	1.7–3.76	<.001	1.58	1.03–2.42	.037
Tumor size	3.31	2.23–4.92	<.001	2.13	1.37–3.3	.001
Surgical type	1.09	0.88–1.35	.429	–	–	–
Pathological type	1.12	0.87–1.46	.378	–	–	–
Necrosis	3.08	2.04–4.64	<.001	1.94	1.24–3.03	.003
Tumor thrombus	6.5	3.95–10.71	<.001	1.44	0.74–2.78	.284
Smoking history	0.87	0.57–1.33	.514	–	–	–
PNI	2.50	1.69–3.71	<.001	1.50	0.98–2.30	.065
GNRI	1.67	1.08–2.56	.021	0.91	0.91–1.45	.687
NLR	0.17	0.12–0.26	<.001	0.27	0.18–0.41	<.001
PLR	0.30	0.20–0.44	<.001	0.42	0.28–0.64	<.001

[*]Analysis with other risk factors respectively, shows the ratio of lower levels over higher levels.

CI = confidence interval, GNRI = geriatric nutritional risk index, NLR = neutrophil–lymphocyte ratio, OS = overall survival, PLR = platelet–lymphocyte ratio, PNI = prognostic nutritional index, RFS = recurrence-free survival.

Among them, age, pT stage, pN stage, Fuhrman grade, tumor size, pathological type, coagulation necrosis, tumor thrombus, and PNI were associated with OS and/or RFS of RCC patients in the univariable model. Subsequently, in multivariate analysis, age, pT stage, tumor size, pathological type, coagulation necrosis, and PNI (hazard ratio [HR] = 2.13, 95%CI: 1.25–3.62, P = .005) were independently correlated with OS (P < .05). However, PNI did not present an independent prognostic effect on RFS (HR = 1.5, 95%CI: 0.98–2.32, P = .065). In contrast, both normal NLR and PLR were showed to have an independent correlation with better OS (HR = 0.39, 95%CI: 0.24–0.64, P < .001 and HR = 0.35, 95%CI: 0.21–0.58, P < .001) and better RFS (HR = 0.27, 95%CI: 0.18–0.41, P < .001 and HR = 0.42, 95%CI: 0.28–0.64, P < .001), respectively.

Next, we reviewed data from different patient cohorts and further verified the prognostic effects of PNI in RCC. 6 studies with a total of 4785 RCC cases and our current participants were included in the meta-analysis.[11–16] Five studies reported the correlation between preoperative PNI and prognosis of RCC, and 2 studies reported the relationship between pre-targeted treatment PNI and prognosis of advanced RCC. The characteristics of cohorts included were summarized in Table 3. The pooled results suggested that preoperative PNI was significantly correlated with OS (HR = 1.57, 95%CI: 1.37–1.80, P < .001) and RFS (HR = 1.69, 95%CI: 1.45–1.96, P < .001, Fig. 2). Meanwhile, pretreatment low PNI was also associated with both OS (HR = 1.78, 95%CI: 1.26–2.53, P = .001) and PFS (HR = 2.03, 95%CI:1.40–2.95, P = .002) of advanced RCC patients (Fig. 3). There was no publication bias observed among these included studies.

4. Discussion/Conclusion

In this study, we found that PNI was a significant predictor for OS and RFS in patients with RCC. Patients who had lower PNI were more likely to have worse prognosis. Through systemically summarizing the published data, we confirmed that PNI was an independent prognostic factor for OS, RFS, and PFS in RCC.

In cancer patients, serum albumin level is recognized not only as a nutrition index, but a biomarker of immune inflammatory reaction.[17] It is reported that serum albumin level was significantly correlated with C-reactive protein level, which is related to the inflammation in the body.[18] On the other hand, lymphocyte is also widely accepted as an important index both on immune inflammatory status and body nutrition.[19,20] Combing lymphocyte count with the serum albumin level, PNI is therefore considered to reflect both cancer-related malnutrition status and cancer-related immune status of patient. In addition, PNI was further found to be associated with long-term prognosis of other types of malignancies, such as esophageal squamous cell carcinoma,[21] gastric cancer,[22] pancreatic cancer,[23] hepatocellular carcinoma,[24] colorectal cancer,[25] lung cancer,[26] and breast cancer.[27]

The relationship between PNI and cancer progress is comprehensive and multifactorial. Based on the cut off value, patients with lower PNI indeed showed worse prognosis in our cohort. In the univariate and multivariate model, prognostic effect of PNI on OS was independently, as well as other well-recognized parameters including age, pT stage, pN stage, Fuhrman grade, tumor size, pathological type, and exist of coagulation necrosis. However, different surgical treatment approaches and the exist of tumor thrombus did not show a prognostic correlation relationship in this study. In addition, we made a comparison with several other nutritional indexes that are often used for prognostic prediction in cancers, and found that the risk correlation of PNI is likely better than that of GNRI, while is no better than that of NLR and PLR respectively. Furthermore, considering that our data provided new but weak evidence on the potential independent correlation between RFS and PNI, a meta-analysis method is therefore used in the following analyses.

In meta-analysis, all of the included studies used ROC method, median, or average value of PNI to define the normal/low PNI status. Although their cut off values were not completely same, it was acceptable as all of them were in the consistent range of 41 to 51. When comparing the correlation between preoperative PNI

Table 3

characteristics of included studies.

	Country	Duration	Type of treatment	Number	Cut off	Follow-up (month)	Multivariate Cox HR (95%CI)	NOS[†]
Peng, 2017[12]	China	2001–2010	RCC/operation	1360	48	67	OS: 1.645 (1.153–2.348), P = .006 PFS: 1.705 (1.266–2.296), P < .001	7
Kwon, 2017 [13]	Korea	2007–2014	mRCC/Targeted therapy	125	41	45	OS: 0.51 (0.30–0.86), P = .011[*] PFS: 0.30 (0.12–0.74), P = .009[*]	8
Cai, 2017[14]	China	2006–2015	mRCC/Targeted therapy;	178	51	22	OS: 1.658 (1.040–2.641)), P = .033 PFS: 1.842 (1.226–2.766), P = .003	7
Jeon, 2016[15]	Korea	1994–2008	RCC/operation	1437	51	69	CSS: 1.51 (1.05–2.19), P = .026 OS: 1.50 (1.09–2.07), P = .031	8
			RCC/operation	1310	51	69	CSS: 1.81 (1.15–2.82), P = .009 OS: 1.63 (1.11–2.39), P = .011 RFS: 1.47 (1.03–2.11), P = .033	
Broggi, 2016[16]	America	2001–2014	RCC/operation	341	45	60-80	OS: 1.73 (1.09–2.76), P = .021 RFS: 2.26 (1.42–3.73), P = .016	8
Hofbauer, 2015[11]	America	1991–2012	RCC/operation	1344	48	40	OS: 0.67 (0.53–0.84), P < .001[*] RFS: 0.51 (0.35–0.76), P = .001[*]	8
Liang, (current)	China	2009–2014	RCC/operation	694	49	61	OS: 2.13 (1.25–3.63), P = .005 RFS: 1.50 (0.98–2.30), P = .065	8

[*] normal prognostic nutritional index (PNI) group vs low PNI group.

[†] Newcastle-Ottawa Scale score.

CSS = cancer specific survival, OS = overall survival, PFS = progression-free survival, RCC = renal cell carcinoma, RFS = recurrence-free survival.
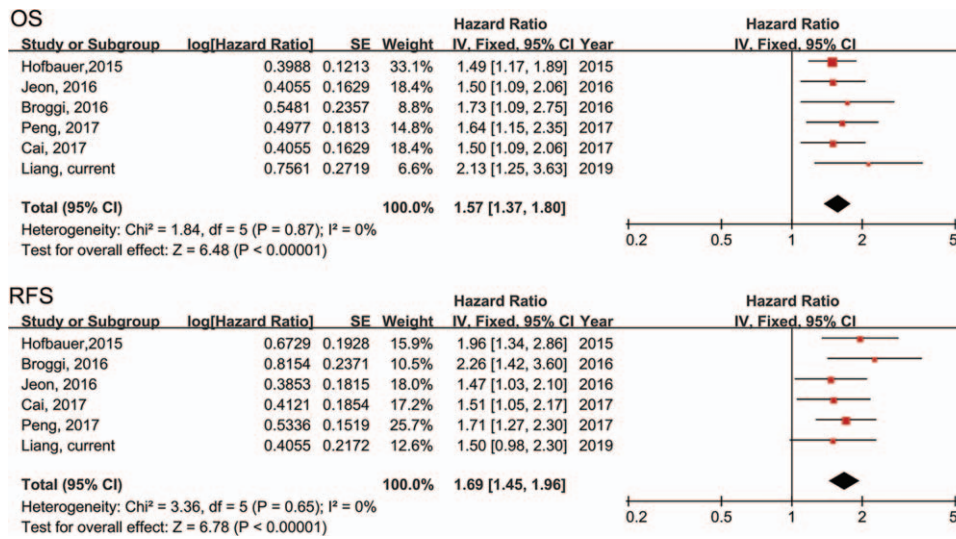
Figure 2. Forrest plots of meta-analyses of the effect of preoperative PNI on outcomes in RCC patients who underwent surgery.
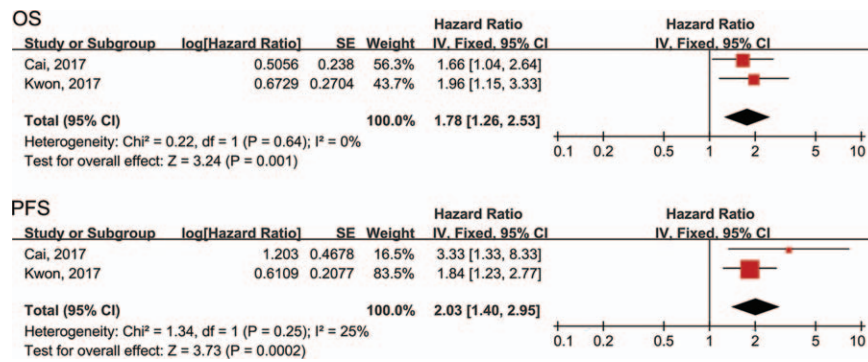

Figure 3. Forrest plots of meta-analyses of the effect of pretreatment PNI on outcomes in advanced RCC patients treated with targeted therapy.

and OS of patients after surgery, both radical and cytoreductive surgery were considered. The whole population included 26.2% cases in T3/T4 stage, 3.7% cases of distant metastasis and 4.3% cases of regional lymph node metastasis. Despite that there is limit research data on the relationship between PNI and cytoreductive surgery, our pooled results indicated that preoperative low PNI (<45–51) significantly contributed to worse OS, regardless of the specific types of surgery.

Although there are only 2 studies reported the clinical significance of PNI in patients underwent targeted therapy, they provided relatively large sample size (n=303) and long-term follow-up data (>22 months). Both 2 studies showed that low PNI was an independent prognostic factor for OS and PFS in advanced RCC patient. However, it should point out that when PNI is considered as a continuous variable, its prognostic value may be less significant. Kwon et al[13] included continuous PNI into multivariate Cox regression model and found that pretreatment PNI was not a prognostic factor for OS (HR=0.96, 95%CI: 0.91–1.00, P=.076) and PFS (HR=0.94, 95%CI: 0.85–1.03, P=.164) in advanced RCC patients who underwent targeted therapy.

The retrospective nature of our study and all the included studies is a main limitation, which may lead to an information bias. Besides, we did not explore the potential prognostic difference among advanced RCC patients who underwent neoadjuvant chemotherapy, radiotherapy or targeted therapy with different PNI level. Future large size, prospective, multi-center studies are needed to provide stronger evidence for the clinical utility of PNI in RCC management.

In conclusion, PNI is an independent prognostic factor in RCC. Patients with pretreatment or preoperative low PNI were more likely to have worse OS, RFS and PFS. Accordingly, PNI may be helpful in outcome prediction and optimize the postoperative management on RCC.

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References

[1] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115–32.

[2] Eggener SE, Yossepowitch O, Pettus JA, et al. Renal cell carcinoma recurrence after nephrectomy for localized disease: predicting survival from time of recurrence. J Clin Oncol 2006;24:3101–6.

[3] Nazha B, Moussaly E, Zaarour M, et al. Hypoalbuminemia in colorectal cancer prognosis: nutritional marker or inflammatory surrogate? World J Gastrointest Surg 2015;7:370–7.

[4] Crumley AB, Stuart RC, McKernan M, et al. Is hypoalbuminemia an indepen- dent prognostic factor in patients with gastric cancer? World J Surg 2010;34:2393–8.

[5] Buzby GP, Mullen JL, Matthews DC, et al. Prognostic nutritional index in gastrointestinal surgery. Am J Surg 1980;139:160–7.

[6] Mullen JL, Buzby GP, Matthews DC, et al. Reduction of operative morbidity and mortality by combined preoperative and postoperative nutritional support. Ann Surg 1980;192:604–13.

[7] Roy LB, Edwards PA, Barr LH. The value of nutritional assessment in the surgical patient. JPEN J Parenter Enteral Nutr 1985;9:170–2.

[8] Poulin E, Langevin H, Vallieres E, et al. Prognostic nutritional index and delayed hypersensitivity tests as a means of predicting hospital morbidity and mortality. Union Med Can 1983;112:18–21.

[9] Smale BF, Mullen JL, Buzby GP, et al. The efficacy of nutritional assessment and support in cancer surgery. Cancer 1981;47:2375–81.

[10] Takushima Y, Abe H, Yamashita S. Evaluation of prognostic nutritional index (PNI) as a prognostic indicator in multimodal treatment for gynecological cancer patients. Gan To Kagaku Ryoho 1994;21:679–82.

[11] Hofbauer SL, Pantuck AJ, de Martino M, et al. The preoperative prognostic nutritional index is an independent predictor of survival in patients with renal cell carcinoma. Urol Oncol 2015;33:68.e61–7.

[12] Peng D, He ZS, Li XS, et al. Prognostic value of inflammatory and nutritional scores in renal cell carcinoma after nephrectomy. Clin Genitourin Cancer 2017;15:582–90.

[13] Kwon WA, Kim S, Kim SH, et al. Pretreatment prognostic nutritional index is an independent predictor of survival in patients with metastatic renal cell carcinoma treated with targeted therapy. Clin Genitourin Cancer 2017;15:100–11.

[14] Cai W, Zhong H, Kong W, et al. Significance of preoperative prognostic nutrition index as prognostic predictors in patients with metastatic renal cell carcinoma with tyrosine kinase inhibitors as first-line target therapy. Int Urol Nephrol 2017;49:1955–63.

[15] Jeon HG, Choi DK, Sung HH, et al. Preoperative prognostic nutritional index is a significant predictor of survival in renal cell carcinoma patients undergoing nephrectomy. Ann Surg Oncol 2016;23:321–7.

[16] Broggi MS, Patil D, Baum Y, et al. Onodera's prognostic nutritional index as an independent prognostic factor in clear cell renal cell carcinoma. Urology 2016;96:99–105.

[17] Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med 1999;340:448–54.

[18] McMillan DC, Watson WS, O'Gorman P, et al. Albumin concentrations are primarily determined by the body cell mass and the systemic inflammatory response in cancer patients with weight loss. Nutr Cancer 2001;39:210–3.

[19] Jung YS, You G, Shin HS, et al. Relationship between geriatric nutritional risk index and total lymphocyte count and mortality of hemodialysis patients. Hemodial Int 2014;18:104–12.

[20] Wolfson M, Strong CJ, Minturn D, et al. Nutritional status and lymphocyte function in maintenance hemodialysis patients. Am J Clin Nutr 1984;39:547–55.

[21] Feng JF, Chen QX. Significance of the prognostic nutritional index in patients with esophageal squamous cell carcinoma. Ther Clin Risk Manag 2014;10:1–7.

[22] Migita K, Takayama T, Saeki K, et al. The prognostic nutritional index predicts long-term outcomes of gastric cancer patients independent of tumor stage. Ann Surg Oncol 2013;20:2647–54.

[23] Wang DS, Luo HY, Qiu MZ, et al. Comparison of the prognostic values of various inflammation based factors in patients with pancreatic cancer. Med Oncol 2012;29:3092–100.

[24] Pinato DJ, North BV, Sharma R. A novel, externally validated inflammation based prognostic algorithm in hepatocellular carcinoma: the prognostic nutritional index (PNI). Br J Cancer 2012;106: 1439–45.

[25] Okada I, Shirahata A, Soda H, et al. Significance of Onodera's prognostic nutritional index for treating unresectable or recurrent colorectal cancer with chemotherapy. Gan Kagaku Ryoho 2012;39: 231–5.

[26] Shunsuke M, Noriyasu U, Koichi F, et al. The significance of the prognostic nutritional index in patients with completely resected non-small cell lung cancer. PLoS One 2015;10:e0136897.

[27] Mohri T, Mohri Y, Shigemori T, et al. Impact of prognostic nutritional index on long-term outcomes in patients with breast cancer. World J Surg Oncol 2016;14:1–5.