

Peripheral Lymphocyte Count, Free/Total PSA Ratio, LUTS Predict The Severity of Prostatic Inflammation in BPH Patients

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Abstract

Objective To study the correlation between peripheral blood lymphocytes, f/t PSA and LUTS symptoms, and prostatic inflammation in BPH patients.

Materials and Methods From May 2020 to October 2020, 120 patients (aged 56-85 years) with BPH undergoing elective transurethral resection of the prostate (TURP) were selected. Peripheral blood lymphocyte counts and f/t PSA values were measured preoperatively, and IPSS scores were assessed. Postoperative prostate tissues were sent for pathological examination, and the relationship between peripheral blood lymphocyte count, TPSA, f/t PSA values, relevant clinical laboratory parameters, and relevant LUTS symptoms and the distribution of prostate tissue inflammation was analyzed.

Results with the aggravation of prostatic inflammation, IPSS score and TPSA value were lower, while f/t PSA value and lymphocyte count were lower. Multivariate logistic regression analysis of 120 BPH patients showed that age (≥ 60) [odds ratio (OR) = 0.29, 95% CI = 0.31-2.10; $P = 0.02$], IPSS score [OR = 1.24, 95% CI = 1.13-1.37; $P < 0.01$], TPSA [OR = 1.10, 95% CI = 1.02-1.19; $P = 0.02$], f/t PSA [OR = 1.03, 95% CI = 0.01-0.15; $P = 0.02$], and lymphocytes [OR = 1.70, 95% CI = 0.78-3.77; $P = 0.04$] were related to the formation of prostatic inflammation in BPH patients.

Conclusion Peripheral blood lymphocyte count, TPSA, LUTS severity, and f/t PSA ratio can predict the severity of prostatic inflammation, which may be used as diagnostic markers for BPH patients with LUTS symptoms who have prostatitis and promote the development of drug treatment for LUTS symptoms in BPH patients with prostatitis.

Introduction

BPH is the most common chronic and slowly progressing urological disease in older men, reaching 80% in men aged 70¹. In clinical practice, it may be associated with prostatic hypertrophy and benign prostatic obstruction, triggering bladder outlet obstruction and LUTS². The pathogenesis and progression of BPH are still not fully understood, but they are likely to be multifactorial, and some studies have shown an association with increased sympathetic activity, hormonal changes, and metabolic syndrome³. Over the past few decades, BPH has been considered an immune-mediated inflammatory disease, and its persistent prostatitis state is a critical factor in the development and progression of BPH as a whole⁴. Prostatic inflammation plays a crucial role in the pathogenesis and progression of TUTS secondary to BPH. LUTS can be defined as symptoms related to the storage or voiding stage, and LUTS has an essential impact on the patient's quality of life. Numerous studies have shown that inflammation promotes the occurrence and development of LUTS symptoms in BPH patients, so it is important to find relevant laboratory parameters to predict the severity of prostate tissue inflammation in BPH patients. This paper investigated the correlation between relevant laboratory parameters and the severity of inflammation in prostate tissue.

Methods

Patients information

We evaluated 120 male patients with BPH who underwent transurethral resection of the prostate (TURP) for LUTS from May 2020 to October 2020. This study was approved by the Medical Ethics Committee of the Second Hospital of Lanzhou University. All patients signed the surgical informed consent, and all relevant techniques and information collection were provided by the Department of Urology, the Second Hospital of Lanzhou University. All methods were performed in accordance with the relevant guidelines and regulations in the methods. Our assessments included IPSS score, blood PSA test, blood and urine routine.

Inclusion criteria

Postoperative pathological examination specimens suggest simple benign prostatic hyperplasia; postoperative pathological examination suggests benign prostatic hyperplasia with mild, moderate, and severe prostatic inflammation; no use of non-steroidal anti-inflammatory drugs, phosphodiesterase type 5 inhibitors, vitamins, and statins within one month before surgery.

Exclusion criteria

Any acute infection within one month before TURP; occasional prostate cancer; previous surgery for hematological malignancies; use of drugs that interfere with peripheral blood parameters within one month before surgery, including non-steroidal anti-inflammatory drugs, phosphodiesterase type 5 inhibitors, vitamins, and statins.

Case removal criteria

Misdiagnosis and misdiagnosis; serious postoperative complications; patients withdraw spontaneously.

Outcome measures

Evaluation of LUTS: Preoperatively using the IPSS score, the IPSS score was classified as "no symptom" (0), "mild symptom" (1–7), "moderate symptom" (8–19), and "severe symptom" (20–35); laboratory index f/t PSA ratio; peripheral blood lymphocyte count; severity of inflammation in the prostate tissue of the surgical specimen, the histological grade of inflammation in the prostate was classified as no prostatic inflammation, no inflammatory cells; mild prostatitis (grade I), scattered inflammatory cell infiltrates in the stroma; moderate prostatitis (grade II), non-confluent lymph nodes; and severe prostatic inflammation (grade III) according to the criteria recommended by the North American Cooperative Prostatitis Research Network (CPCRN) and the International Collaborative Prostatitis Network (IPCN).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics25.0; Enumeration data are expressed as a percentage, Data were expressed as mean \pm standard deviation for continuous variables and

compared between groups using Student t-test or the Mann-Whitney U test as appropriate. The Pearson Chi-square test and Fisher exact test were used to comparing the categorical variables. For multivariate analysis, continuous variables, such as age, IPSS, were dichotomized with the median. When $P < 0.05$, there was a significant difference.

Results

120 patients (aged 56 to 85 years) were included, including those with inflammation in the prostate tissue ($n = 84$) and those without inflammation in the prostate tissue ($n = 34$). Comparison between the two groups: age (76.51 ± 13.21 vs 63.83 ± 9.35), IPSS score (19.21 ± 7.06 vs 27.97 ± 5.64), f/t PSA (0.29 ± 0.14 vs 0.19 ± 0.09), lymphocytes (1.58 ± 0.80 vs 1.26 ± 0.59) (Table 1); after grouping according to prostate inflammation, with the severity of prostate inflammation, the main indicator of LUTS symptoms IPSS score ($P < 0.05$); on the other hand, the severity of prostate inflammation and f/t PSA ratio and lymphocyte values were negatively correlated ($P < 0.05$). Further Spearman correlation analysis revealed that lymphocytes and f/t PSA ratio were significantly associated with the severity of prostate inflammation ($P < 0.05$) (Table 2); multivariate logistic regression analysis of 120 BPH patients indicated that age (≥ 60) [odds ratio (OR) = 0.29, 95% CI = 0.31–2.10; $P = 0.02$], IPSS score [OR = 1.24, 95% CI = 1.13–1.37; $P < 0.01$], TPSA [OR = 1.10, 95% CI = 1.02–1.19; $P = 0.02$], f/t PSA [OR = 1.03, 95% CI = 0.01–0.15; $P = 0.02$], and lymphocytes [OR = 1.70, 95% CI = 0.78–3.77; $P = 0.04$] were associated with prostate inflammation formation in BPH patients. There were no differences in secondary outcomes between the groups (Table 3).

Table 1
General information of prostate inflammation in 120 patients with BPH

| | prostate inflammation | |
|--------------------------------------|-----------------------|---------------|
| | Yes (n = 86) | No (n = 34) |
| Age, year | 76.51 ± 13.21* | 63.83 ± 9.35* |
| IPSS score | 19.21 ± 7.06* | 27.97 ± 5.64* |
| FPSA, ng/ml | 0.76# | 1.04# |
| TPSA, ng/ml | 3.43# | 6.08# |
| f/t PSA | 0.29 ± 0.14* | 0.19 ± 0.09* |
| Lymphocyte, 10 ⁹ /L | 1.58 ± 0.80# | 1.26 ± 0.59* |
| White blood cell, 10 ⁹ /L | 7.09 ± 2.50* | 6.68 ± 2.63* |
| Urine leukocyte, per/hp | 5.50# | 22.08# |
| *: mean ± stanstandard;#: Median | | |

Table 2
Comparison of IPSS score, f/t PSA ratio and lymphocyte level among four groups

| Prostatic inflammation grade | N | IPSS score | FPSA, ng/ml | TPSA, ng/ml | f/t PSA | Lymphocyte, 10 ⁹ /L |
|----------------------------------|----|---------------|-------------|-------------|-------------|--------------------------------|
| No | 34 | 19.21 ± 7.06* | 0.76# | 3.43# | 0.29 ± 0.14 | 1.58 ± 0.80 |
| I | 58 | 27.28 ± 5.32* | 0.91# | 5.02# | 0.21 ± 0.07 | 1.42 ± 0.60 |
| II | 10 | 26.30 ± 3.30* | 0.72# | 7.98# | 0.16 ± 0.06 | 1.11 ± 0.54 |
| III | 18 | 31.11 ± 6.69* | 1.78# | 20.12# | 0.10 ± 0.09 | 0.84 ± 0.26 |
| P | | P = 0.02 | P = 0.15 | P < 0.01 | P < 0.01 | P = 0.01 |
| *: mean ± stanstandard;#: Median | | | | | | |

Table 3
Univariate and multivariate analysis of risk factors of prostatic inflammation

| | Univariate analysis | | | multivariate analysis | | |
|---------------------------------------|---------------------|-----------|-------|-----------------------|-----------|-------|
| | OR | 95% CI | P | OR | 95% CI | P |
| Age (>= 60) | 0.51 | 0.24–1.10 | 0.09 | 0.29 | 0.31–2.10 | 0.02 |
| IPSS score | 1.23 | 1.13–1.33 | <0.01 | 1.24 | 1.13–1.37 | <0.01 |
| FP5A, ng/ml | 1.33 | 0.83–2.15 | 0.24 | 1.25 | 0.34–4.64 | 0.74 |
| TP5A, ng/ml | 1.10 | 1.02–1.19 | 0.02 | 0.97 | 0.77–1.22 | 0.80 |
| f/t PSA | 0.56 | 0.01–0.13 | <0.01 | 1.03 | 0.01–0.15 | 0.02 |
| Lymphocyte, 10 ^{*9} /L | 1.70 | 0.78–3.77 | 0.04 | 0.86 | 0.35–2.12 | 0.75 |
| White blood cell, 10 ^{*9} /L | 0.94 | 0.81–1.10 | 0.44 | 1.00 | 1.00-1.02 | 0.34 |
| Urine leukocyte, per/hp | 1.01 | 1.00-1.01 | 0.30 | 1.01 | 0.99–1.04 | 0.25 |

Discussion

In the ZhangQ et al study⁵, the authors stated that prostate tissue inflammation was positively associated with LUTS symptoms. This suggests that early anti-infective therapy can relieve LUTS in BPH patients when they have prostatitis. A meta-analysis of randomized controlled trials concluded that non-steroidal anti-inflammatory drugs improve LUTS and prostatic blood flow status⁶. Besides, higher grades of prostatic inflammation have also been found to predict inadequate response to α -adrenergic blockers and 5- α reductase inhibitors in BPH patients with LUTS. The study by Sugimoto M et al⁷ stated that tadalafil provided reasonable control of LUTS symptoms in BPH patients with prostatic inflammation. Therefore, BPH patients with LUTS with prostatic inflammation may benefit from medical treatment, while BPH patients without prostatic inflammation may not. Prostatic inflammation and body mass index play an essential role in the development of BPH patients with LUTS^{8,9}. It is essential how to identify BPH patients with LUTS who have prostatic inflammation. However, it is a challenging clinical problem. Prostatitis can be empirically confirmed by pathology in patients undergoing a prostate biopsy, but most patients with BPH afflicted with LUTS do not undergo prostate biopsy. It has been demonstrated that some systemic inflammatory response indicators C-reactive protein, soluble tumor necrosis factor- α receptor II, interleukins, neutrophil/lymphocyte ratio, and peripheral white blood cell count correlate with LUTS severity in BPH patients^{10,11}. For measures such as interleukins, it is unlikely to be integrated into daily practice due to high costs. In our study, we found that peripheral lymphocyte counts were associated with prostatic inflammation. The findings confirm those of previous work by Fujita K et al¹²; this suggests that peripheral blood lymphocyte counts are related to the severity of LUTS symptoms of BPH.

Taken together, our findings show that peripheral blood lymphocytes can predict prostate tissue inflammation severity in BPH patients to some extent. However, clinical urologists often judge BPH patients with prostatic inflammation based on clinical characteristics such as the severity of LUTS, response to drugs, prostate volume, and the presence of prostatic calcification, which is often subjective and lacks objective evidence¹³. Our study stated that peripheral blood lymphocyte count and f/tPSA ratio were positively correlated with prostatic inflammation and LUTS symptom severity. In summary, peripheral blood lymphocyte count and f/tPSA ratio can effectively predict the severity of prostate tissue inflammation in BPH patients. However, the number of samples in this study is relatively small, so before clinical practice, multicenter and evidence-based testing is needed, and further validation is needed to determine its clinical utility.

Conclusion

Peripheral blood lymphocyte count, f/tPSA ratio combined with LUTS symptoms are able to predict prostate tissue inflammation to some extent.

Declarations

Authors contribution

Shun Wan wrote and edited the manuscript; Xiao-Hong Sun collected patient data; Yong-Shuai Lin, Yu-Qiang Fu, and Gong-Jun Guo analysed the data; Zhi Yang and Fang-Ming Du substantial contributions to the conception; Jun Mi reviewed the manuscript. All authors reviewed the manuscript.

Conflict of interest

The authors have declared that no conflict of interest exists.

Notes

The authors alone are responsible for the content and writing of the article.

Accordance statement

All methods were performed in accordance with the relevant guidelines and regulations in the methods.

Data availability

All data generated or analysed during this study are included in this published article (and its Supplementary Information files).

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