Somalia Turkiye Medical Journal (STMJ)
V. 02, No. 04, 2023
doi: 10.58322/stmj.v2i4.33
http://www.stmedj.com
ISSN 2958-2849

Research Article

Predictive Factors for Detection of Clinically Significant Cancer in Repeat Prostate Biopsy

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Received September 11th, 2023

Accepted October 10th, 2023

Abstract **Introduction:** This study aims to identify predictive factors for detecting clinically significant cancer in the second biopsy among patients who underwent two prostate biopsies. **Materials and Methods:** Between 2016 and 2022, our clinic conducted prostate biopsies in response to elevated prostate-specific antigen (PSA) levels. When the initial pathology did not reveal cancer, patients who subsequently underwent a second biopsy due to the detection of atypical small acinar proliferation (ASAP) and persistent PSA elevation were included in this study. Data from 103 patients were retrospectively evaluated. The initial biopsy followed a 12-quadrant routine protocol. The second biopsy was performed within three months for ASAP cases and six months later for cases with persistent PSA elevation. Pathological staging utilized the Gleason scoring system, with scores of 7 and above indicating clinically significant cancer. Patients were stratified by age (under 65 and 65 and over), and whether their PSA values six months post-initial biopsy exceeded 20%. Statistical analysis employed Fisher's exact test, with a significance threshold set at $p<0.05$. **Results:** Of the 103 patients included in the study, cancer was detected in 13 (12.6%) during the second biopsy. Among these, 5 (4.8%) exhibited clinically insignificant cancers meeting active surveillance criteria, while 8 (7.8%) demonstrated a Gleason score of 7 or higher. No significant difference in cancer detection or identification of clinically significant cancer was observed between patients with ASAP at the first biopsy and those without ($p=0.982$). However, the rate of clinically significant cancer was notably higher at 15.4% in patients with a PSA increase of over 20%, compared to 3.1% in those without an increase ($p=0.024$). Furthermore, clinically significant cancer was identified in 14.2% of patients aged 65 and over, as opposed to 1.9% in those under 65 ($p=0.019$). **Conclusions:** This study highlights a higher detection rate of clinically significant cancer in patients with a PSA value increase of more than 20% compared to their initial PSA, as well as in individuals aged 65 and over, among those who underwent a prostate biopsy due to elevated PSA levels initially deemed benign. Timely consideration of a second biopsy is crucial for these patient cohorts.

Keywords Prostate; biopsy; ASAP; cancer

Introduction

Prostate cancer (PCa) stands as the second most prevalent malignancy in men and ranks as the fifth leading cause of global mortality. Elevated plasmatic levels of prostate-specific antigen (PSA> 4 ng/mL), a glycoprotein predominantly expressed by prostate tissue, serve as the basis for detecting many cases of prostate cancer. However, given that non-cancerous individuals may also exhibit elevated PSA levels, tissue biopsy remains the gold standard for confirming the presence of cancer (1). Prostate biopsy outcomes encompass a spectrum of findings, ranging from PCa to benign prostatic hyperplasia (BPH), high-grade prostate intraepithelial neoplasia (HGPIN), and atypical small acinar proliferation (ASAP) (2). This study seeks to elucidate the predictive factors for identifying clinically significant cancer in the second biopsy among cases where the initial biopsy yielded no evidence of prostate cancer.

Materials and Methods

Between 2016 and 2022, our clinic conducted prostate biopsies in response to elevated prostate-specific antigen (PSA) levels. In cases where no cancer was detected in the initial pathology, patients who subsequently underwent a second biopsy due to the detection of atypical small acinar proliferation (ASAP) and the persistence of elevated PSA were enrolled in this study. The data of 103 patients were retrospectively accessed and evaluated. The initial biopsy adhered to a 12-quadrant routine protocol. This procedure was performed with the patient in the lateral decubitus position, employing standard grayscale ultrasonography and a 7.5 MHz rectal probe (Mindray M5, Shenzhen, China). A biopsy needle of 18 Gauge and an automatic biopsy gun (GEOTEK Estacore, Daventry, UK) were utilized.

For patients with ASAP, the second biopsy was conducted within three months, while those with persistent PSA elevation underwent the procedure six months after the initial biopsy. Pathological

staging utilized the Gleason scoring system, with a Gleason score of 7 or higher indicating clinically significant cancer. Additionally, patients were categorized by age, distinguishing those under 65 from those who were not.

Statistical Analysis

The statistical analysis employed the Statistical Package for the Social Sciences version 22 (SPSS Inc, Chicago, USA). The normal distribution of the data was assessed using the Shapiro-Wilk test. Fisher's exact test was employed for statistical comparisons. A p value below 0.05 was considered statistically significant in the analysis.

Results

A total of 103 patients were included in the study. Cancer was detected in 13 (12.6%) patients during the second biopsy. Among these cases, 5 (4.8%) were classified as clinically insignificant cancers, meeting the criteria for active surveillance, while 8 (7.8%) exhibited a Gleason score of 7 or higher.

No significant difference was observed in the detection of cancer or clinically significant cancer during the second biopsy between individuals with or without ASAP in the initial biopsy (p =0.982).

In cases where there was a PSA increase of more than 20%, the rate of clinically significant cancer stood at 15.4%, whereas it was notably lower at 3.1% in those without such an increase (p=0.024). Furthermore, the prevalence of clinically significant cancer was notably higher at 14.2% in individuals aged 65 and over, in contrast to a lower rate of 1.9% in those younger than 65 (p=0.019) (Table 1).

Table 1. Comparison of the cases according to the pathology results and other parameters

	Benign	Clinically insignificant cancer	Clinically significant cancer	p value
Number of patients (103)	90 (87,4%)	5 (4,8%)	8 (7,8%)	
First biopsy result: ASAP (+)	34 (87,2%)	2 (5,1%)	3(7,7%)	0,982
First biopsy result ASAP (-)	56 (87,5%)	3(4,7%)	5 (7,8%)	
PSA increase>20% (+)	32 (82%)	1 (2,6%)	6 (15,4%)	0,024*
PSA increase>20% (-)	58(90,7%)	4 (6,2%)	2 (3,1%)	
Age≥65	42 (85,8)	0	7 (14,2%)	0,019*
Age<65	48 (%88,9)	5(9,2)	1 (1,9%)	

**p-value is significant below 0.05*

Discussion

Prostate-specific antigen (PSA) remains the cornerstone of screening studies for prostate cancer. Elevated PSA levels above 4.0 ng/ml serve as an indication for prostate biopsy, with an escalating probability of adenocarcinoma as PSA values rise (4). Additionally, reports indicate that prostate cancer is detected in 5-20% of biopsies performed for various indications in patients with PSA values at or below 4.0 ng/ml (5).

In cases where the initial biopsy yields no evidence of prostate cancer, a re-biopsy may be warranted. European urology guidelines recommend re-biopsy in instances of elevated and high PSA levels, suspicious findings on rectal examination, the presence of atypical small acinar proliferation (ASAP), detection of high-grade prostate intraepithelial neoplasia (HGPIN) in multiple quadrants, and findings on multiparametric MRI (3).

ASAP is encountered in roughly 5% of prostate biopsies, and approximately 30-40% of patients with ASAP demonstrate biopsy-detectable prostate cancer within five years (9). Current guidelines advise a repeat biopsy within 3-6 months following the initial ASAP diagnosis due to the high likelihood of cancer detection on repeat biopsy (7, 8). In alignment with this, our study also implemented a second biopsy within three months for patients with ASAP identified in the first biopsy. The probability of encountering a Gleason score exceeding 6, indicative of high-grade cancer, on repeat biopsy following an ASAP diagnosis, exhibits significant variation across studies, ranging from 8.0% to 66.7% (6).

PSA velocity (PSAV), which reflects changes in PSA levels over time has been proposed to augment prostate cancer detection. It is posited that a rapidly increasing PSA may signal an elevated risk for a prostate cancer diagnosis, even in cases where PSA levels are within the conventional biopsy threshold. Consequently, current National Comprehensive Cancer Network (NCCN) guidelines suggest that men with PSAV≥0.35 ng/ml per year should contemplate biopsy, even if their PSA levels fall below the usual biopsy threshold (10). The American Cancer Society advances a similar recommendation for PSAV ≥0.75 ng/ml per year and PSA levels between 4-10 ng/ml (11). The European Association of Urology (EAU) advocates for biopsy when PSAV exceeds 0.60 ng/ml per year (12). In our study, we re-measured PSA six months
after the initial biopsy. Those exhibiting a 20% increase above the initial value demonstrated a heightened detection rate of clinically significant prostate cancer.

Prostate cancer is infrequently diagnosed in younger men (under 50), comprising only 2% of all cases. The mean age at diagnosis is 68, with 85% of diagnoses occurring in individuals over 65. Autopsy series reveal microscopic disease rates of 30% in the fourth decade, 50% in the sixth decade, and 75% in individuals over 85 (10). In our study, the clinically significant cancer

detection rate was notably elevated among individuals aged 65 and over, aligning with broader epidemiological trends.

It is worth noting that the absence of a Multiparametric MR imaging system at our institution during the study period represents a limiting factor in our research.

Conclusion

While prostate biopsy stands as a safe and effective diagnostic procedure, it is imperative to acknowledge the associated risks of complications and financial considerations. Furthermore, the notion of repeat biopsy may induce anxiety in patients. Therefore, a judicious patient selection process is crucial in order to enhance the likelihood of a positive biopsy outcome and diminish the necessity for unnecessary procedures. Predictive factors play a pivotal role in this regard. Specifically, among patients who underwent prostate biopsy due to elevated PSA levels initially deemed benign, those demonstrating a follow-up PSA measurement exceeding 20% compared to the initial PSA, coupled with an age surpassing 65, exhibited significant predictive value. These findings constitute noteworthy contributions to our study.

Conflict of Interest

The authors disclose no potential conflicts of interest about this study.

Ethical Approval

Approval from the Clinical Research Ethics Committee of Samsun University was obtained under protocol number SÜKAEK-2022/4/7.

Funding

This study did not receive any external funding.

References

1. Rawla P. Epidemiology of Prostate Cancer. *World J Oncol* 2019;10(2):63-89.

2. Kim TS, Ko KJ, Shin SJ, et al. Multiple cores of high grade prostatic intraepithelial neoplasia and any core of atypia on first biopsy are significant predictor for cancer detection at a repeat biopsy. *Korean J Urol* 2015;56(12):796-802.
3. Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. *Eur Urol* 2017;71(4):618-629.
4. Cooner WH, Mosley BR, Rutherford CL, et al. Prostate cancer detection in a clinical urological practice by ultrasonography, digital rectal examination and prostate specific antigen. *J Urol* 1990; 143(8):1146-1152.
5. Catalona WJ, Smith DS, Ratliff TL, et al. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. *N Engl J Med* 1991;324(9):1156-1161.
6. Imanaka T, Yoshida T, Taniguchi A, et al. Implementation of repeat biopsy and detection of cancer after a diagnosis of atypical small acinar proliferation of the prostate. *Mol Clin Oncol* 2020;13(6):67.
7. Carroll PR, Parsons JK, Andriole G, et al. Prostate cancer early detection, version 1.2014. Featured updates to the NCCN Guidelines. *J Natl Compr Canc Netw* 2014;12(9):1211-1219.
8. Heidenreich A, Bastian PJ, Bellmunt J, et al. EAU guidelines on prostate cancer Part 1: Screening, diagnosis, and local treatment with curative intent-update 2013. *Eur Urol* 2014;65:124–137.
9. Kim H, Kim JK, Choe G, et al. Clinical strategy of repeat biopsy in patients with atypical small acinar proliferation (ASAP). *Sci Rep* 2021;11(1):23143.
10. Bell KJ, Del Mar C, Wright G, et al. Prevalence of incidental prostate cancer: A systematic review of autopsy studies. *Int J Cancer* 2015;137(7):1749-1757.
11. Schroder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. *N Engl J Med* 2009;360:1320–1328.
12. Thompson IM, Chi C, Ankerst DP, et al. Effect of finasteride on the sensitivity of PSA for detecting prostate cancer. *J Natl Cancer Inst* 2006; 98:1128–1133.
13. Heidenreich A, Aus G, Bolla M, et al. EAU guidelines on prostate cancer. *Eur Urol* 2008;53:68–80.