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ORIGINAL RESEARCH

Preoperative prognostic nutritional index and nomogram predicting recurrence-free survival in patients with primary non-muscle-invasive bladder cancer without carcinoma in situ

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Background and objectives: Among the cancers of the urogenital system, bladder cancer is ranked second both in incidence and mortality, and hence, a more accurate estimate of the prognosis for individual patients with non-muscle-invasive bladder cancer (NMIBC) is urgently needed. Prognostic nutritional index (PNI) which is based on serum albumin levels and peripheral lymphocyte count has been confirmed to have prognostic value in various cancers. The aim of this study was to clarify the prognostic value of PNI in patients with NMIBC.

Methods: Data of 329 patients with NMIBC were evaluated retrospectively. Recurrence-free survival (RFS) was assessed using the Kaplan–Meier method, and the equivalences of survival curves were tested by log-rank tests. The univariate and multivariate analyses were performed using the Cox proportional hazards regression model. Discrimination of the nomogram was measured by the concordance index. A p-value of <0.05 was considered statistically significant.

Results: In univariate analysis, age, tumor focality, tumor size, tumor grade, pathological T stage and preoperative PNI were significantly associated with RFS. Multivariate analysis identified PNI as an independent predictor of RFS in patients with NMIBC. According to these independent predictors, a nomogram for the prediction of recurrence was developed.

Conclusion: PNI can be regarded as an independent prognostic factor for predicting RFS in NMIBC. The nomogram could be useful to improve personalized therapy for patients with NMIBC.

Keywords: non-muscle-invasive bladder cancer, prognostic nutritional index, nomogram, prognosis, recurrence-free survival

Introduction

Bladder cancer (BCa) is the 6th most commonly diagnosed cancer in the male population worldwide according to the latest published global cancer statistics.[1] The majority of BCa occurs in men, and there is about a 10-fold variation in incidence rates internationally. Among the cancers of the urogenital system, BCa is ranked second both in incidence and mortality. Worldwide, the age-standardized mortality rate (per 100,000 person-years) of BCa was 3.2 among men versus 0.9 among women in 2012.[1] Approximately 75% of patients with BCa present with a non-muscle-invasive bladder cancer (NMIBC).[2] NMIBC includes Ta (noninvasive papillary carcinoma), T1 (tumor invading subepithelial connective tissue) and CIS (carcinoma in situ: "flat tumor"). The patients usually require follow-up chemotherapy or BCG treatment to prevent the tumor recurrence after surgery.[3]

Increasing evidence shows that nutritional deficiencies and systemic inflammatory response (SIR) might play important roles in the development and progression of human cancer.[4,5] For example, neutrophil-to-lymphocyte ratio which is widely used as a biomarker of SIR has been reported to be associated with worse clinical outcomes in NMIBC.[6] The prognostic nutritional index (PNI) which was described by Onodera et al is based on serum albumin levels and peripheral lymphocyte count,[7] and several studies have confirmed its prognostic value in various cancers, such as hepatocellular carcinoma, lung cancer, renal cancer, colorectal carcinoma and so on.[8–11]

The most frequently used prognostic model for individual BCa patients is the European Organization for the Research and Treatment of Cancer-Genito-Urinary Cancer Group (EORTC-GUCG) risk scoring system; however, this system is mainly designed for European population. The nomogram, which is a statistical instrument accounting for numerous variables to predict the outcome of an individual patient, was reported by Hong et al for prediction of recurrence-free survival (RFS) in patients with NMIBC.[12,13] However, the nomogram has limitations such as indefinite subgroup and lack of some hematologic indexes. Thus, a more accurate prognostic model for patients with NMIBC is needed.

To our knowledge, the value of PNI in predicting RFS in NMIBC has not been investigated yet. Thus, we decided to clarify the prognostic value of preoperative PNI among patients who had undergone transurethral resection of bladder tumor (TURBT) for NMIBC and establish a nomogram to predict RFS for individual patients after surgery.

Methods
Patients

This retrospective analysis included clinicopathological and follow-up data of 329 patients with NMIBC who had undergone TURBT at the Department of Urology at the Qilu Hospital of Shandong University from January 2008 to December 2013. Patients who met the following conditions were included in this study: (1) full data on preoperative peripheral lymphocyte count and serum albumin level were available; (2) absence of autoimmune disease and cancer in other systems, or received neo-adjuvant chemotherapy and radiotherapy; (3) pathological type was Ta or T1 urothelial carcinoma without CIS; (4) presence of primary NMIBC; (5) distant metastasis was excluded before surgery; (6) received intravesical chemotherapy by epirubicin or pirarubicin postoperatively, the regimen of which was once a week for 6–8 times and then once a month for at least 6 times; and (7) full data on follow-up were available. All clinical investigations in our study were conducted in accordance with the Declaration of Helsinki. This study was approved by the Institutional Ethics Committee of the Qilu Hospital of Shandong University. Written informed consent was obtained from all the patients in this study.

All patients underwent routine hematologic examination, computerized tomography, transabdominal ultrasound, cystoscopy, urinary cytology and/or tissue biopsy for diagnosis of NMIBC before surgery. Pathological T stages were uniformly adjusted according to the 2009 TNM classification which was approved by the Union Internationale Contre le Cancer (7th edition), and tumor grade was assessed based on the 1973 World Health Organization (WHO) classification guidelines.[14] Preoperative baseline clinicopathological and laboratory data, such as age, gender, history of smoking, symptoms, tumor size and pathological type, were obtained from the electronic medical records and reviewed. Negative symptoms were defined as having no symptom related to BCa, and was only detected by routine examination, whereas positive symptoms were defined as having gross or microscopic hematuria, urgent urination, dysuresia or flank pain. The tumor size was defined as the longest diameter of the general postoperative pathological specimens. PNI was then calculated with the following formula as previously described: $10\times$ serum albumin levels (g/dL) $+0.005\times$ peripheral lymphocyte count (per mm^3).[7]

All patients were regularly followed up with physical examination, routine urine and blood tests, biochemical tests and cystoscopy every 3 months for the first 2 years, every 6 months in the next 3 years and yearly thereafter for more than 5 years, and excretory urograms and/or computed tomography scans were obtained every year for 5 years after TURBT.

RFS rates and EORTC-GUCG risk scoring system

Visible or suspicious lesions were removed by TURBT. Due to limited patients suffering BCa progression in this study, RFS was identified as the end point in this study. RFS was defined as the time interval from the date of the initial TURBT to the date of recurrence which was confirmed by histopathology. The most frequently used prognostic model for an individual patient with NMIBC is the EORTC-GUCG risk scoring system. According to this risk scoring system of disease recurrence and progression, the definitions of risk are as follows: (1) low risk: primary, solitary, Ta, low grade/ G1, <3 cm and no CIS; (2) intermediate risk: all tumors not defined in the 2 adjacent categories (between the category of low and high risk); and (3) high risk: a) T1 tumor, b)

high grade/G3 tumor, c) CIS, and d) multiple and recurrent and large (>3 cm) Ta G1G2 tumors (all conditions must be present in this point).[15]

Statistical analysis

The peripheral lymphocyte count, serum albumin level and PNI are shown as the mean and standard deviation (SD). Correlations between categorical variables were evaluated by the Pearson's chi-square test or Fisher's exact test in this study. The probable cutoff value for the PNI was determined by applying receiver operating curve (ROC) analysis, and the most optimal cutoff value was used for further analysis. In RFS analysis, the Kaplan–Meier method was used to evaluate the survival rates in different groups, and the equivalences of the survival curves were tested by log-rank tests. Besides, the Cox proportional hazards regression model was applied in univariate and multivariate analyses.

Based on the multivariable model, a nomogram was constructed to predict 1-, 3- and 5-year RFS. The nomogram provides a graphic representation linking an individual patient's multivariable prognostic factors to the RFS probability of a patient with NMIBC. Discrimination is measured by the concordance index (c-index) which is the area under the curve of an ROC curve. A scale of 1.0 represents perfect predictions, and 0.5 is the equivalent of a coin toss. The calibration of the model is assessed visually with calibration plots. A 45° line indicates perfect calibration – when the predictive value of the model perfectly matches the patient's actual risk. Any deviation above or below the 45° line indicates underprediction or overprediction, respectively. A 2-sided p-value was used in our analyses, and a p-value of <0.05 was considered to be statistically significant. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows, version 23.0; IBM Corporation, Armonk, NY, USA) program and R (version 3.1.2; R Foundation, Vienna, Austria; https://www.r-project.org/).

Results
Baseline clinicopathological characteristics

Of the 367 patients with NMIBC who underwent TURBT at our institution from January 2008 to December 2013, 38 were excluded as they did not meet the inclusion criteria. The mean (SD) follow-up duration was 43.9 (27.1) months. The clinicopathological characteristics of 329 patients are shown in Table 1. Of the total, 262 (79.6%) were male and 67 (20.4%) were female, and the mean (SD) age of the study cohort was 62.90 (12.50) years. Among the patients, 92 (28.3%) had a

Table 1 Clinicopathological characteristics of 329 patients with NMIBC stratified by EORTC-GUCG risk group

	All patients (n=329)	Low risk (n=31)	Intermediate risk (n=189)	High risk (n=109)	p-value
Gender, n (%)					
Male/female	262 (79.6)/67 (20.4)	23 (74.2)/8 (25.8)	148 (78.3)/41 (21.7)	91 (83.5)/18 (16.5)	0.413
Age (years)					
Mean ± SD	62.90±12.50	58.32±12.98	61.76±12.98	66.16±10.75	0.001
Median (range)	63 (28–89)	66 (28–88)	63.5 (32–89)	67 (32–85)	
History of smoking, n (%)					
Yes	93 (28.3)	11 (35.5)	53 (28.0)	29 (26.6)	0.622
No	236 (71.7)	20 (64.5)	136 (72.0)	80 (73.4)	
Symptoms, n (%)					
Positive	259 (78.1)	23 (74.2)	140 (74.1)	96 (88.1)	0.014
Negative	70 (21.9)	8 (25.8)	49 (25.9)	13 (11.9)	
Tumor focality, n (%)					
Unifocal	206 (62.6)	31 (100.0)	107 (56.6)	68 (62.4)	0.272
Multifocal	123 (37.4)	0 (0.0)	82 (43.4)	41 (37.6)	
Tumor size, n (%)					
≤1 cm	61 (18.6)	11 (35.5)	37 (19.6)	13 (11.9)	<0.001
1–3 cm	155 (47.1)	20 (64.5)	84 (44.4)	51 (46.8)	
≥3 cm	113 (34.3)	0 (0.0)	68 (36.0)	45 (41.3)	
Tumor grade, n (%)					
G1	55 (16.7)	31 (100.0)	24 (12.7)	0 (0.0)	<0.001
G2	189 (57.5)	0 (0.0)	165 (87.3)	0 (0.0)	
G3	85 (25.8)	0 (0.0)	0 (0.0)	85 (100.0)	
Pathological T stage, n (%)					
pTa	247 (75.1)	31 (100.0)	189 (100.0)	27 (24.8)	<0.001
pT1	82 (24.9)	0 (0.0)	0 (0.0)	82 (75.2)	

Abbreviations: NMIBC, non-muscle-invasive bladder cancer; EORTC-GUCG, European Organization for the Research and Treatment of Cancer; SD, standard deviation.

history of smoking and 259 (78.1%) had positive symptoms. Multifocal tumors were found in 123 (37.4%) patients. Tumors in 61 (18.6%) patients were <1 cm, in 155 (47.1%) between 1 and 3 cm and in 113 (34.3%) >3 cm. Tumor grade was G1 in 55 (16.7%), G2 in 189 (57.5%) and G3 in 85 (25.8%) patients. Pathological T stage was pTa in 247 (75.1%) and pT1 in 82 (24.9%) patients.

Stratification of patients by EORTC-GUCG risk scoring system

According to the EORTC-GUCG risk scoring system, 31 patients were regarded to have low risk of recurrence, 189 intermediate risk of recurrence and 109 high risk of recurrence. The relationships between clinicopathological characteristics and EORTC-GUCG risk system are shown in Table 1. Statistically significant differences were noticed in age and symptoms among different risk groups.

Prognostic value of the EORTC-GUCG risk scoring system in predicting RFS in patients with NMIBC

During the follow-up period, 125 of the 329 patients (38.0%) experienced intravesical recurrence: 5 (16.1%) in low-risk group, 61 (32.3%) in intermediate-risk group and 59 (54.1%) in high-risk group. The Kaplan–Meier survival analysis showed that the EORTC-GUCG risk scoring system was significantly associated with RFS, and the patients in the higher-risk group had shorter RFS (p<0.001) (Figure 1).

Prognostic value of the preoperative PNI in predicting RFS in patients with NMIBC

The median (range) preoperative serum albumin level was 43.0 (26.3–54.3) g/L, and the median peripheral lymphocyte count was 1.76 (0.44–4.59) ×10^9/L. The patients were divided into 2 groups according to the optimal cutoff value of PNI (52.57). Based on this cutoff value, 160 (48.6%) patients were categorized as high-PNI group, while the remaining 169 (51.4%) as low-PNI group.

The relationships between clinicopathological characteristics and PNI are shown in Table 2. Age and tumor grade were found significantly related with preoperative PNI.

Overall, RFS rate of patients with NMIBC was 82.7% (272/329) at 1 year, 66.1% (205/310) at 3 years and 43.2% (89/206) at 5 years. The mean time of recurrence (SD) was 19.9 (17.3) months. Furthermore, 1-, 3- and 5-year RFS stratified by preoperative PNI were also identified in this study: 1-year RFS rate was 76.9% in low-PNI group and 88.8% in high-PNI group (p=0.004); 3-year RFS rate was 55.4% in
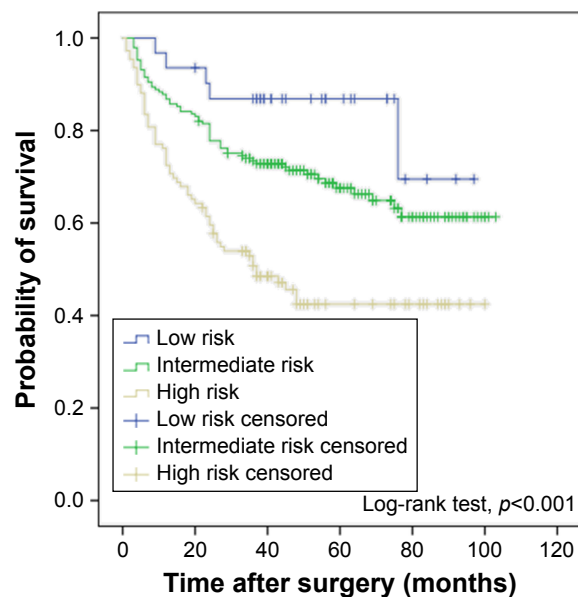
Figure 1 Kaplan–Meier survival curves for recurrence-free survival of all patients with non-muscle-invasive bladder cancer stratified by EORTC-GUCG risk scoring system.
Abbreviation: EORTC-GUCG, European Organization for the Research and Treatment of Cancer.

low-PNI group and 77.1% in high-PNI group (p<0.001); and 5-year RFS rate was 29.6% in low-PNI group and 58.2% in high-PNI group (p<0.001). The Kaplan–Meier survival analysis showed that preoperative PNI was significantly associated with RFS (p<0.001, Figure 2). Thus, low preoperative PNI could predict poorer RFS.

Furthermore, we evaluated whether the PNI in different EORTC-GUCG groups was associated with the RFS. No difference was found in patients of low-risk group for RFS (p=0.815, Figure 3A), but statistically significant difference was found in patients of intermediate-risk group (p=0.013, Figure 3B) and high-risk group (p=0.044, Figure 3C).

In univariate analysis, no difference for RFS was found in gender, history of smoking and symptoms. Age (<50 or ≥50), tumor focality (unifocal or multifocal), tumor size (≤1, 1–3 or ≥3 cm), tumor grade (G1, G2 or G3), pathological T stage (pTa or pT1) and preoperative PNI (low or high) were significantly associated with RFS (Table 2). To clarify the independent prognostic value of preoperative PNI for RFS, multivariate Cox proportional hazards regression analysis using age, tumor focality, tumor size, tumor grade, tumor stage and preoperative PNI as covariates was performed which revealed that age (hazard ratio [HR] =2.007, 95% confidence interval [CI] 1.036–3.885, p=0.039), tumor

Table 2 Clinicopathological characteristics of 329 patients with NMIBC stratified by PNI
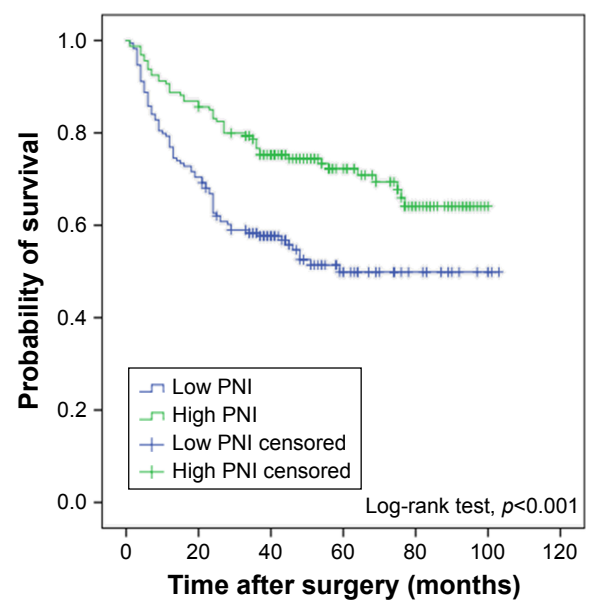
	PNI		*p*-value
	<52.57 (n=169)	≥52.57 (n=160)	
Gender, n (%)			
Male/female	135 (79.9)/ 34 (20.1)	127 (79.4)/ 33 (20.6)	0.909
Age (years)			
Mean ± SD	64.45±12.83	61.26±11.95	0.02
Median (range)	67 (32–88)	61 (28–89)	
History of smoking, n (%)			
Yes	52 (30.8)	41 (25.6)	0.300
No	117 (69.2)	119 (74.4)	
Symptoms, n (%)			
Positive	138 (81.7)	121 (75.6)	0.182
Negative	31 (18.3)	39 (24.4)	
Tumor focality, n (%)			
Unifocal	101 (59.8)	105 (65.6)	0.272
Multifocal	68 (40.2)	55 (34.4)	
Tumor size, n (%)			
≤1 cm	30 (17.7)	31 (19.4)	0.382
1–3 cm	75 (44.4)	80 (50.0)	
≥3 cm	64 (37.9)	49 (30.6)	
Tumor grade, n (%)			
G1	27 (16.0)	28 (17.5)	0.032
G2	88 (52.0)	101 (63.1)	
G3	54 (32.0)	31 (19.4)	
Pathological T stage, n (%)			
pTa	120 (71.0)	127 (79.4)	0.079
pT1	49 (29.0)	33 (20.6)	
Albumin (g/L)			
Mean ± SD	40.82±3.30	45.07±2.92	<0.001
Median (range)	41.4 (26.3–48.2)	44.8 (37.0–54.3)	
Lymphocyte (×10⁹/L)			
Mean ± SD	1.50±0.42	2.22±0.64	<0.001
Median (range)	1.49 (0.44–2.89)	2.16 (0.6–4.59)	

Abbreviations: NMIBC, non-muscle-invasive bladder cancer; PNI, prognostic nutritional index; SD, standard deviation.

Figure 2 Kaplan–Meier survival curves for recurrence-free survival of patients with non-muscle-invasive bladder cancer stratified by PNI.
Abbreviation: PNI, prognostic nutritional index.

focality (HR =1.484, 95% CI 1.039–2.119, p=0.030), tumor grade (G1, G2 or G3; HR =2.603, 95% CI 1.186–5.713 and HR =2.933, 95% CI 1.228–7.003, p=0.015, respectively), tumor stage (pTa or pT1; HR =1.737, 95% CI 1.108–2.724, p=0.016) and PNI (low or high; HR =0.598, 95% CI 0.410–0.870, p=0.007) were independent predictors of RFS in patients with NMIBC (Table 3).

Nomogram in predicting 1-, 3- and 5-year RFS rates in patients with NMIBC

According to the multivariable Cox model, patient's age, tumor focality, tumor grade, tumor stage and preoperative PNI had a significant effect on RFS. The nomogram can be used to predict the probability of BCa recurrence at 1, 3 and 5 years after primary surgery (Figure 4). The accuracy of this

prediction model was relatively high, with a *c*-index of 0.697. Calibration is another important indicator of the nomogram. The calibration plots showed only a limited deviation from the ideal predictions (Figure 5).

Discussion

The results of the present study showed patients stratified by EORTC-GUCG risk scoring system were statistically different in RFS outcomes (p<0.001), which indicated accuracy of our patients' data. The RFS rates of the low-PNI group were significantly lower than those of the high-PNI group, and our results revealed that PNI was an independent prognostic factor associated with RFS in patients with NMIBC. To the best of our knowledge, this is the first study to investigate the association among PNI, pathological factors, age and RFS outcomes in a cohort of patients with NMIBC and to establish a nomogram using these prognostic factors.

PNI was originally proposed as a marker to predict the nutritional and immunological statuses of cancer patients before gastrointestinal surgery. It was initially reported by Buzby et al, using the following formula: PNI (percent) =158−16× serum albumin level (g/100 mL)−0.78× triceps skinfold (mm)−0.20× serum transferrin level (mg/100 mL)−5.8× cutaneous delayed hypersensitivity reactivity.[16] Onodera et al defined PNI as a simple linear predictive model calculated
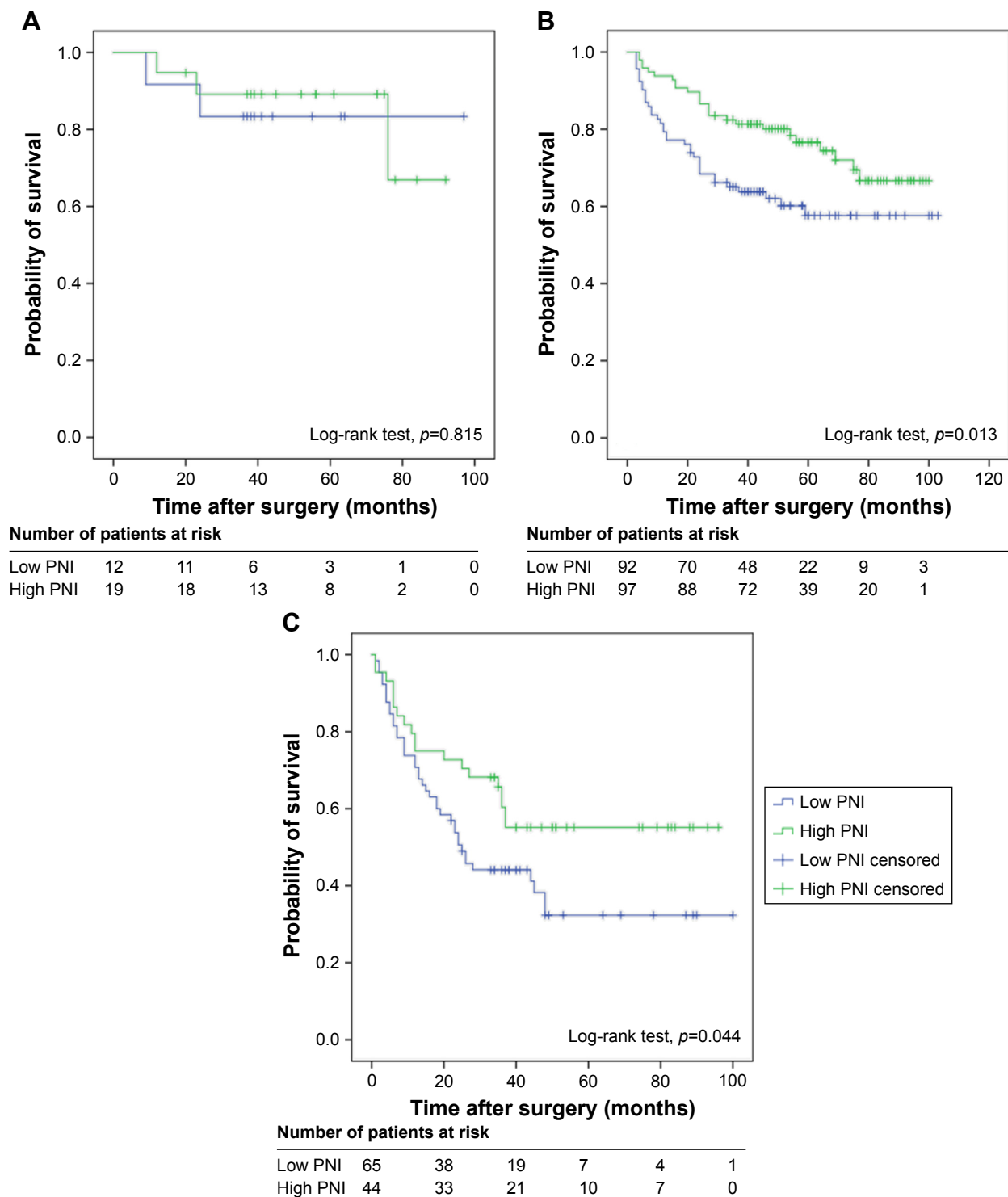
Figure 3 Kaplan–Meier survival curves for different EORTC-GUCG risk groups of patients with non-muscle-invasive bladder cancer stratified by PNI: (**A**) low risk; (**B**) intermediate risk; and (**C**) high risk.
Abbreviations: EORTC-GUCG, European Organization for the Research and Treatment of Cancer; PNI, prognostic nutritional index.

by serum albumin and peripheral lymphocyte count.[7] Then, PNI was reported as a prognostic index in various types of human cancers.[8–11] However, the optimal cutoff value of PNI to predict the overall survival (OS), cancer-specific survival, progression-free survival and RFS outcomes remains

unclear. Jeon et al reported a PNI of 51 for renal carcinoma, and used a minimum *p*-value approach to identify the cutoff point.[10] Mori et al reported a PNI of 50 for non-small-cell lung cancer in their study, and the optimal cutoff value was calculated by ROC curve.[17] In the present study, the optimal

Table 3 Univariate and multivariate Cox proportional hazards regression analyses of RFS in 329 patients with NMIBC

Variable	Univariate		Multivariate	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Gender				
Male	1 (reference)	0.827		
Female	1.049 (0.685–1.606)			
Age (years)				
<50	1 (reference)	0.004	1.000 (reference)	0.039
≥50	2.562 (1.342–4.891)		2.007 (1.036–3.885)	
History of smoking				
No	1 (reference)	0.833		
Yes	1.043 (0.705–1.544)			
Symptoms				
Positive	1 (reference)	0.238		
Negative	0.758 (0.478–1.201)			
Tumor focality				
Unifocal	1 (reference)	0.013	1.000 (reference)	0.030
Multifocal	1.564 (1.100–2.224)		1.484 (1.039–2.119)	
Tumor size (cm)				
≤1	1 (reference)			
1–3	1.835 (1.024–3.291)	0.041		
≥3	2.477 (1.373–4.466)	0.003		
Tumor grade				
G1	1 (reference)		1.000 (reference)	
G2	3.165 (1.455–6.885)	0.004	2.603 (1.186–5.713)	0.017
G3	6.030 (2.727–13.336)	<0.001	2.933 (1.228–7.003)	0.015
Tumor stage				
pTa	1 (reference)	<0.001	1.000 (reference)	0.016
pT1	2.563 (1.784–3.682)		1.737 (1.108–2.724)	
PNI				
<52.57	1 (reference)	<0.001	1.000 (reference)	0.007
≥52.57	0.510 (0.354–0.733)		0.598 (0.410–0.870)	

Abbreviations: RFS, recurrence-free survival; NMIBC, non-muscle-invasive bladder cancer; HR, hazard ratio; CI, confidence interval; PNI, prognostic nutritional index.
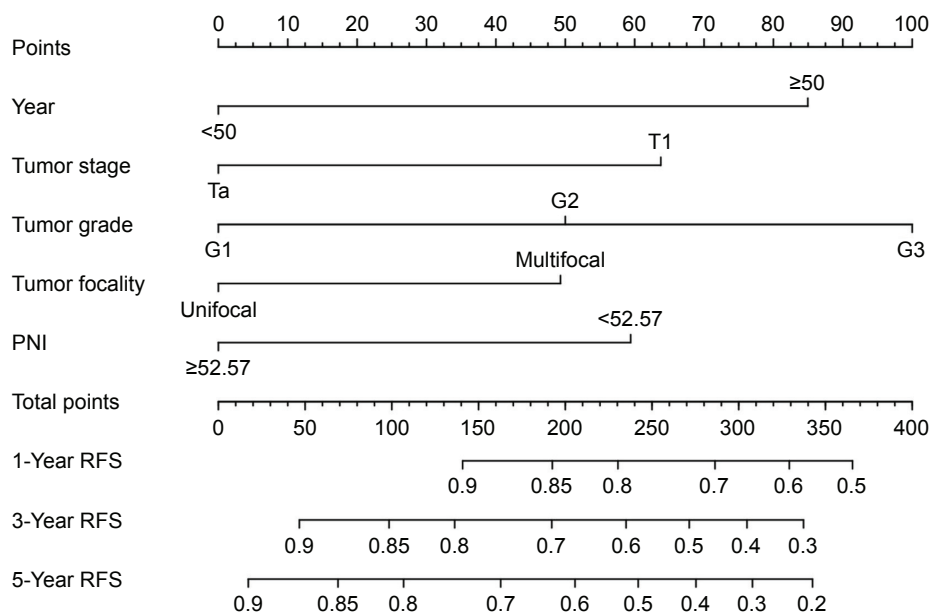

Figure 4 Nomogram for predicting RFS in patients with non-muscle-invasive bladder cancer.
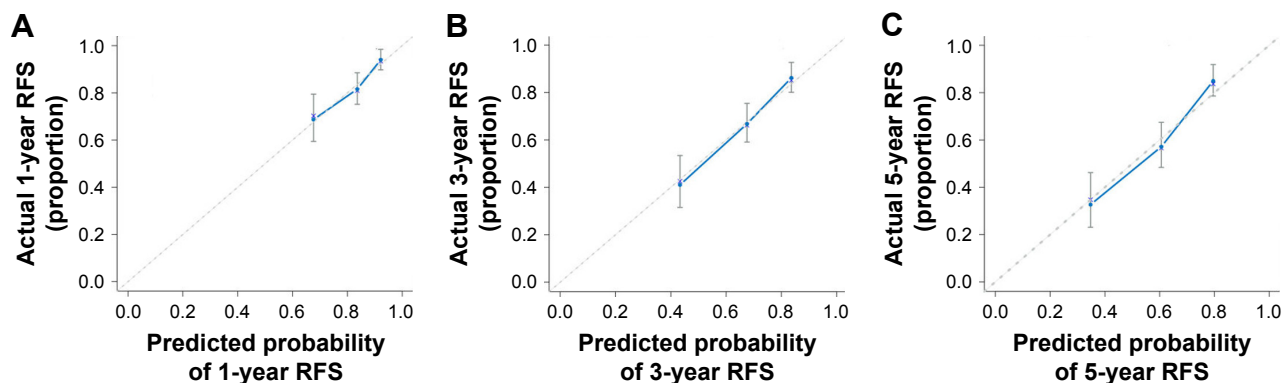**Abbreviations:** RFS, recurrence-free survival; PNI, prognostic nutritional index.

Figure 5 Calibration curves for internal validation of estimating RFS in patients with non-muscle-invasive bladder cancer: (**A**) 1-year outcome; (**B**) 3-year outcome; and (**C**) 5-year outcome.
Abbreviation: RFS, recurrence-free survival.

cutoff value of PNI was 52.57 which was similar to that of patients with breast cancer (52.4).[18] The following reasons could cause uncertainty in PNI: first, different tumors had different biological characteristics, and patients' status was heterogeneous; second, limited number of patients could lead to a bias in cutoff value; and third, different statistical methods could result in different cutoff values.

It is well known that serum albumin level is one of the most widely used markers for evaluating nutritional status, and malnutrition is closely associated with poor prognosis and low quality of life and weakens the human defense mechanisms, including anatomic barriers, cellular and humoral immunity and phagocyte function.[19,20] Gregg et al reported nutritional deficiency, as measured by preoperative weight loss, body mass index and serum albumin, was a strong predictor of 90-day mortality and poor OS in patients with BCa who underwent radical cystectomy.[21] However, Ataseven et al suggested there was no correlation between hypoalbuminemia and body mass index (BMI) in patients with epithelial ovarian cancer, but hypoalbuminemia could reflect prognosis.[20]

Another component in PNI is lymphocyte, which plays a fundamental role in the cell-mediated immune response in the formation and progression of tumor.[22] The importance of lymphocytes has been clarified in several studies which have shown that lymphocytopenia is associated with poor survival outcome, independent of clinicopathological characteristics in patients with muscle-invasive BCa.[23,24] The causes of tumor-induced lymphocytopenia remain to be elucidated in detail, and one potential reason is the result of impaired lymphocyte homeostasis and enhanced lymphocyte apoptosis.[25] Meanwhile, tumor cells also express higher levels of proapoptotic molecules such as Fas ligand, resulting in increased destruction of lymphocytes via activation of the

extrinsic pathway of apoptosis.[26] Thus, lymphocytopenia may be a surrogate marker of tumor-associated immune suppression. Taken together, PNI may serve as an indicator of nutritional status, SIR and immunity, and low PNI may lead to poorer outcome.

Several noteworthy findings were identified in this study. This is the first study to report PNI as an independent prognostic factor and combine age, tumor stage, tumor grade and tumor focality in a single predictor model to evaluate the prognosis of patients with NMIBC followed by intravesical chemotherapy. We also noticed that tumor size was not an independent factor to predict RFS which was included in the EORTC-GUCG risk scoring system, but the accuracy of internal calibrations in the nomogram was high. This could be explained by the limited number of patients.

Nomograms are considered the most accurate model to predict outcomes after surgical treatment, so far.[27] By applying points to the 5 variables, we can estimate the probability of recurrence for individual patients easily. Nomograms could guide clinicians in personalized clinical decision-making.[28] PNI can be measured at low cost, and routinely and easily in clinical practice, so it is convenient to establish a nomogram using PNI.

The limitation of the present study is inherent to its retrospective design. Moreover, single-institution cohorts might have more complete datasets, yet they might be biased by institutional practice patterns, which can be overcome by the use of multi-institutional or national databases.[29] Furthermore, a number of the patients in the present study had shortage of follow-up time. Only 206 patients were involved in the analysis of 5-year OS. Another limitation is that in the present study the nomogram was only internally validated, and external validation should be further investigated with a large multicenter cohort. However, even considering these

limitations, the present study suggests PNI as a potential independent prognostic factor for RFS in patients with NMIBC and provides a nomogram for patients with NMIBC who undergo TURBT and are then treated with intravesical chemotherapy to evaluate probability of recurrence.

Conclusion

The present study investigates the value of preoperative PNI as an independent prognostic factor to predict RFS of patients with NMIBC. The serum albumin and peripheral lymphocytes can be measured at low cost, and routinely and easily in clinical practice. Moreover, the nomogram which includes age, tumor stage, tumor grade, tumor focality and PNI could be useful to improve personalized multidisciplinary therapy for patients with NMIBC.

Acknowledgments

Disclosure

None of the contributing authors have any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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