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ORIGINAL RESEARCH

Association Between Neutrophil-to-Lymphocyte Ratio and Benign Prostatic Hyperplasia: Results from the TCLSIH Cohort Study

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Purpose: The prevalence of benign prostatic hyperplasia (BPH) in the general Chinese adult male population has risen sharply over the past few decades. Increasing evidence suggests that inflammation plays an important role in the pathogenesis of BPH. To better understand the role of inflammation in the pathogenesis of BPH, we can use the neutrophil-to-lymphocyte ratio (NLR) because it is a simple and effective marker of inflammation and immunity. This study aims to prospectively investigate the association between NLR levels and the prevalence of BPH in a general Chinese adult male population.

Patients and Methods: This study included a total of 15,783 male participants free from BPH at baseline. NLR was measured according to the complete blood count. BPH was defined as total prostate volume (TPV) ≥30 mL, and TPV was determined by transabdominal ultrasonography. Multivariable Cox proportional hazards models were fitted to calculate hazards ratios (HRs) and corresponding 95% confidence intervals (CIs) for BPH risk with NLR levels.

Results: During a median follow-up of 2.7 years, 5078 BPH cases were documented. After adjusting for age, body mass index, smoking, alcohol, education, occupation, income, physical activity, total energy intake, personal and family history of disease, and inflammation markers, the multivariable-adjusted HRs of BPH were 1.00 (reference), 1.08 (95% CIs 0.99, 1.17), 1.10 (95% CIs1.02, 1.19), and 1.12 (95% CIs1.03, 1.21), respectively, for participants with NLR in the first, second, third, and fourth quartiles (P for trend <0.01).

Conclusion: Higher NLR levels were associated with a higher risk of BPH in Chinese adult male population. Our findings support the notion that NLR levels may be an important target for BPH prevention and intervention.

Keywords: neutrophil to lymphocyte ratio, inflammation, benign prostatic hyperplasia, prospective cohort study

Introduction

Prostate cancer (PCa) is the second most prevalent cancer type diagnosed worldwide and the major cause of cancer-related death among human beings.[1] Benign prostatic hyperplasia (BPH) is the most prevalent prostate condition affecting men as they age and a significant risk factor for PCa development.[2] Moreover, BPH may cause symptoms of the lower urinary tract (LUTS) due to increased smooth muscle tone and resistance[3] and blockage of the proximal urethra.[4]

Although several theories with empirical support tackle this point, the causes of BPH are multifactorial and not fully understood. A growing body of literature that recognized inflammation of the prostate plays a particularly critical role in the initiation and evolution of BPH and the progression of symptoms,[5] and most of the studies underline that it has a causal or predictive role.[6] Infections, hormonal changes, nutritional factors, immunological reactions, environmental factors, genetic

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predisposition, and even urine reflux inside the prostate's collecting duct are all potential causes of inflammation.[7] Meanwhile, a number of growth factors and cytokines may support an inflammatory process in the prostate.

The neutrophil-to-lymphocyte ratio (NLR) has gained popularity as a biomarker for determining the overall level of inflammation in recent years.[8] It is also easy to measure and an inexpensive parameter that can be easily calculated from complete blood counts (CBCs).[3] Multiple studies have clearly shown that the potential role of NLR in urology has generated considerable attention. For example, evidence suggests that NLR has a role, both in biochemical failure in prostate cancer and the spontaneous passage of ureteral stones.[9,10] Extensive research has revealed that NLR is related to severe LUTS and intravesical prostatic protrusion (IPP) in men with BPH.[3,11,12] However, small sample sizes limit the findings of all of these studies. Until now, there has been a lack of a well-designed prospective cohort to determine a causal relationship between NLR levels and the prevalence of BPH in the first place.

To address this research gap, the major purpose of the prospective cohort study was to investigate whether NLR levels are associated with the risk of BPH in a large-scale Chinese adult male population.

Methods

Study Design and Participants

The Tianjin Chronic Low-Grade Systemic Inflammation and Health (TCLSIH) cohort study (clinicaltrials.gov UMIN000027174) included this investigation. The cohort had been described in detail in our previous studies.[13,14] This is in line with the ethical guidelines of the 1975 Declaration of Helsinki. The Institutional Review Board of Tianjin Medical University approved the study's protocols and procedures under approval number TMUhMEC 201430, and each participant signed a written informed consent form. Also, this study complies with STROBE guidelines for cohort studies.

From January 2010 to December 2020, 35,238 Chinese adult male participants were enrolled in the TCLSIH cohort study; participants who had received at least one health examination and questionnaire, including physical examination, blood tests, socio-demographic characteristics, and lifestyle questionnaires. Among these individuals, we excluded 4828 participants who were lost to follow-up (follow-up rate: 86.3%). We also excluded participants with other prostate diseases (n=2682) and those with cardiovascular disease (CVD) (n=2875), cancer (n=1618), or did not undergo neutrophil and lymphocyte counts (n=1583), had BPH or a prior history of treatment for BPH (n=5869) at baseline. The final study sample included 15,783 people after these exclusions. Figure 1 displays a flowchart of the participant selection process.

Definition of Newly Diagnosed BPH

Previous studies have investigated the relative adequacy of transabdominal and transrectal ultrasonography for prostatic measurements, replacing gold-standard transrectal studies with cheaper, easier, and less invasive transabdominal studies in large-scale population screening.[15] At both baseline and subsequent follow-up examinations, prostate disease was tested using transabdominal ultrasonography.[16] BPH was defined as total prostate volume (TPV) $\geq$ 30 mL[16] according to a previous study. TPV was determined by transabdominal ultrasonography (7–12 MHz, Royal Philips) and calculated as elliptical volume (height$\times$ width$\times$ length$\times$ $\pi/6$).[17] Using trained professional staff, transabdominal ultrasonography with TPV measurements was performed. A first-time BPH developed as a result of the follow-up period.

Assessment of NLR

Using venipuncture at the elbow, fasting blood samples were taken from each participant in the morning. An automated hematology analyzer was used to measure the leukocyte, neutrophil, and lymphocyte counts, which were expressed as 1000 cells/mm^3. The NLR was calculated as the ratio of the neutrophil count to the lymphocyte count. To investigate how the NLR levels are associated with the prevalence of BPH, we divided them into quartiles and continuous variables.

Assessment of Other Variables

Height (m) and weight (kg) were measured using calibrated equipment for anthropometric measurements. Weight/height^2 (kg/m^2) was used to calculate the body mass index (BMI). Waist circumference was measured according to a standardized protocol (to the closest 0.1 cm).

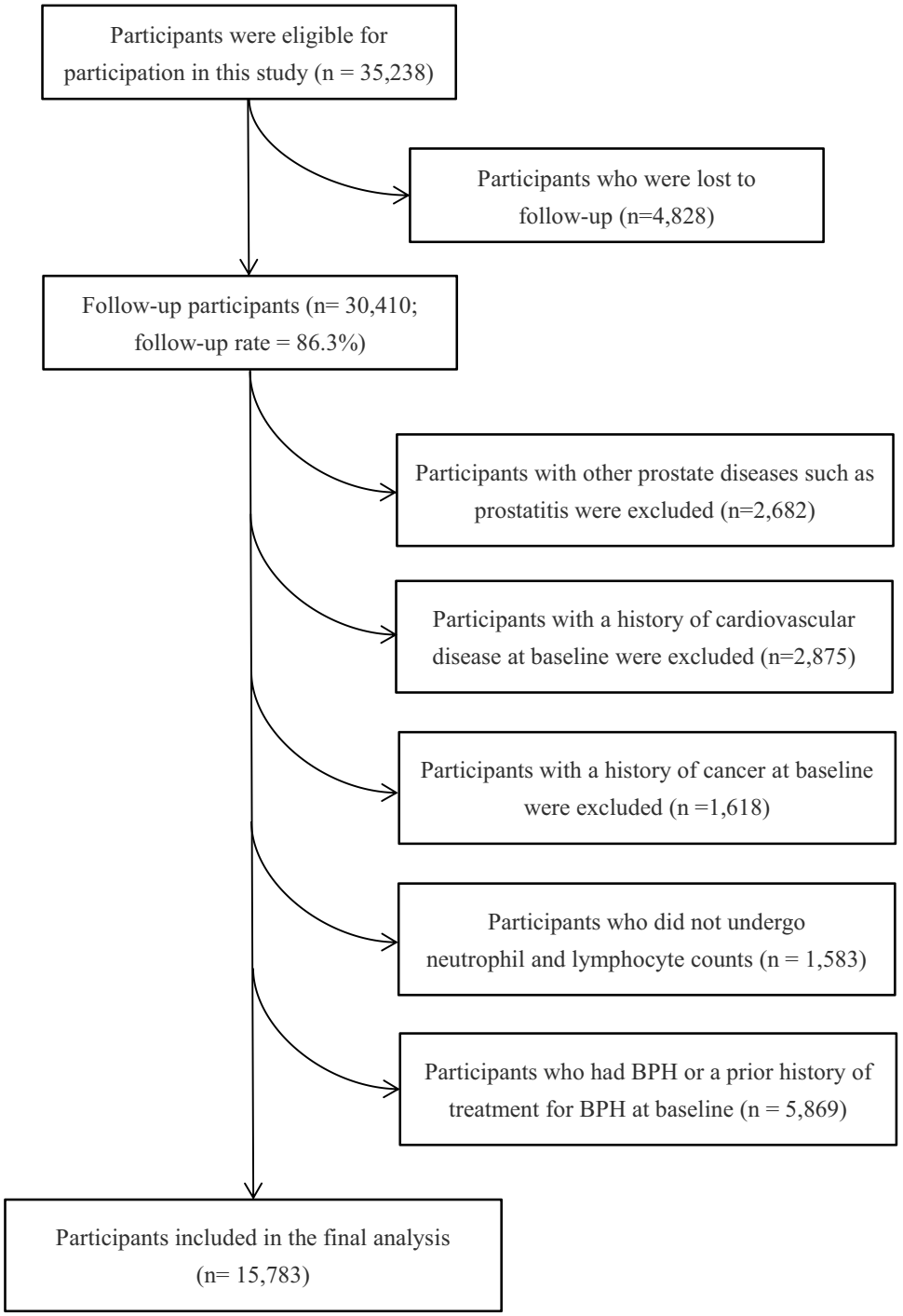

Figure 1 Flow diagram of study participant selection.
Note: BPH was defined as TPV ≥ 30 mL.
Abbreviation: BPH, benign prostatic hyperplasia.

Fasting blood glucose (FBG), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), and high-sensitivity C-reactive protein (hsCRP) were all measured in fasting blood samples. An FBG level of ≥7.0 mmol/L or a self-reported history of diabetes mellitus were considered indicators of diabetes mellitus.[18] TC ≥ 5.17 mmol/Lor TG ≥ 1.7 mmol/L or LDL-C ≥3.37 mmol/L, or the usage of antilipemic medications have been defined as hyperlipidemia.[19] Blood pressure (BP) was measured at least twice by trained nurses using automatic BP monitors (A&D Company, Ltd., Tokyo, Japan).[20] Prior to

taking BP measurements, participants rested for at least 5 min in a calm area, and measurements were then taken in the upper right arm.[21] The measurements were separated by at least 1 min. Systolic BP of ≥140 mmHg and/or diastolic BP of ≥90 mmHgor a history of hypertension were both considered to be indicators of hypertension.[22]

Social and demographic variables were also assessed, including age, smoking and drinking status, educational level, occupation, monthly household income, and individual and family history of disease were obtained from a health status questionnaire. A simplified version of the International Physical Activity Questionnaire (IPAQ), which records the amount of time spent engaging in vigorous-intensity activities, moderate-intensity activities, walking, and sitting during the past 7 days, was used to measure physical activity (PA).[23] Total PA was estimated using the formula metabolic equivalent hours per week [Metabolic equivalent (MET)× hours/week].[23] To determine the usual dietary intake, a 100 food items validated extended self-administered food frequency questionnaire (FFQ) was employed. Data from the FFQ and the Chinese food composition table were combined to determine each participant's average daily energy intake.[24]

Statistical Analysis

The presence of normal distributions for continuous variables is checked using the Kolmogorov–Smirnov test. The clinical characteristics and blood tests taken at baseline on the participants are listed. Descriptive data are presented as the geometric mean (95% confidence intervals, CI) for continuous variables and as a percentage for categorical variables. The person-time of follow-up time for each participant was calculated from the completion of the initial survey to the last time of follow-up, the date of incident BPH occurred, or loss to follow-up, whichever came first.

To determine if NLR levels were associated with the risk of BPH, we used the proportional hazards Cox model. A significant level of interaction terms between quartile categories of NLR and follow-up time was examined to evaluate the proportional hazard assumption. Three progressively multivariable Cox regression models were fitted. In model 1, crude hazard ratios (HRs) with their corresponding 95% confidence intervals (CIs) were calculated. In model 2, the participants adjusted for age and BMI. Model 3, additionally adjusted for smoking status, alcohol drinking status, educational level, occupation, household income, PA, total energy intake, hypertension, hyperlipidemia, family history of the disease (including CVD, hypertension, and diabetes mellitus), and inflammatory markers (hsCRP and ALT). Adjustment for inflammatory markers was performed to assess the effect of inflammation on the associations with the prevalence of BPH. By modeling these quartiles as ordinal variables, tests of linear trends within categories of NLR quartiles were assessed.

All statistical tests were two-tailed, with a P value < 0.05 being statistically significant. The SAS version 9.4 (SAS Institute, Inc., Cary, NC) was used for all analyses.

Results

Characteristics of Study Subjects

The study's participants had an average age of 44.1 ±10.3 years. Table 1 shows the basic characteristics associated with incident BPH. Males with BPH had a higher average age than men without BPH (P< 0.0001). Participants with BPH tended to have a lower level of ALT, "Animal foods" dietary pattern score, education (P< 0.0001), and household income (P= 0.01), but had a higher level of BMI, waist, TC, TG, LDL, FBG, SBP, DBP, and "Sweets" dietary pattern score (P< 0.0001). They tend to have a history of hypertension and hyperlipidemia and a family history of CVD, hypertension, and diabetes mellitus (P< 0.0001). Men with BPH had a spread between smoking, drinking, and employment status. Otherwise, no significant differences were observed between groups.

Association Between NLR Levels and Risk of BPH

During a median follow-up of 2.7 years and 42,517 person-years, we documented a total of 5078 participants with incident BPH. The association between NLR levels and the prevalence of BPH is shown in Table 2. NLR levels were positively associated with the presence of BPH in all models. Following final multiple adjustments, the HRs of BPH were

Table 1 Participant Baseline Characteristics by BPH Status (n = 15, 783)[a]

Characteristics	BPH		*P* value[b]
	No	Yes	
No. of subjects	10,705	5078	–
Age (years)	41.7 (34.0, 48.0)[c]	49.2 (43.4, 54.7)	<0.0001
BMI (kg/m^2)	25.8 (23.5, 27.9)	26.1 (24.0, 28.1)	<0.0001
Waist (cm)	88.5 (82.0, 94.0)	89.9 (84.0, 96.0)	<0.0001
TC (mmol/L)	4.90 (4.26, 5.40)	4.95 (4.33, 5.49)	<0.0001
TG (mmol/L)	1.75 (0.99, 2.07)	1.82 (1.03, 2.15)	<0.0001
LDL (mmol/L)	2.90 (2.36, 3.39)	2.96 (2.41, 3.43)	<0.0001
HDL (mmol/L)	1.24 (1.03, 1.41)	1.24 (1.02, 1.40)	0.59
FBG (mmol/L)	5.32 (4.80, 5.50)	5.58 (4.90, 5.70)	<0.0001
ALT (U/L)	28.4 (16.0, 33.0)	27.0 (16.0, 31.0)	<0.0001
SBP (mmHg)	124.9 (115.0, 135.0)	127.7 (115.0, 135.0)	<0.0001
DBP (mmHg)	80.5 (70.0, 87.0)	83.1 (75.0, 90.0)	<0.0001
hsCRP (mg/L)	1.69 (0.50, 1.74)	1.73 (0.50, 1.70)	0.41
Physical activity (MET-hour/week)	21.9 (4.87, 27.1)	22.7 (4.40, 27.9)	0.62
Total energy intake (kcal/day)	2483.3 (1694.0, 3028.6)	2439.4 (1681.2, 2929.1)	0.35
"Healthy" dietary pattern score	0.01 (−0.38, 0.25)	−0.01 (−0.39, 0.24)	0.37
"Sweets" dietary pattern score	−0.04 (−0.58, 0.42)	0.07 (−0.52, 0.54)	<0.0001
"Animal foods" dietary pattern score	0.03 (−0.38, 0.22)	−0.06 (−0.47, 0.09)	<0.0001
Smoking status (%)			<0.0001
Current smoker	61.2	49.2	–
Ex-smoker	5.09	8.21	–
Non-smoker	33.7	42.6	–
Drinker status (%)			<0.0001
Everyday	24.6	25.7	–
Sometime	13.4	17.4	–
Ex-drinker	4.85	5.91	–
Non-drinker	3.53	3.56	–
Education (≥ College graduate, %)	75.1	67.4	<0.0001
Employment status (%)			<0.0001
Managers	47.5	52.1	–
Professionals	18.2	15.1	–
Other	34.3	32.8	–
Household income (≥ 10,000 Yuan, %)	45.9	43.1	0.01
Individual history of disease (%)			
Hypertension	29.3	41.9	<0.0001
Hyperlipidemia	54.1	58.4	<0.0001
Family history of disease (%)			
CVD	29.6	39.8	<0.0001
Hypertension	50.7	57.7	<0.0001
Diabetes mellitus	24.2	28.0	<0.0001

Notes: BPH was defined as TPV ≥ 30 mL. [b]Analysis of variance or logistic regression analysis. [c]Adjusted geometric mean [Descriptive data are presented as the geometric mean (95% confidence intervals, CI) for continuous variables and as a percentage for categorical variables] (all such values).

Abbreviations: [a]BPH, benign prostatic hyperplasia; BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; FBG, fasting blood glucose; ALT, alanine aminotransferase; SBP, systolic blood pressure; DBP, diastolic blood pressure; hsCRP, high-sensitivity C-reactive protein; CVD, cardiovascular disease; TPV, total prostate volume.

1.00 (reference), 1.08 (95% CIs 0.99, 1.17), 1.10 (95% CIs1.02, 1.19), and 1.12 (95% CIs1.03, 1.21), respectively, for participants with NLR in the first, second, third, and fourth quartiles (P for trend < 0.01). The data for participant cohort for each NLR quartile are shown in Table 3.

Table 2 Adjusted Relationships of NLR to BPH (n = 15,783)

	Quartiles of Neutrophil to Lymphocyte Ratio (Range)				*P* for Trend[a]
	The First Quartile Group	The Second Quartile Group	The Third Quartile Group	The Fourth Quartile Group	
Serum neutrophil to lymphocyte ratio (range)	0.25–1.33	1.33–1.65	1.65–2.07	2.07–20.7	–
No. of subjects	2763	2685	2661	2596	–
Person-years of follow-up	11,122	10,671	10,443	10,281	–
No. of BPH[b]	1184	1262	1274	1358	–
Crude	1.00 (reference)	1.10 (1.02–1.20)[c]	1.14 (1.05–1.23)	1.23 (1.14–1.33)	<0.0001
Adjusted for age and BMI	1.00 (reference)	1.09 (1.00–1.17)	1.11 (1.03–1.20)	1.12 (1.03–1.21)	0.0052
Multiple adjusted[d]	1.00 (reference)	1.08 (0.99–1.17)	1.10 (1.02–1.19)	1.12 (1.03–1.21)	0.0062

Notes: [a]*P* for trend was calculated across quartiles using multivariable Cox regression models. [b]BPH was defined as TPV ≥ 30 mL. [c]Adjusted hazard ratios (95% confidence interval) (all such values). [d]Additionally adjusted for smoking status (categorical; current smoker, ex-smoker, or non-smoker), alcohol drinking status (categorical; everyday drinker, sometime drinker, ex-drinker, or non-drinker), educational level (categorical: < or ≥ college graduate), occupation (categorical; managers, professionals, and other), household income (categorical: < or ≥ 10,000 Yuan), physical activity (continuous; MET-hour/week), total energy intake (continuous; kcal/ day), hypertension (yes or no), hyperlipidemia (yes or no), family history of disease (including cardiovascular disease, hypertension, and diabetes mellitus [each yes or no]), high-sensitivity C-reactive protein (continuous: mg/L), and alanine aminotransferase (continuous: U/L).

Abbreviations: NLR, neutrophil to lymphocyte ratio; BPH, benign prostatic hyperplasia; BMI, body mass index; TPV, total prostate volume.

Table 3 Participant Baseline Characteristics for Each NLR Quartile (n = 15, 783)[a]

Characteristics	The First Quartile Group	The Second Quartile Group	The Third Quartile Group	The Fourth Quartile Group	*P* value[b]
No. of subjects	3947	3947	3935	3954	–
Age (years)	43.2 (35.2, 50.4)[c]	43.9 (36.6, 50.8)	44.0 (36.2, 51.0)	45.3 (37.7, 52.6)	<0.0001
BMI (kg/m^2)	25.7 (23.5, 27.7)	25.9 (23.7, 28.0)	26.0 (23.8, 28.1)	25.9 (23.7, 27.9)	<0.001
Waist (cm)	88.2 (82.0, 94.0)	88.9 (83.0, 95.0)	89.2 (83.0, 95.0)	89.4 (83.0, 95.0)	<0.0001
TC (mmol/L)	4.94 (4.31, 5.48)	4.92 (4.31, 5.45)	4.92 (4.27, 5.47)	4.86 (4.25, 5.41)	0.002
TG (mmol/L)	1.74 (0.94, 2.06)	1.77 (1.01, 2.15)	1.81 (1.03, 2.09)	1.77 (1.02, 2.09)	0.14
LDL (mmol/L)	2.94 (2.39, 3.42)	2.93 (2.39, 3.41)	2.92 (2.36, 3.41)	2.89 (2.37, 3.37)	0.07
HDL (mmol/L)	1.27 (1.04, 1.44)	1.24 (1.03, 1.40)	1.23 (1.02, 1.39)	1.22 (1.01, 1.38)	<0.0001
FBG (mmol/L)	5.35 (4.80, 5.50)	5.43 (4.80, 5.50)	5.39 (4.80, 5.50)	5.44 (4.80, 5.60)	0.008
ALT (U/L)	28.6 (16.0, 33.0)	28.2 (16.0, 33.0)	28.4 (16.0, 33.0)	26.5 (16.0, 31.0)	<0.0001
SBP (mmHg)	125.1 (115.0, 135.0)	125.6 (115.0, 135.0)	125.9 (115.0, 135.0)	126.7 (115.0, 135.0)	<0.001
DBP (mmHg)	80.8 (72.0, 88.0)	81.4 (75.0, 90.0)	81.5 (75.0, 90.0)	82.1 (75.0, 90.0)	<0.0001
hsCRP (mg/L)	1.42 (0.43, 1.43)	1.51 (0.50, 1.67)	1.72 (0.51, 1.80)	2.16 (0.58, 2.10)	<0.0001
Physical activity (MET-hour/week)	22.6 (4.20, 28.0)	21.6 (4.95, 26.0)	22.2 (4.55, 27.6)	22.2 (4.40, 27.0)	0.79
Total energy intake (kcal/day)	2505.6 (1703.7, 3024.6)	2486.0 (1690.7, 3040.4)	2470.8 (1719.5, 2954.9)	2408.1 (1647.4, 2949.6)	0.32
"Healthy" dietary pattern score	−0.01 (−0.38, 0.24)	−0.01 (−0.38, 0.25)	0.03 (−0.38, 0.26)	−0.03 (−0.40, 0.23)	0.36
"Sweets" dietary pattern score	0.01 (−0.56, 0.50)	0.01 (−0.56, 0.46)	−0.02 (−0.54, 0.43)	0.01 (−0.58, 0.45)	0.77
"Animal foods" dietary pattern score	0.02 (−0.41, 0.20)	0.01 (−0.42, 0.19)	0.01 (−0.41, 0.20)	−0.04 (−0.40, 0.13)	0.21
Smoking status (%)					0.004
Current smoker	59.5	57.5	56.3	55.9	–
Ex-smoker	6.16	6.61	5.82	5.79	–
Non-smoker	34.3	35.9	37.8	38.3	–
Drinker status (%)					0.58
Everyday	26.0	24.0	24.3	25.6	–
Sometime	14.5	15.0	15.4	13.8	–
Ex-drinker	5.24	5.24	5.18	5.08	–
Non-drinker	3.65	3.45	3.48	3.59	–
Education (≥ College graduate, %)	74.4	74.1	73.5	68.0	<0.0001
Employment status (%)					0.28
Managers	49.1	48.0	48.5	51.3	–
Professionals	16.9	17.5	17.6	16.1	–
Other	34.0	34.5	33.9	32.6	–

(*Continued*)

Table 3 (Continued).

Characteristics	The First Quartile Group	The Second Quartile Group	The Third Quartile Group	The Fourth Quartile Group	*P* value[b]
Household income (≥ 10,000 Yuan, %)	46.6	46.5	44.7	41.8	0.005
Individual history of disease (%)					
Hypertension	30.9	32.6	33.6	36.2	<0.0001
Hyperlipidemia	55.0	56.4	55.6	54.9	0.50
Family history of disease (%)					
CVD	32.4	35.0	33.9	31.6	0.02
Hypertension	52.6	52.9	53.7	53.8	0.71
Diabetes mellitus	25.2	25.4	26.3	25.4	0.73

Notes: BPH was defined as TPV ≥ 30 mL. [b]Analysis of variance or logistic regression analysis. [c]Adjusted geometric mean [Descriptive data are presented as the geometric mean (95% confidence intervals, CI) for continuous variables and as a percentage for categorical variables] (all such values).

Abbreviations: [a]NLR, neutrophil to lymphocyte ratio; BPH, benign prostatic hyperplasia; BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; FBG, fasting blood glucose; ALT, alanine aminotransferase; SBP, systolic blood pressure; DBP, diastolic blood pressure; hsCRP, high-sensitivity C-reactive protein; CVD, cardiovascular disease; TPV, total prostate volume.

In addition, we performed a sensitivity analysis excluding participants with diabetes (n=1030) in the final model. The results are similar to our previous analysis (data not shown).

Discussion

In this large prospective cohort study of adult males in China, we found that higher NLR levels were associated with a higher risk of BPH after adjustment for a wide range of potential confounding variables. We believe that this is the first large-scale population-based study on NLR levels and the risk of BPH to be carried out in Asia.

From the biological view, it is well-known that NLR is a recognized surrogate marker for inflammatory states in the body and can easily be determined from a peripheral blood sample using a complete blood count.[25] In the general population, scarce data are available on the association between NLR levels and on the risk of BPH. Kang et al conducted a case–control study using normal controls, with 538 men in the control group and 269 men in the case group, and showed that the prevalence of BPH was substantially correlated with increased NLR levels.[26] Similarly, Ozer et al found that NLR was positively associated with severe International Prostate Symptom Score (IPSS), TPV, prostate-specific antigen (PSA), and Maximum urinary flow rate (Qmax) values.[3] Furthermore, Chung et al investigated the association between NLR and IPP in male BPH, and their findings demonstrated that NLR might be used as a surrogate marker for IPP with certain morphological abnormalities.[12] In our cohort study with 15,783 participants, a positive association between NLR levels and the risk of BPH was observed. Reasons for the discrepancy between these findings remain unclear, which may partly be due to the small sample size, cross-sectional design, particular patient population, and incomplete control of confounding factors.

Epithelial and stromal cell proliferation in the periurethral and transition zone is a symptom of BPH.[27] In the past few decades, it has been clear how androgens, growth factors, and inflammation all play a role in the occurrence and progression of BPH.[6] BPH is an immune-mediated inflammatory illness characterized by a persistent prostatic inflammatory state (PIS).[28] Inflammation was found in 43% of the 3942 surgically generated BPH specimens, 69% of which were chronic inflammation.[29] Histological inflammation is commonly found in BPH specimens, and it affects the biological characteristics of BPH, such as patient symptoms, prostate volume, and PSA levels.[30] Several studies have shown how immune cell infiltration and pro-inflammatory mediators contribute to the pathophysiology of BPH.[31]

Important serum indicators for illness diagnosis, prognosis, and treatment evaluation include inflammatory cytokines.[8] The most prevalent types of leukocytes, neutrophils, are crucial for starting and controlling innate and adaptive immunity. Another critical component of circulating leukocytes that facilitates adaptive immune response and collaborates closely with innate immunity are lymphocytes. As a measure of systemic inflammation for the current analysis, we used NLR, a ratio that depicts the interaction between two distinct immune pathways. NLR has dramatically associated with prostate tissue inflammation in a recent study with 183 patients who underwent transurethral resection of

the prostate.[30] Considering the association between NLR and prostatic inflammation and the potential for prostatic inflammation to contribute to the development of BPH, it is plausible to believe that the presence of BPH and NLR is significantly correlated.[26] During the study, we also found that participants with BPH tended to have a lower level of ALT. This result is in accordance with a recent study that demonstrates association between development of nonalcoholic fatty liver disease, a metabolic aberration-associated disease, and prostate volume.[32,33] In this study, there was no significant difference between the CRP in the groups. The outcome is identical to the previous one, when men with elevated CRP levels were not more likely to experience rapid in creases in prostate volume, obstructive LUTS, or PSA level.[34]

In comparison to earlier studies, the current study has several significant advantages. Unlike research done in particular clinical populations, the participants in this analysis were selected from a large sample size and are hence more generalizable. In addition, the association between NLR levels and the risk of BPH was also adjusted for a number of potential confounding variables. However, when adjusting for these potential confounders, the results were still statistically significant, indicating that increased NLR levels are independently associated with a higher risk of BPH. It goes without saying that the current study has several limitations. First, in participants with elevated NLR levels, we were unable to explore the pathophysiology of the progression of BPH. BPH is not exclusively caused by inflammation, and several additional causes are probably involved in this morphological alteration. In order to ascertain if the progression of BPH varies with NLR over time in men who first present with BPH, more study on this topic is required. Nevertheless, we believe the current study offers substantial initial information on the association between NLR levels and the risk of BPH. Second, there are still many unidentified variable factors that could affect the association between NLR levels and the risk of BPH, even after we have adjusted for some potentially confounding variables. Finally, the age range in our study is broad (18–90 years). As a result, the relatively brief follow-up period (median: 2.7 years) and youthful participant population may underestimate the association between NLR and the risk of BPH. Although the follow-up period was brief, the sample size of the study was sufficient to increase the statistical validity of our conclusions. To support our findings, additional long-term studies are needed.

Conclusion

In summary, our study demonstrates that, even after adjusting for potential confounding variables, there is a positive association between NLR levels and the risk of BPH in Chinese adult male population. This study highlights the significant association between NLR levels and the risk of BPH, supporting the possibility that NLR levels can be used to predict the risk of BPH. These results back up the notion that inflammation and BPH are related. BPH does not pose a life-threatening hazard, but its symptoms might impair a patient's quality of life. Further experimental and long-term studies are needed to clarify the biological mechanisms of BPH and ascertain whether the elevated level of NLR is a result of BPH.

Abbreviations

NLR, neutrophil-to-lymphocyte ratio; BPH, benign prostatic hyperplasia; PCa, prostate cancer; LUTS, lower urinary tract symptoms; CBCs, complete blood counts; IPP, intravesical prostatic protrusion; BMI, body mass index; TCLSIH, Tianjin Chronic Low-Grade Systemic Inflammation and Health; CVD, cardiovascular disease; TPV, total prostate volume; Qmax, Maximum urinary flow rate; IPSS, International Prostate Symptom Sore; FBG, fasting blood glucose; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; ALT, alanine aminotransferase; BP, blood pressure; PA, Physical activity; IPAQ, International Physical Activity Questionnaire; MET, Metabolic equivalent; FFQ, food frequency questionnaire; HRs, crude hazard ratios; CIs, confidence intervals; PSA, prostate-specific antigen; PIS, prostatic inflammatory status.

Data Sharing Statement

The raw/processed data required to reproduce these findings cannot be shared at this time as the data also form part of an ongoing study.

Ethics Approval and Informed Consent

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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