Retrospective Study

Evaluate the prognostic nutritional index value on the prognosis of Chinese patients with high/extremely high-risk prostate cancer after radical prostatectomy

Yang F et al. PNI in prostate cancer patients

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Abstract

BACKGROUND

The incidence of prostate cancer (PCa) is on the rise in China. The risk level of patients with PCa was associated with the disease-free survival rate at 10 years after radical prostatectomy. Predicting prognosis in advance according to the degree of risk can provide reference for patients, especially for the treatment options and postoperative adjuvant treatment measures of high-risk/extremely high-risk patients.

AIM

To explore the predictive value of prognostic nutritional index (PNI) for biological recurrence in Chinese patients with high/extremely high risk PCa after radical prostatectomy.

METHODS

The biochemical test results and clinical data of 193 patients who underwent radical prostatectomy for the first time from January 2015 to December 2020 were retrospectively collected. The PNI value of peripheral blood within 1 week before surgery was calculated, and during the follow-up period, prostate specific antigen ≥ 0.2 ng/mL was considered to have biological recurrence. The receiver operating curve (ROC) was used to calculate the optimal critical value and area under the curve (AUC) of the patients. According to the critical value, the progression-free survival time of the high PNI group and the low PNI group was compared. The independent influencing factors of the patients' prognosis were obtained by COX proportional hazard regression model.

RESULTS

The non-biological recurrence rates of 1-year, 3-year and 5-year were 92.02%, 84.05% and 74.85%, respectively. The optimal critical value for PNI to predict biological recurrence was 46.23, the AUC was 0.789 (95%CI: 0.651-0.860, P < 0.001). The sensitivity
and specificity were 82.93%, 62.30%, respectively. In accordance with the optimal critical value of ROC curve (46.23), 193 patients were further divided into high PNI group (PNI ≤ 46.23, n = 108) and low PNI group (PNI > 46.23, n = 85). The incidence of postoperative complications in high PNI group was lower than that in low PNI group (21.18% vs 38.96%). The Kaplan-Meier survival analysis showed that the overall survival rate at 5 years in the low PNI group was 87.96% (13/108), which was lower than that in the high PNI group (61.18%, 33/85) (P < 0.05). Low PNI (HR = 1.74 P = 0.003) and positive incisal margin status (HR = 2.14 P = 0.001) were independent predictors of biological recurrence in patients with high/extremely high risk PCa.

CONCLUSION
The PNI value has predictive value for the prognosis of patients with high/extremely high risk PCa, and it is an independently prognostic factor. Patients with low PNI value have shorter time of non-biological recurrence after prostatectomy. It is expected that the combined prediction of other clinicopathological data will further improve the accuracy and guide postoperative adjuvant therapy to improve the quality of prognosis.

**Key Words:** High/extremely high-risk; Prostate cancer; Prognostic nutrition index; Prognostic evaluation; Radical prostatectomy

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**Core Tip:** Radical prostatectomy is currently the main treatment for prostate cancer (PCa). However, the incidence of postoperative complications and tumor progression remains high, and patients are highly prone to recurrence or metastasis. Therefore, it is crucial to explore more and more effective biomarkers to evaluate the prognosis of patients. Prognostic nutritional index (PNI) is an indicator of reflecting body's
nutritional status and immune level. At present, there are few studies on the relationship between PNI and the prognosis of patients with high-risk/extremely high-risk PCa. This study aims to explore the PNI value on the prognostic of patients with high-risk/extremely high-risk PCa after radical prostatectomy. The results showed that PNI value was an independent factor of influencing the prognosis of patients with high-risk/extremely high-risk PCa.

INTRODUCTION

The results of the Globocan project showed that prostate cancer (PCa) was one of the most common cancers in men. In the United States, PCa ranked first in incidence and third in mortality among male cancer patients. The incidence of PCa was related to race and diet structure and other factors. In China, the incidence of PCa is relatively low, but with the aging of the population, the westernization of lifestyle, the progress of detection methods and the development of tumor screening, the incidence of PCa is also rising. Another study reported that the incidence of PCa in China was 5.3/100000, and the mortality was 2.5/100000[1,2]. Currently, radical prostatectomy is the main treatment option, and there is still a great possibility of recurrence or metastasis after surgery. According to PAS, T classification and Gleason's cancer score, patients with PCa were classified as low risk, medium risk and high risk. The risk level was related to the 10-year disease-free survival rate after radical prostatectomy. 10-year disease-free survival rates at low, medium and high risk were 83%, 46% and 29%, respectively[3,4]. Predicting the prognosis information in advance according to the degree of risk can provide reference for patients, especially for the treatment options and postoperative adjuvant treatment measures of high/extremely high-risk patients.

Prognostic nutritional index (PNI) was initially proposed to predict the immunogenicity and risk of gastrointestinal surgery by albumin and lymphocytes, but it was later found that PNI was correlated with the prognosis of many tumors. At present, PNI is considered to have predictive significance in the prognosis of lung cancer[5], melanoma[6], esophageal cancer[7], and it is considered that low PNI is related
to poor prognosis. Currently, there are few studies on the relationship between PNI and the prognosis of patients with high-risk/extremely high-risk PCa. This study intends to investigate the predictable value of PNI on the prognosis of patients with high-risk/extremely high-risk PCa after radical prostatectomy.

MATERIALS AND METHODS

**Research data**

The clinical data of 193 patients with PCa who were first treated in our hospital from January 2013 to December 2016 were retrospectively collected. All patients and their families signed informed consent forms. Inclusion criteria as follows: (1) PCa was first diagnosis by pathology, and surgical resection was performed; (2) The blood test report and other data were complete and informed consent was obtained; and (3) Per the National Comprehensive Cancer Network (NCCN) criterion, it was identified as high/extremely high-risk PCa, high risk: T3a or prostate specific antigen (PSA) > 20 ng/mL or Gleason score ≥ 8, and extremely high-risk: T3b-4. Exclusion criteria as follows: (1) Patients had other serious diseases or tumors; and (2) Patients had postoperative infection. This study had been approved by Medical Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology.

**Clinical data collection**

The clinical data of all patients were collected by consulting medical records and calling for follow-up, including age, history of chronic diseases, incisal margin status, capsule invasion, nerve invasion and postoperative adjuvant therapy.

**Research indicators**

**PNI value:** Peripheral venous blood was collected from all patients within one week before operation for blood routine, blood biochemistry and PSA value detection. The PNI value was calculated from the total number of peripheral serum albumin and blood
lymphocytes. Calculation formula: PNI = albumin value (g/L) + 5 × total lymphocyte count (10⁹/L).

Follow-up and outcome indicators: Patients were followed up by telephone, outpatient visits and reviewing medical records. Paper questionnaires were filled in to record patients’ postoperative data and disease progression. Follow-up included patients’ survival status (recurrence and death) and survival time. The biological recurrence indicator was PSA. When PSA ≥ 0.2 ng/mL, biological recurrence occurred. The starting point of follow-up was postoperative pathological diagnosis, and the end point was outcome events (recurrence and death). The overall survival (OS) was the time from the starting point to the end point or the last follow-up. Death due to reasons other than PCa or no recurrence before the end of follow-up period was regarded as withdrawal or termination.

Statistical analysis
The data were entered into Epidata and corrected logically. SPSS21.0 was used to analyze the data. Rate or constituent ratio was used to described count data. The rate or composition ratio between groups was compared by the chi-square test. The area under the curve (AUC) was obtained by receiver operating curve (ROC). The sensitivity and specificity of PNI were evaluated by the AUC. Calculating the Yordon index was used to determine the optimal critical value of PNI. The progression-free survival was compared between the two groups of patients with PNI by Kaplan-Meier survival analysis. The influencing factors of biological recurrence were analyzed by COX proportional hazard regression model. P < 0.05 was considered statistically significant.

RESULTS
ROC curve analysis
The survival outcome was regarded as the dependent variable to draw the ROC curve of PNI value. The results showed that the AUC was 0.789 (95% CI: 0.651-0.860, \( P < 0.001 \)). When the critical value of PNI for the diagnosis of biological recurrence was 46.23, the Joden index was the maximum, so the optimal critical value of PNI was 46.23. Under this threshold, the sensitivity and specificity of PNI diagnosis were 82.93% and 62.30%, respectively, as shown in Figure 1.

**PNI grouping of patients with different characteristics**

In line with the optimal critical value of ROC curve (46.23), 193 patients were further divided into high PNI group (PNI ≤ 46.23, \( n = 108 \)) and low PNI group (PNI > 46.23, \( n = 85 \)). There were no significant differences in the rates of high PNI group and low PNI group in patients with different age, chronic disease history, incisal margin status, capsule invasion, nerve invasion and postoperative adjuvant therapy. There was comparability between the two groups of patients with different PNI, as shown in Table 1.

**Postoperative complications in different PNI groups**

After radical prostatectomy in 193 patients with high/extremely high-risk PCa, there were 8 cases of incision infection, 8 cases of postoperative bleeding, 7 cases of abdominal infection, 5 cases of rectal injury, 7 cases of postoperative penile erection dysfunction, 6 cases of bladder-urethral anastomotic stenosis, 8 cases of urethral stenosis, 3 cases of lymphatic cyst, 9 cases of urinary fistula, and 6 cases of pulmonary embolism. There were 59 cases of postoperative complications. The incidence of postoperative complications in high PNI group was lower than that in low PNI group (21.18% vs 38.96%), as shown in Table 2.

**Cancer progression-free period of patients with high/extremely high-risk PCa in different PNI groups**
A total of 46 patients died of PCa 5 years after operation, and the survival rate at 5 years was 76.17%. Postoperative progression-free survival curves were plotted using Kaplan-Meier survival analysis in patients with high/extremely high risk PCa. The results showed that the OS rate at 5 years in the low PNI group was 87.96% (13/108), which was lower than that in the high PNI group (61.18%, 33/55), and the difference was statistically significant ($P < 0.05$). The 5-year low PNI group had shorter progression-free survival ($P < 0.001$), poor prognosis and higher postoperative biological recurrence rate, as shown in Figure 2.

**Single factor and multiple factors analysis of COX proportional hazard regression model**

At the end of follow-up, biological recurrence was considered as the dependent variable (biological recurrence $Y = 1$, no biological recurrence $Y = 0$), PNI group, age, chronic disease history, incisal margin status, capsule invasion, nerve invasion and postoperative adjuvant therapy were considered as independent variables in the COX proportional hazard regression model. Single factor results showed that the factors affecting the biological recurrence of PCa patients included PNI grouping, age, history of chronic diseases, incisal margin status, capsule invasion, and nerve invasion ($P < 0.05$). The above factors with statistically significant effects on biological recurrence of patients were included in the multivariate COX proportional hazard regression model. The results showed that low PNI (HR = 1.74 $P = 0.003$) and positive incisal margin status (HR = 2.14 $P = 0.001$) were independent predictors of biological recurrence in patients with high/extremely high-risk PCa. Specifically, the prognostic biological recurrence in patients with low PNI was 1.74 times that in patients with high PNI, and the prognostic biological recurrence was 2.14 times higher in patients with positive incisal margin status than that in patients with negative incisal margin status, as shown in Table 3.

**DISCUSSION**
Lymphocytes and albumin were used to reflect the immune nutritional status of patients for PNI. PNI in a variety of cancers is expected to be considered as a predictor of therapeutic effect, and a large number of related studies have suggested that low PNI has connection with poor prognosis of cancer[9]. Surgical stress may cause a series of metabolic changes in patients, consume nutrients such as protein and fat in the early metabolic period[10]. Although serum albumin cannot be directly used as a nutrient by the body, but its half-life of up to 20 d can reflect the reserve level of nutrients such as amino acids in patients. Low albumin level reduces plasma osmotic pressure, resulting in reduced tolerance and absorption capacity of intestinal nutrients. Intestinal hyperosmotic nutrition agents also absorb the liquid in the intestinal wall like the intestinal cavity[11], and serum albumin is closely related to a variety of tumor regulators. Some studies believe that serum albumin contributes to cell stability and DNA replication[12]. Lymphocytes are an important part of the immune system, which can secrete tumor necrosis factor-α, interferon-γ and other cytokines to inhibit tumor progression. At the same time, lymphocytes have an important inhibitory effect on postoperative inflammation. The low level of lymphocytes mostly indicate immune dysfunction[13]. Immunity and nutrition play an important role in the disease progression and prognosis of patients. Peripheral blood albumin and lymphocytes make a reliable predictive analysis for the prognosis of cancer patients.

PCA is a heterogeneous disease, ranging from inertia to high invasiveness. Approximately 15% of patients with PCA are diagnosed as high risk. However, the high mortality rate in men with high-risk/very high-risk PCA remains a challenge, estimated at 14.2% after radical prostatectomy[14,15]. In order to identify the risk of PCA earlier and accurately, so as to develop effective diagnosis, treatment and rehabilitation models, the risk of PCA is managed by classification. At present, there are many PCA classification methods, but it is difficult to determine the core percentage involved in the tumor reliably and repeatedly, most of them are based on T stage, PSA and Gleason score to classify patients. This study refers to the classification criteria of the NCCN[16].
The ROC curve results of this study showed that the optimal critical value of PNI for predicting PCa biological recurrence was 46.23, and the AUC was 0.789, indicating that the results of PNI for predicting biological recurrence had good authenticity and was a relatively accurate prediction index. The optimal diagnostic critical value of PNI for postoperative recurrence of non-small cell lung cancer was 45.7, and the optimal critical value for the survival outcome of urothelial carcinoma was 46.91. However, in another PCa study, the optimal prognostic critical value was 50.2. Combined with the results of this study, the optimal predictive critical value of PNI for the prognosis of cancer patients may be mostly between 45-50. Elevated PSA is an important early detection marker of PCa in most clinically significant PCa, but prostatic hyperplasia and prostatitis can also lead to PSA elevation. The results of this study (sensitivity 82.93%, specificity 62.30%) are consistent with the characteristics of low specificity. The progression-free survival of patients in the low PNI group was shorter than that of patients in the high PNI group, which was similar to the previous findings in a variety of cancers. However, in this survey, there might be misdiagnosis in judging biological recurrence only by PSA value.

AUC = 0.789 indicated that the diagnostic value of prognosis was still limited. The fitting results of COX proportional hazard regression model also showed that PNI < 46.23 was an independent factor of influencing the poor prognosis of patients with PCa after operation, and the positive incisal margin status could also promote biological recurrence. At the same time, some research results showed that PNI was correlated with some pathological data, suggesting that PNI combined with other clinical or pathological data can improve the accuracy in predicting the prognosis of PCa patients.

This study is a retrospective study of patients in a hospital. There may be a bias in admission rate. The clinical and pathological data of the included patients are not comprehensive enough, and other nutritional or immune indicators of the patients are not considered. There may be information bias. There is no further grouping analysis for the case of PNI < 46.23. It is expected that a multicenter prospective study with a
large sample will be done in the future to have a deeper investigation of patients and further explore the prognostic impact of PNI in PCa patients.

CONCLUSION
In summary, PNI value has predictive significance for prognosis in patients with high/extremely high-risk PCa after radical prostatectomy, which can help doctors to evaluate the prognosis of patients at an early stage. The prognosis of patients with high PNI is better than that of patients with low PNI. Preventive postoperative adjuvant therapy can help patients to prolong progression-free survival.
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Li Chen, Ping Bai, Xiangyi Kong, Shaolong Huang, Zhongzhao Wang, Xiangyu Wang, Yi Fang, Jing Wang. "Prognostic Nutritional Index (PNI) in Patients With Breast Cancer Treated With Neoadjuvant Chemotherapy as a Useful Prognostic Indicator", Frontiers in Cell and Developmental Biology, 2021


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