

Is the Prognostic Nutritional Index a Predictor of Urolithiasis?

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What's known on the subject? and What does the study add?

The prognostic nutritional index (PNI) is calculated using serum albumin and lymphocyte counts and is thought to provide information about nutritional status, inflammation, and immunity. PNI has been frequently studied in malignancies. Studies examining the relationship between PNI and many malignancies are available in the literature. However, studies examining the relationship between PNI and urolithiasis are limited. Considering the relationship between albumin and stone disease and the effect of lymphocytes on inflammation and immunity, PNI may be a marker of urolithiasis. In our study, a low PNI value was associated with urolithiasis. PNI, given that it does not require additional testing, and can be calculated using routine blood tests, and is associated with urolithiasis, can give clinicians a preliminary understanding of patients with urolithiasis.

Abstract

Objective: Prognostic nutritional index (PNI) is a parameter that reflects nutritional status and inflammation. It is calculated from serum albumin and lymphocyte count. Our study investigated whether PNI has a predictive value in urolithiasis.

Materials and Methods: Data of patients who applied to Ağrı Training and Research Hospital with renal colic between January 2017 and December 2024 were retrospectively examined. Three hundred forty-eight patients were included in the stone group and 627 patients were included in the control group. Patients' age, gender, smoking, hypertension, and diabetes history, body mass index, hemoglobin level, glomerular filtration rate (GFR), blood urea nitrogen, uric acid levels, sodium, potassium, calcium, white blood cell count (WBC), neutrophil count, lymphocyte count, albumin, neutrophil/lymphocyte ratio (NLR), and PNI levels were compared.

Results: No statistically significant difference existed between the demographic data and the patients' comorbidities. In the stone patients group and the control group, mean GFR was 88.04 [standard deviation (SD): 13.21], 93.90 (SD: 13.17); mean WBC was 8910 (SD: 1629), 8268 (SD: 1562); mean neutrophil count was 6040 (SD: 1416), 4933 (SD: 1283); mean lymphocyte count was 2070 (SD: 879), 2535 (SD: 944); mean NLR was 3.62 (SD: 2.1), 2.34 (SD: 1.41); PNI was 30.73 (SD: 6.85), 53.66 (SD: 6.94) ($p < 0.001$, all).

Conclusion: PNI value was lower in stone patients than in the control group. PNI may be a parameter predicting stone formation. Additionally, the predictive value can be strengthened with the NLR value.

Keywords: Prognostic nutritional index, urolithiasis, kidney stone

Introduction

Urinary system stone disease is prevalent, seen in 1–20% of people worldwide (1). Stone disease attracts attention with the high recurrence rates. However, there are studies with different

recurrence rates. Old studies that dominate the literature report a recurrence risk of approximately 50% in 5 years (2). Being one of the most common diseases in the world, this condition, with its high prevalence and high recurrence rates, leads to increased treatment costs and complications (3).

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Prognostic nutritional index (PNI) is a score that includes serum albumin and lymphocyte levels, which was first used to evaluate nutritional status and surgical risk in gastrointestinal surgery patients (4). It is calculated using the albumin level, which reflects nutritional status, and the lymphocyte count, which can indicate inflammation (5). Various formulas calculated based on platelet, neutrophil, lymphocyte, and C-reactive protein levels are used as both nutritional and inflammation parameters. One of these, PNI, has generally been studied in cancers (6). The ratios of these parameters have been frequently shown to be prognostic factors in various diseases (7).

Our study examined patients who presented to our clinic with renal colic complaints. These patients were divided into two groups according to their computed tomography results: patients with and without urinary system stones. We aimed to compare the PNI values of these two groups. We aimed to investigate whether PNI is a predictor of urolithiasis.

Materials and Methods

The data of patients who applied to the Urology Department of Ağrı Training and Research Hospital, a tertiary hospital in Türkiye, with renal colic between January 2017 and December 2022, were retrospectively examined. The ethics committee approval for the study was received from Ağrı İbrahim Çeçen University Clinical Research Ethics Committee (approval number: 109, date: 27.03.2025). Patients who were younger than 18 years of age, had a previous diagnosis of cancer, had a history of major surgery such as gastrointestinal system surgery, had a history of trauma, had a history of chronic inflammatory disease, had end-stage liver or kidney disease, were receiving systemic steroid therapy, did not undergo computed tomography, and had incomplete data were excluded from the study. After screening, two groups were formed: patients with and without stones. As a result, 975 patients were included: 348 patients in the group with urolithiasis (group 1) and 627 patients in the control group (group 2). Age, gender, hemoglobin levels, white blood cell count (WBC), neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio (NLR), glomerular filtration rate (GFR), uric acid, blood urea nitrogen, sodium, potassium, calcium, and albumin levels, body mass index, hypertension history, smoking history, and diabetes history of patients in both groups were recorded. PNI was calculated using the formula determined by Onodera et al. (5) in 1984. This formula is calculated using the serum albumin level and the total lymphocyte count in the blood and is formulated as "10 x albumin (g/dL) + 0.005 x total lymphocyte count/mm³". All these data were recorded, and the PNI levels were examined to determine whether they differed between the stone patients and the control group. Thus, whether PNI has a predictive value for stone formation was investigated.

Statistical Analysis

SPSS Version 28.0.0.0 (IBM, Chicago) was used for statistical analysis. The Student's t-test was used for parametric distribution values when comparing two group means. The chi-square test was used to compare categorical parameters. The normality of continuous variables was assessed using analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Continuous variables were presented as mean \pm standard deviation (SD) for normally distributed data and median (interquartile range) for non-normally distributed data. To calculate the cut-off value of the PNI, receiver operating characteristic (ROC) curve analysis was performed (Figure 1). A cut-off value of 53.275 was found [area under curve (AUC): 0.62, 95% confidence interval (CI): 0.583-0.656]. For practical purposes, 53.3 will be used as a cut-off value. Patients whose PNI <53.3 and PNI \geq 53.3 were compared based on the presence or absence of a stone by using the chi-square test. The significance level (α) was set at 0.05 for all analyses. The minimum number of samples required for the study was calculated by performing power analysis at an 80% power value.

Results

There was no statistically significant difference in the patients' age, gender, smoking history, hypertension history, diabetes history, body mass index, hemoglobin levels, blood urea nitrogen, uric acid, sodium, potassium, calcium, and albumin values between the two groups (Table 1).

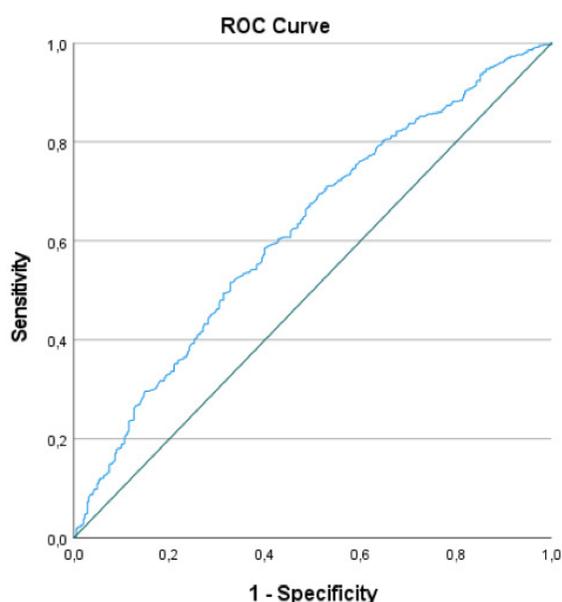
While the mean GFR value was 88.04 (SD: 13.21)/mm³mL/min/1.73 m² in group 1, the mean GFR value was 93.90 (SD: 13.17) mL/min/1.73 m² in group 2 ($p < 0.001$). The mean WBC value was 8910 (SD: 1629)/mm³ in group 1 and 8268 (SD: 1562)/mm³ in group 2 ($p < 0.001$). The mean neutrophil count was 6040 (SD: 1416)/mm³ in group 1 and 4933 (SD: 1283)/mm³ in group 2 ($p < 0.001$). Mean lymphocyte count was found to be 2070 (SD: 879)/mm³ in group 1 and 2535 (SD: 944)/mm³ in group 2 ($p < 0.001$). Mean NLR values were found to be 3.62 (SD: 2.1) in group 1 and 2.34 (SD: 1.41) in group 2 ($p < 0.001$). When PNI values were compared, mean PNI value was found to be 50.73 (SD: 6.85) in group 1 and 53.66 (SD: 6.94) in group 2 ($p < 0.001$).

ROC curve analysis was performed to calculate the cut-off value of the PNI level (Figure 1). 53.275 was found to be a cut-off value (AUC: 0.62, 95% CI: 0.583-0.656). For practical purposes and with the knowledge that it does not affect the results, the value 53.3 will be used from this stage of the article onwards. Patients whose PNI <53.3 and PNI \geq 53.3 were compared using the chi-square test, based on their stone presence. 43.6% of patients who had PNI <53.3 had a urinary stone, while 26% of the PNI \geq 53.3 group had a stone (OR: 2.2, 95% CI: 1.67-2.88) (Table 2).

Table 1. Patient characteristics, laboratory values, prognostic nutritional index, and neutrophil-lymphocyte ratios of stone formers and control groups

Parameters	Group 1 (n=348)	Group 2 (n=627)	p-value
Age, mean (SD)	39.54 (8.47)	39.82 (8.61)	0.623
Gender, n (%)			
Male	193 (55.5)	358 (57.1)	0.621
Female	155 (44.5)	269 (42.9)	
Smoking history, n (%)	113 (33.4)	190 (33.2)	0.947
Missing data	10 (2.9)	55 (8.8)	-
Hypertension, n (%)	47 (14.0)	74 (12.3)	0.447
Missing data	13 (3.8)	25 (4.0)	-
Diabetes mellitus, n (%)	36 (10.8)	61 (10.3)	0.808
Missing data	14 (4.0)	33 (5.3)	-
Body mass index (kg/m ²), mean (SD)	22.95 (4.43)	22.67 (4.07)	0.340
Hemoglobin (gr/dL), mean (SD)	13.63 (1.25)	13.76 (1.13)	0.111
Glomerular filtration rate (mL/min/1.73m ²), mean (SD)	88.04 (13.21)	93.90 (13.17)	<0.001*
Blood urea nitrogen (mg/dL), mean (SD)	17.68 (4.14)	17.36 (4.18)	0.245
Uric acid (mg/dL), mean (SD)	4.72 (0.81)	4.68 (0.82)	0.574
Sodium (mEq/L), mean (SD)	139.72 (3.03)	139.37 (3.24)	0.092
Potassium (mEq/L), mean (SD)	4.51 (0.42)	4.50 (0.41)	0.612
Calcium (mg/dL), mean (SD)	9.48 (0.82)	9.53 (0.86)	0.375
White blood count (/mm ³), mean (SD)	8910 (1629)	8268 (1562)	<0.001*
Neutrophil (/mm ³), mean (SD)	6040 (1416)	4933 (1283)	<0.001*
Lymphocyte (/mm ³), mean (SD)	2070 (879)	2535 (944)	<0.001*
Albumin (g/dL), mean (SD)	4.04 (0.53)	4.1 (0.55)	0.097
Neutrophil/lymphocyte ratio, mean (SD)	3.62 (2.1)	2.34 (1.41)	<0.001*
Prognostic nutritional index, mean (SD)	50.73 (6.85)	53.66 (6.94)	<0.001*

*: Clinically significant, SD: Standard deviation

**Figure 1.** ROC curve analysis of groups according to PNI values
PNI: Prognostic nutritional index, ROC: Receiver operating characteristic**Table 2. Comparative analysis of having stone or not, according to prognostic nutritional index cut-off values**

	PNI <53.3 (n=537)	PNI ≥53.3 (n=438)	p-value
Patient with urinary stones, n (%)	234 (43.6)	114 (26)	<0.001*
Patient without urinary stones, n (%)	303 (56.4)	324 (74)	

Odds ratio: 2.2; 95% confidence interval: 1.67-2.88, *: Clinically significant, PNI: Prognostic nutritional index

Discussion

Our study showed that patients with stones had lower PNI values than the control group. In addition, the cut-off value of PNI in terms of stone formation risk was found to be 53.3. These results indicate that it can provide insight to the physician without additional cost and intervention, since it is obtained from routinely checked blood parameters, and it is cheap and easily accessible.

The PNI was first used by Buzby et al. (4) in 1980 to predict surgical risk. Onodera et al. (5) used the formula more straightforwardly and focused only on serum albumin and lymphocyte levels. It was studied to predict the prognosis of many cancers, especially gastrointestinal system malignancies (8). Lymphocytes can indicate inflammation levels as well as immune status (9). Serum albumin is related to nutritional status and, as it is a negative acute phase reactant, to inflammation (10). For all these reasons, PNI can serve as an important marker reflecting nutritional status, immunity, and inflammation. A recent study by Wang et al. found that higher PNI levels were associated with a reduced prevalence of urolithiasis (11). The results of this study support our findings. Lee et al. (12) used the controlling nutritional status score to assess the recurrence rate of urolithiasis and demonstrated that patients with poorer nutritional status experienced faster recurrence. They also found a significant negative correlation between nutritional status and stone recurrence. Both studies reflect the relationship between nutritional status and urinary system stones. Our study found that lower PNI levels are associated with a higher prevalence of urinary stones. PNI is considered to be affected by albumin and lymphocytes. Albumin may reflect protein-energy malnutrition, while lymphocytes may be associated with impaired immunity due to malnutrition. As a result, malnutrition may affect stone formation.

One component in the PNI formula is albumin. Albumin is the most common protein in plasma and is an indicator of nutritional status (10). Albumin is a molecule that can support stone formation by participating in the matrix structure of urinary system stones. At the same time, it acts as an inhibitor of stone formation in urine (13). There are many studies examining the relationship between protein and albumin and stones. Reddy et al.'s (14) study shows that high protein intake increases the formation of urinary system stones. One study showed that patients with normal calcium levels were fed a diet with lower animal protein, which reduced the risk of stone formation (15). Another two randomized controlled studies concluded that a low-protein diet did not positively affect stone recurrence (16,17). Another study stated that the risk of urolithiasis formation depends on the type of protein taken (18). A study evaluating the risk factors for urolithiasis after exogenous albumin intake concluded that there was no change in urine parameters (19). Another study comparing stone patients with controls showed that serum albumin levels of both groups were similar (20). Recent systematic reviews have demonstrated inconsistent evidence on the relationship between protein intake and the risk of stone formation (21). In our study, the two groups had no difference in albumin levels. We think the inconsistent findings in the literature regarding the association between albumin and urolithiasis make the use of a combined marker, such as PNI, more important.

In a study conducted by Mao et al. (22), NLR level was found to be related to stone prevalence. Another recently published case-control study concluded that NLR levels were higher and lymphocyte levels were lower in stone patients (23). In another study, it was concluded that neutrophil and NLR levels in stone patients were similar to those in the control group (24). Another notable study concluded that a decreased lymphocyte percentage plays a significant role in stone formation (20). In our study, neutrophil count and NLR were higher, while lymphocyte count was lower in the urolithiasis group. It has been shown that inflammation plays an important role in stone disease. Considering this situation, we think that the inflammatory profile in patients with stones is also related to the increase in neutrophils. In addition, our results are similar to studies showing a decrease in lymphocyte count in patients with urolithiasis (22,23). This supports the increase in NLR and the reduction in PNI.

In our study, WBC levels were higher in patients with stones. We believe this is due to the inflammation parameters and the high neutrophil count. In our study, the neutrophil count was higher in the urolithiasis group, but the lymphocyte count was lower. Considering that the neutrophil count was dominant in the leukocyte distribution, the lower WBC count in the urolithiasis group is an expected result. In addition, GFR was found to be lower in the stone group in our study. This is an expected result because there may be pathologies such as stone-related obstruction and impaired oral intake.

In our research, PNI values were lower in patients with stones. We think, using a combined marker that is affected by nutritional status, immunity, and inflammation may be important in diagnosing urolithiasis. We also think it is important to obtain it from a routinely applied test, which is cheap, easily accessible, and does not require additional examination. In addition, our study concluded that NLR is higher in stone patients. Combining parameters can provide important information regarding diagnosing patients with stones, advanced tests, and predicting recurrence. Since none of these require additional tests, we believe this combined use will significantly benefit physicians.

In our study, the PNI cut-off value for determining the urolithiasis risk was 53.3. Our study concluded that urinary system stone disease risk increases below this value. This value can be used practically by clinicians. Different cut-off values have been used in the literature—especially in cancer patients (6,25). The fact that PNI is an index mostly studied on malignancy makes direct comparison difficult. Multiple studies should support this value, and statistical analyses should determine this support. However, we still believe it can be a catalyst for other studies in the literature.

Study Limitations

Our study had some significant limitations. First, the retrospective nature of our study was the most important limitation. Second, the small number of patients was also a limitation. Another limitation is that genetic predisposition, occupational exposure, and environmental factors cannot be thoroughly examined. Additionally, patients' smoking, diabetes, and hypertension histories were retrieved from the hospital system. We consider this a limitation due to the potential for errors by physicians or healthcare professionals entering this information. In addition, these patients could not be followed for a long time was another limitation.

Conclusion

PNI is a score that reflects nutritional status and immune status. Our study found that the PNI value was low in patients with stones, suggesting that it is a parameter that predicts stone formation. In addition, NLR levels were higher in patients with stones. PNI is very important because it can be obtained from routine tests, is cheap and easily accessible, and predicts the risk of stone formation. Using it together with NLR can strengthen its predictive value. Nevertheless, more prospective and extensive studies with a larger number of patients are needed.

Ethics

Ethics Committee Approval: The ethics committee approval for the study was received from Ağrı İbrahim Çeçen University Clinical Research Ethics Committee (approval number: 109, date: 27.03.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ç.C., U.A., K.T., E.D., Concept: Ç.C., K.T., E.D., Design: Ç.C., Data Collection or Processing: K.T., E.D., Analysis or Interpretation: U.A., E.D., Literature Search: Ç.C., K.T., Writing: Ç.C., U.A., K.T., E.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

- Sorokin I, Mamoulakis C, Miyazawa K, Rodgers A, Talati J, Lotan Y. Epidemiology of stone disease across the world. *World J Urol.* 2017;35:1301-1320. [\[Crossref\]](#)
- Uribarri J, Oh MS, Carroll HJ. The first kidney stone. *Ann Intern Med.* 1989;111:1006-1009. [\[Crossref\]](#)
- Pearle MS, Calhoun EA, Curhan GC; Urologic Diseases of America Project. Urologic diseases in America project: urolithiasis. *J Urol.* 2005;173:848-857. [\[Crossref\]](#)
- Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg.* 1980;139:160-167. [\[Crossref\]](#)
- Onodera T, Goseki N, Kosaki G. [Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. *Nihon Geka Gakkai Zasshi.* 1984;85:1001-1005. Japanese. [\[Crossref\]](#)
- Ellez HI, Keskinilic M, Semiz HS, Arayici ME, Kisa E, Oztop I. The prognostic nutritional index (PNI): a new biomarker for determining prognosis in metastatic castration-sensitive prostate carcinoma. *J Clin Med.* 2023;12:5434. [\[Crossref\]](#)
- Shu W, Tao W, Chunyan H, Jie F, Yuan L, Yan X, Huan Z, Liang X. Preoperative nutritional evaluation of prostate cancer patients undergoing laparoscopic radical prostatectomy. *PLoS One.* 2022;17:e0262630. [\[Crossref\]](#)
- Yang Y, Gao P, Song Y, Sun J, Chen X, Zhao J, Ma B, Wang Z. The prognostic nutritional index is a predictive indicator of prognosis and postoperative complications in gastric cancer: a meta-analysis. *Eur J Surg Oncol.* 2016;42:1176-1182. [\[Crossref\]](#)
- Marelli-Berg FM, James MJ, Dangerfield J, Dyson J, Millrain M, Scott D, Simpson E, Nourshargh S, Lechler RI. Cognate recognition of the endothelium induces HY-specific CD8+ T-lymphocyte transendothelial migration (diapedesis) in vivo. *Blood.* 2004;103:3111-3116. [\[Crossref\]](#)
- Fuhrman MP. The albumin-nutrition connection: separating myth from fact. *Nutrition.* 2002;18:199-200. [\[Crossref\]](#)
- Wang L, Yu Y, Jiang Z, Lin F, Zhong Y, Wang C, Huang S, Xu Z. Inverse association between prognostic nutritional index and kidney stone prevalence: a population-based study. *PLoS One.* 2025;20:e0318254. [\[Crossref\]](#)
- Lee HY, Kang HW, Kim K, Ha YS, Kim WT, Kim YJ, Yun SJ, Kim WJ, Lee SC. Nutritional status assessed by the controlling nutritional status (CONUT) score as a predictor of recurrence of urolithiasis. *Investig Clin Urol.* 2021;62:553-559. [\[Crossref\]](#)
- Khan SR, Kok DJ. Modulators of urinary stone formation. *Front Biosci.* 2004;9:1450-1482. [\[Crossref\]](#)
- Reddy ST, Wang CY, Sakhaee K, Brinkley L, Pak CY. Effect of low-carbohydrate high-protein diets on acid-base balance, stone-forming propensity, and calcium metabolism. *Am J Kidney Dis.* 2002;40:265-274. [\[Crossref\]](#)
- Borghi L, Schianchi T, Meschi T, Guerra A, Allegri F, Maggiore U, Novarini A. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. *N Engl J Med.* 2002;346:77-84. [\[Crossref\]](#)
- Hiatt RA, Ettinger B, Caan B, Quesenberry CP Jr, Duncan D, Citron JT. Randomized controlled trial of a low animal protein, high fiber diet in the prevention of recurrent calcium oxalate kidney stones. *Am J Epidemiol.* 1996;144:25-33. [\[Crossref\]](#)
- Dussol B, Iovanna C, Rotily M, Morange S, Leonetti F, Dupuy P, Vazi A, Saveanu A, Loundou A, Berland Y. A randomized trial of low-animal-protein or high-fiber diets for secondary prevention of calcium nephrolithiasis. *Nephron Clin Pract.* 2008;110:c185-c194. [\[Crossref\]](#)
- Ferraro PM, Mandel EI, Curhan GC, Gambaro G, Taylor EN. Dietary protein and potassium, diet-dependent net acid load, and risk of incident kidney stones. *Clin J Am Soc Nephrol.* 2016;11:1834-1844. [\[Crossref\]](#)
- Hattori CM, Tiselius HG, Heilberg IP. Whey protein and albumin effects upon urinary risk factors for stone formation. *Urolithiasis.* 2017;45:421-428. [\[Crossref\]](#)
- Tang K, Liu H, Jiang K, Ye T, Yan L, Liu P, Xia D, Chen Z, Xu H, Ye Z. Predictive value of preoperative inflammatory response biomarkers for metabolic syndrome and post-PCNL systemic inflammatory response syndrome in patients with nephrolithiasis. *Oncotarget.* 2017;8:85612-85627. [\[Crossref\]](#)

21. Van Elswyk ME, Weatherford CA, McNeill SH. A systematic review of renal health in healthy individuals associated with protein intake above the US recommended daily allowance in randomized controlled trials and observational studies. *Adv Nutr.* 2018;9:404-418. [\[Crossref\]](#)
22. Mao W, Wu J, Zhang Z, Xu Z, Xu B, Chen M. Neutrophil-lymphocyte ratio acts as a novel diagnostic biomarker for kidney stone prevalence and number of stones passed. *Transl Androl Urol.* 2021;10:77-86. [\[Crossref\]](#)
23. Butt AJ, Khawar MB, Afzal A, Bhalli Au, Hashmi MATS, Afzal N, Hamid SE, Shahzaman S, Habiba U, Shah SS. Neutrophil-to-lymphocyte ratio and monocyte-to-HDL ratio as a biomarker of urolithiasis. *Comparative Clinical Pathology.* 2023;32:783-788. [\[Crossref\]](#)
24. Manjunath T, Barua SK, Sarma D, Bagchi PK, Phukan M. Correlation of hematological inflammatory biomarkers in patients with urolithiasis: a prospective case control study. 2021. [\[Crossref\]](#)
25. Li B, Lu Z, Wang S, Hou J, Xia G, Li H, Yin B, Lu W. Pretreatment elevated prognostic nutritional index predicts a favorable prognosis in patients with prostate cancer. *BMC Cancer.* 2020;20:361. [\[Crossref\]](#)