Chronic Inflammation on Prostate Needle Biopsy as a Significant Predictor of the Lower Incidence Risk of Prostate Cancer

jiatong zhou
Tianjin Medical University Second Hospital
guangyu sun
Tianjin Medical University Second Hospital
ranlu liu (16622080858@163.com)
Tianjin Medical University Second Hospital

Research Article

Keywords: chronic inflammation, prostate antigen density, prostate cancer

Posted Date: February 25th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-258933/v1

Abstract

Purpose: At present, there is no clear relationship between prostatitis and prostate cancer(PCa). Therefore, in order to further understand the inflammation of prostate tissue and the occurrence of PCa, we conducted this study.

Method: A total of 686 patients were enrolled in the study. All patients underwent prostate biopsy in our hospital. A retrospective analysis of the biopsy results was performed to assess the association between chronic inflammation and the risk of PCa.

Result: Of the 686 patients, 354 were diagnosed with PCa, and 332 were benign. A total of 403 patients had prostate inflammation. PCa patients had lower prostate volume and transition zone volume than benign group(p□0.001). Compared with benign group, PCa patients had lower PSA and PSA density (PSAD)(p□0.001). We also found that the probability of inflammation in PCa patients is lower than that in the benign group (p□0.001). In multivariate analyses, chronic inflammation was negatively correlated with the incidence of PCa□OR=0.80; p=0.015). Conclusion: Chronic inflammation in biopsy tissue might serve as a predicted factor for low incidence risk of PCa.

Introduction

According to the American Cancer Society,prostate cancer(PCa) was the most common cancer among men in 2015, which was the second leading cause of tumor deaths in American men during the same period[1]. PCa mortality in South America and South Africa is much higher than in Asia[2]. Prostate-Specific Antigen (PSA) is the most valuable and universal serological marker currently used to screen for PCa[3]. However, in the clinical application of PSA test, we are often misled by the abnormal increase in PSA due to other factors[4, 5].Prostate inflammation is one of the most common causes of abnormally elevated PSA, including asymptomatic or chronic prostatitis[6, 7], which is one of the most important factors that cause unnecessary biopsy in a large number of patients[8]. A bacterial infection caused inflammation of the prostate, causing damage to prostate epithelial cells and further causing malignant of prostate cells, which may be one of the mechanisms[9]. Although chronic inflammation is common in biopsy tissues, its mechanism in the development of PCa is still unclear[9]. Therefore, to further investigate whether inflammation had a significant relationship with the incidence risk of PCa, we performed this study.

Patients And Methods

We retrospectively analyzed the records of 831 patients who underwent transperineal prostate biopsy for the first time in Tianjin medical University Second Hospital from January 2016 to January 2019. A total of 686 patients were included in this study after main included criteria were as follows: 1) abnormal digital rectal examination(DRE), 2) abnormal DRE and elevated PSA, 3) Abnormal DRE with normal PSA.

The main exclusions of distant metastases, had less than 14 needles, had a previous history of prostate surgery, had urinary tract infections, and also those who were on a catheter.

Collection and use of patient data.

All data of patients were collected and analyzed retrospectively. Including the age (years) and body mass index (BMI, kg/m^2) of each patient. PSA was measured by immuno-radiation test (normal range: 0-4ng/ml). Use TRUS to measure prostate volume and TZ before biopsy. Use collected data to calculate PSA density(PSAD).

Each biopsy core needed to be systematically evaluated by an experienced pathologist use the following issues: Chronic inflammation criteria included the following findings: (1) Inflammatory cells infiltrate the prostate matrix;(2) Inflammatory cell infiltration is mainly composed of lymphocytes and mixed plasma cells, and (3) Distribution around cell infiltration.

Statistical analysis

We used SPSS.22 to statistically analyze the data, used mean ± SD to represent continuous variables, chi-square test to compare binary variables, univariate and multivariate analysis to select independent risk factors. All $p < 0.05$ was considered statistically significant.

Results

Of the 686 patients included, 407 (59%) patients had chronic inflammation in prostate, 354 (51.6%) patients were diagnosed PCa, and 332(48.4%) patients were diagnosed the benign group. In Table 1, we had shown baseline clinical characteristics of our cohort. Comparing the clinical characteristics of PCa and the benign group, we found that age is not an important factor in predicting the risk of prostate cancer($p = 0.97$). Chronic inflammation of the prostate could reduce the risk of PCa(p□0.001). And we also observed that patients with smaller PV and TZ had low incidence of PCa. Serum PSA levels($p = 0.022$) and PSA density (PSAD)($p < 0.001$) were also significantly higher in the PCa group than the benign group in univariate analysis. In multivariate analyses, chronic inflammation played an important role in the incidence of PCa(OR = 0.8; $p = 0.015$) in Table 2. In addition, we also found that the higher PSAD, the greater the incidence risk of PCa(p□0.001). Also, The ROC curves of PSAD was 0.45 (area under curve 0.85, sensitivity 0.75, specificity 0.86).

Discussion

In our study, we demonstrated that chronic inflammation was inversely related to the incidence of PCa. We concluded that inflammation of prostate puncture tissue may reduce the probability of malignant transformation of prostate gland epithelium. At present, inflammation was an important factor in the occurrence and development of many malignant tumors. Cervical cancer, HCC, esophageal cancer, and gastric cancer all have clear models about the relationship between inflammation and tumor progression.

However, the specific relationship between inflammation and the occurrence and progression of PCa remains unclear. Gurel et al found that chronic inflammation was associated with a higher incidence of PCa [10], while large clinical trial data reported by Moreira et al presented that chronic inflammation was independently associated with low incidence risk of PCa [11]. Besides, there were some researches showed that inflammation might not play a role in the incidence of PCa [12–14]. We had recognized that chronic inflammation in the prostate may cause proliferative inflammatory atrophy (PIA) and that PIA was associated with high-grade prostate intraepithelial neoplasia (HGPIN). Bills et al found that PIA enhanced the progression of PCa [21], while Brasil et al evaluated 100 radical prostatectomy specimens and found there was no significant association between PIA and PCa[10]. Coussens et al proposed the close connection between chronic inflammation and gastric, liver, colon, and bladder cancer[14]. For suppressing the inflammatory response, the risk of tumorigenesis could be further reduced[15]. Deu to chronic inflammation was related to oxidative stress-mediated by the cyclooxygenase gene pathway, inhibiting this pathway may reduce the risk of cancers. Observational studies of PCa suggested that NSAID might play a protective factor in reducing the incidence of PCa[17]. However, the protective effects of NSAIDs had been challenged and questioned in other studies, they had shown an increasing risk of PCa after taking NSAIDs [18, 19]. Therefore, our conclusion still needed to be further verified, and we should consider whether there was a difference in the impact of inflammation on prostate cells in different ranges of PSA levels.

There are several limitations to the present study. First, The number of subjects included in this study is small, and a large number of multicenter studies are still needed to confirm our conclusion. Also, we only found that inflammation may affect the incidence of PCa, but did not further consider whether the inflammation affected the occurrence of Gleason score. In addition, we only selected patients with patients with PSA 4-50ng/ml for study, and did not conduct stratified study on different PSA range.

Conclusion

The main view was that chronic inflammation might have a protective effect on reducing the incidence of PCa, and be independently associated with low-grade PCa in patients. The second conclusion was that the combination of PSAD and inflammation could reduce the number of unnecessary repeat biopsy.

Declarations

Ethics approval

The study was approved by the Regional Ethical Review Board in Tianjin medical university second hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

Funding

This project was support by: Tianjin Science and technology committee(19ZXDBSY00050). The founding bodies had no influence on the design of the study, data collection, data analysis, and interpretation of data; or writing of the manuscript.

Authors' contributions

Conception and Design: JZ and RL; Extraction of Data: GS and JZ;

Drafting the Article: JZ and GS; Revising It for Intellectual Content: JZ, RL; Final Approval of the Completed Article: JZ, GS, RL. All authors read and approved the final manuscript.

Acknowledgments

We owe our thanks to Guangyu Sun and Jiatong Zhou for their work on revising and data extracting in this manuscript.

Further information

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this

References

1. Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ, He J. CA Cancer J Clin CA: a cancer journal for clinicians. 2016;66(2):115–32.
2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359–86.
3. Stephan C, Jung K, Lein M, Diamandis EP. PSA and other tissue kallikreins for prostate cancer detection. Eur J Cancer. 2007;43(13):1918–26.
4. Oesterling JE. Prostate specific antigen: a critical assessment of the most useful tumor marker for adenocarcinoma of the prostate. J Urol. 1991;145(5):907–23.
5. Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E. Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. N Engl J Med. 1987;317(15):909–16.

6. Okada K, Kojima M, Naya Y, Kamoi K, Yokoyama K, Takamatsu T, Miki T. Correlation of histological inflammation in needle biopsy specimens with serum prostate- specific antigen levels in men with negative biopsy for prostate cancer. Urology. 2000;55(6):892–8.
7. Chang SG, Kim CS, Jeon SH, Kim YW, Choi BY. Is chronic inflammatory change in the prostate the major cause of rising serum prostate-specific antigen in patients with clinical suspicion of prostate cancer? Int J Urol. 2006;13(2):122–6.
8. Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, Petros JA, Andriole GL. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. N Engl J Med. 1991;324(17):1156–61.
9. Sfanos KS, De Marzo AM. Prostate cancer and inflammation: the evidence. Histopathology. 2012;60(1):199–215.
10. Wang W, Bergh A, Damber JE. Morphological transition of proliferative inflammatory atrophy to high-grade intraepithelial neoplasia and cancer in human prostate. Prostate. 2009;69(13):1378–86.
11. Porcaro AB, Novella G, Mattevi D, Bizzotto L, Cacciamani G, Luyk ND, Tamanini I, Cerruto MA, Brunelli M, Artibani W. Chronic Inflammation in Prostate Biopsy Cores is an Independent Factor that Lowers the Risk of Prostate Cancer Detection and is Inversely Associated with the Number of Positive Cores in Patients Elected to a First Biopsy. Curr Urol. 2016;9(2):82–92.
12. Kuang AG, Nickel JC, Andriole GL, Castro-Santamaria R, Freedland SJ, Moreira DM. Both acute and chronic inflammation are associated with less perineural invasion in men with prostate cancer on repeat biopsy. BJU Int. 2019;123(1):91–7.
13. Thun MJ, Henley SJ, Patrono C. Nonsteroidal anti-inflammatory drugs as anticancer agents: mechanistic, pharmacologic, and clinical issues. J Natl Cancer Inst. 2002;94(4):252–66.
14. Gridley G, McLaughlin JK, Ekbom A, Klareskog L, Adami HO, Hacker DG, Hoover R, Fraumeni JF Jr. Incidence of cancer among patients with rheumatoid arthritis. J Natl Cancer Inst. 1993;85(4):307–11.
15. De Marzo AM, Platz EA, Sutcliffe S, Xu J, Grönberg H, Drake CG, Nakai Y, Isaacs WB, Nelson WG. Inflammation in prostate carcinogenesis. Nat Rev Cancer. 2007;7(4):256–69.
16. Strawson J. Nonsteroidal anti-inflammatory drugs and cancer pain. Curr Opin Support Palliat Care. 2018;12(2):102–7.
17. Langman MJ, Cheng KK, Gilman EA, Lancashire RJ. Effect of anti-inflammatory drugs on overall risk of common cancer: case-control study in general practice research database. BMJ. 2000;320(7250):1642–6.
18. Dennis LK, Lynch CF, Torner JC. Epidemiologic association between prostatitis and prostate cancer. Urology. 2002;60(1):78–83.
19. Murtola TJ, Gurel B, Umbehr M, Lucia MS, Thompson IM Jr, Goodman PJ, Kristal AR, Parnes HL, Lippman SM, Sutcliffe S, Peskoe SB, Barber JR, Drake CG, Nelson WG, De Marzo AM, Platz EA. Inflammation in Benign Prostate Tissue and Prostate Cancer in the Finasteride Arm of the Prostate Cancer Prevention Trial. Cancer Epidemiol Biomarkers Prev. 2016;25(3):463–9.

20. Ekbom A, Helmick C, Zack M, Adami HO. Ulcerative colitis and colorectal cancer. A population-based study. N Engl J Med. 1990;323(18):1228–33.

Tables

Table 1 Characteristics of the study population are summarized Abbreviation: PCa, prostate cancer; tPSA, total prostate specific antigen; PSAD, prostate specific antigen density; OR, odds ratio

	PCa(n=354)	Benign（n =332）	OR	p
Age(years)	70.7 ± 65.30	73.9 ± 60.80	1.18	0.97
tPSA (ng/mL), mean ± SD	22.1 ± 9.80	16.1 ± 7.80	2.5	0.022
Prostate volume (mL), mean ± SD	32.4 ± 16.70	54.7 ± 20.0	0.95	<0.001
Transition zone (mL), mean ± SD	17.6 ± 13.40	35.5 ± 14.6	0.9	<0.001
PSAD（ng / mL^2）, mean ± SD	0.83 ± 0.41	0.35 ± 0.23	16.42	<0.001
chronic inflammation			0.82	<0.001
YES	144	263		
NO	210	69		

Table 2 Univariate analysis and Multivariate analysis for risk factors for the incidence of PCa

Abbreviation: tPSA, total prostate-specific antigen; PSAD, prostate-specific antigen density; OR, odds ratio

	Univariate analysis		Multivariate analysis	
OR p	OR p			
Age(years)	1.18	0.97		
tPSA	2.5	0.022	1.68	0.06
Prostate volume	0.95	<0.001	0.99	0.08
Transition zone	0.9	<0.001	0.95	0.06
PSAD	16.42	<0.001	22.71	<0.001
chronic inflammation	0.82	<0.001	0.8	0.015