Is High Grade Prostatic Intraepithelial Neoplasia a Risk Factor for Prostate Cancer?—A Local Study

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Abstract

Objective: To determine the consequence of recognizing high grade prostatic intraepithelial neoplasia (HGPIN) & its extent on initial sextant prostatic biopsy then identifying its associated risk of finding prostate cancer on subsequent biopsy. **Patients and methods**: Seventy-one men were subjected to transrectal ultrasound guided sextant prostate biopsy due to elevated serum prostate specific antigen (S.PSA) > 4 ng /ml, an abnormal digital rectal examination (DRE) and/or transrectal ultrasound (TRUS) findings. The number, percentage, as well as bilateral and multifocal involvement of specimens positive for HGPIN were recorded in every patient. The percentage of cancer detected in these patients on repeat biopsy within 1 year of the initial biopsy was also recorded. **Results**: The mean age and mean S.PSA level of our patients was 59.9 years and 7.9 ng/ml respectively. Of the 71 patients studied, initial biopsy revealed that (32.4%) had benign prostatic hyperplasia (BPH), (36.62%) had carcinoma, (25.35%) had HGPIN and (5.63%) had chronic prostatitis. On repeat biopsy within 1 year of initial biopsy cancer of the prostate was detected in 33.3% of our patients who were diagnosed with HGPIN on 1st biopsy. All of them had multifocal involvement on the initial biopsy. **Conclusion**: Recognizing HGPIN on 1st biopsy (particularly multifocal involvement) is associated with great risk of prostate cancer development on subsequent biopsy, thus comprehensive follow-up of these patients is necessary.

Keywords

HGPIN, Prostate Cancer, Biopsy

1. Introduction

In urinary tract histopathology, HGPIN is considered prostatic gland anomaly

and thought to antecede the development of adenocarcinoma of the prostate [1] [2].

Prostatic intraepithelial neoplasia (PIN) was previously classified into various aspects, depending on the level of atypical cell. It was categorized as PIN1, 2 or 3, in order of increasing irregularities of the cell. For the time being, PIN1 indicates low grade PIN, PIN2 and PIN3 are gathered together as HGPIN [3]. Only HGPIN appeared to be a risk factor for prostate adenocarcinoma. Because LGPIN is not important and does not need repeat biopsy or therapy, it is not recorded in the histopathology reports. Thus, PIN has become synonymous to HGPIN [4].

On a subsidiary biopsy, given a diagnosis of a HGPIN, the incidence of identifying prostatic cancer is approximately 30% [5].

HGPIN is presently known to be the most probably precursor of invasive adenocarcinoma of the prostate for epidemiological, morphological, genetic, clinical and spatial causes [6]. HGPIN raises the hazard 15-times higher in comparison to those without HGPIN and provides the greatest risk proportion in developing cancer of the prostate [7].

The incidence, range & degree of HGPIN seem to increase with the age of the patient [8] [9] & its prevalence is the same in white & black races [10].

Patients viewed by urologists practically have PIN in 4.4% - 25% of recent needle biopsies. Those subjected to transurethral resection (TUR) have the highest probability of PIN ranging from 2.8% to 33% [11] [12].

HGPIN & prostate cancer have the same morphometric and phenotypic properties. HGPIN occurs mostly in the peripheral zone & is seen in sites that are continuous with prostate cancer [13] [14]. A rise in the rate of aneuploidy and angiogenesis as the grade of PIN progresses are further proof that HGPIN is an important predictive factor for prostate cancer [15] [16]. HGPIN and prostate cancer participate in the same genetic alterations [17] [18].

The presence of HGPIN warns both the patient and the clinician that it may progress to clinically significant prostatic tumor.

Biopsy remains the ultimate procedure for discovering HGPIN & early invasive cancer, however noninvasive methods including blood analyses, are being estimated. Serum PSA levels are perhaps increased in patients with HGPIN [19].

The aim of this study is to highlight the significance of recognizing HGPIN on initial prostatic biopsy and to evaluate the relationship between HGPIN and the future development of prostate cancer on subsequent biopsies.

2. Patients and Methods

This study was carried out at the urology department of Al-Yarmouk Teaching Hospital in the period between January 2014 and January 2017, it included 71 men with an age ranged from 50 to 80 years complaining of bladder outlet obstructive symptoms (BOO). Patients were evaluated by full history taking & thorough physical examination including digital rectal examination (DRE) & investigations by doing urinalysis, urine culture & sensitivity, blood sugar, CBC, blood

urea, serum creatinine & serum prostate specific antigen (PSA). Abdominal & pelvic ultrasound & Transrectal ultrasound (TRUS) were performed on all patients. Inclusion criteria included men (n = 71) with elevated S.PSA level > 4 ng/ml, an abnormal DRE and/or TRUS findings. No patients had a prior diagnosis of prostate tumor, or had received radiotherapy, chemotherapy or androgen deprivation therapy.

In every patient we calculated the volume of the prostate using the TRUS then we calculated the PSA density by dividing the total S.PSA by the prostatic volume.

Prostatic biopsies were taken from all patients under transrectal U/S guidance& antibiotics cover. They were obtained in a systematic sextant biopsy technique with the patient in left decubitus position using an automatic biopsy gun with an 18-gauge needle. Further biopsies were also pointed to the suspicious areas. Each biopsy specimen was coded according to its site (apex, mid, base) and side (right or left) and collected in an isolated container. All biopsy specimens were examined by one pathologist.

The diagnosis of HGPIN in our pathology database was established when it was identified in at least one of the six prostatic biopsies obtained, also the bilateral & multifocal involvement (the presence of HGPINP in 2 or more biopsy specimens) were recorded in every case.

Men diagnosed with HGPIN underwent repeat second sextant biopsies of the prostate within 1 year of the 1st biopsy.

3. Results

A total of 71 patients were included in the study, their mean age was 59.9 y. (range 50 - 80). The mean S.PSA level was 7.9 ng/ml (range 4.9 - 43.31) Table 1.

Prostatic biopsies were obtained due to elevated S. PSA in 52 patients, abnormal DRE in 8 patients and abnormal TRUS in 11 men Table 2.

Table 1. The patients' characteristics.

Patient's characteristic	Mean (SD)
Age, years	59.9 (0.232)
S.PSA, ng/ml	7.9 (0.300)
Prostatic volume, ml	49.1 (0.364)
PSA density	0.16 (0.008)

Table 2. Indications of prostatic biopsy in our patients.

Indication	No. of patients (%)
Elevated S.PSA	52 (73.23)
Abnormal DRE	8 (11.27)
Abnormal TRUS	11 (15.5)
Total	71 (100)

Of the 71 patients studied, initial biopsies revealed 23 men (32.4%) had benign prostatic hyperplasia, 26 patients (36.62%) had cancer, 18 patients (25.35%) had HGPIN & 4 patients (5.63) had chronic prostatitis (**Figure 1**)

HGPIN was present bilaterally in five of the 18 patients (27.7%) while multifocal involvement was present in 7 cases (38.8%) as shown in **Figure 2**.

On the repeat biopsy obtained after 12 months of the initial biopsy, cancer of the prostate was detected in 6 (33.3%) out of 18 patients diagnosed with HGPIN. All of those [6] patients had multifocal HGPIN on the initial biopsy.

4. Discussion

In our study the mean age was 59.9 years while the median S.PSA level was 7.9 ng/ml. These values were comparable to those recorded in studies made by Geoman *et al.* [7], Schoenfield *et al.* [20] and Arzoz Fabregas *et al.* [21].

In the current study initial prostatic biopsy was done because of elevated S.PSA in 73.23%, suspicious DRE in 11.27% and an abnormal TRUS finding in
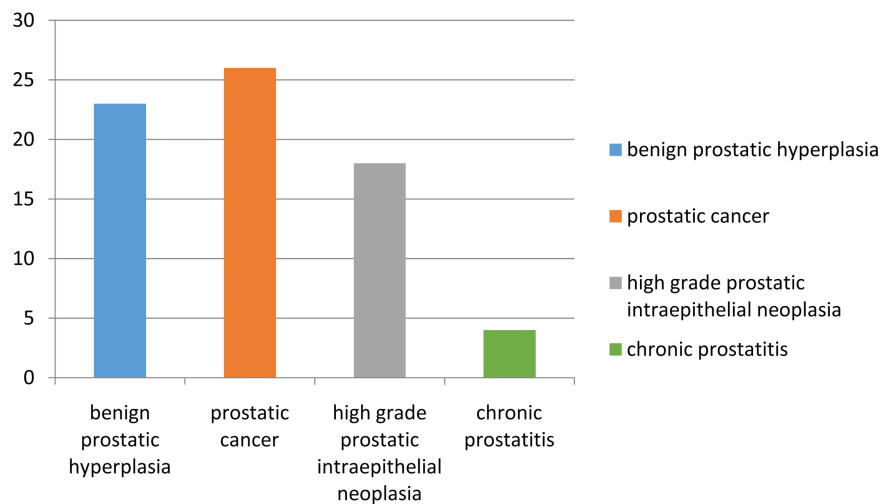
Figure 1. Initial prostatic biopsy findings.
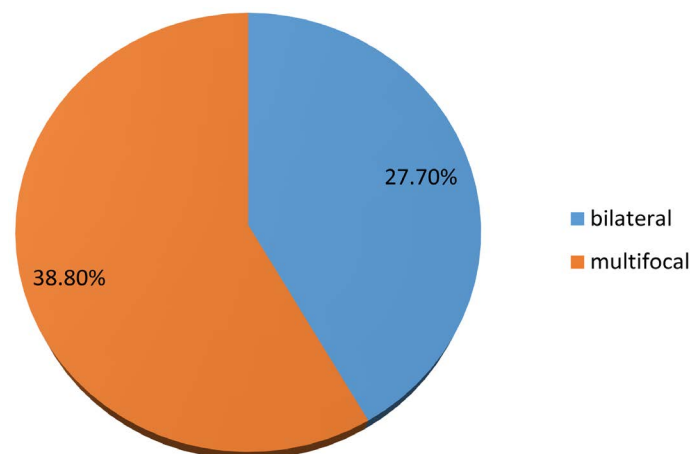
Figure 2. Bilateral & multifocal involvement of HGPIN.

15.5%. These results agreed with that of Geoman *et al.* [7].

In the present study the incidence of HGPIN on the initial biopsy was (25.35%). This was in accordance with Schoenfield *et al.* (22%) [20], De Nunzio *et al.* (22%) [22] and Bostwick (4.4% - 25%) [2], but it was in disagreement with other studies (Goeman *et al.* (11.2%) [7], Abdel-kalek *et al.* (2.7%) [23], Bostwick *et al.* (9%) [24] and Borboroglu *et al.* (9.8%) [25]).

Prostatic cancer was identified on repeat biopsy in (33.3%) of our patients with HGPIN on the 1st biopsy; all of them were with multifocal involvement on the initial biopsy. This finding was in consistence with Kronz *et al.* [26] and Schoenfield *et al.* [20] who found cancer of the prostate on the 2nd biopsy in third of their patients having HGPIN on the 1st biopsy with higher rate of cancer detection in multifocal than unifocal HGPIN. This indicates that the prostate cancer risk is increased with the increase in the number of specimens found to have HGPIN on the 1st biopsy. Our result also agreed with that of Bostwick *et al.* [2], Abdel-khalek *et al.* [23] and Rosser *et al.* [27], However, it disagreed with studies that revealed lower prostate detection rate (De Nunzio *et al.* [22], Kamoi *et al.* [28] and Epstein & Herawi [29]) and other studies with higher prostate detection rate (Keetch *et al.* [30] and Borboroglu *et al.* [25]).

5. Conclusion

Patients recognized with HGPIN are at great risk of developing cancer of the prostate on subsequent prostate biopsy particularly those diagnosed with multifocal HGPIN on initial biopsy so close follow-up of these patients is recommended.

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