KJU
Korean Journal of Urology

www.kjurology.org
DOI:10.4111/kju.2010.51.1.21

Urological Oncology

Outcome of Prostate Biopsy in Men Younger than 40 Years of Age with High Prostate-Specific Antigen (PSA) Levels

Jin Bak Yang, Byong Chang Jeong, Seong Il Seo, Seong Soo Jeon, Han Yong Choi, Hyun Moo Lee

Department of Urology, Sungkyunkwan University School of Medicine, Seoul, Korea

Purpose: Prostate cancer is rarely diagnosed in men younger than 40 years of age. At present, the available data show a low rate of cancer detection from prostate-specific antigen (PSA) screening of this group of young men. We analyzed the outcome of prostate biopsy results in patients of this age group with a high PSA.

Materials and Methods: Between October 1997 and August 2008, a total of 81 men less than 40 years of age were referred from the Health Care Promotion Center as the result of elevated PSA levels. Six men with prostatitis were excluded. The remaining 75 men were asymptomatic and had normal findings on the digital rectal examination (DRE) and were selected to have a transrectal ultrasound-guided prostate biopsy for suspected prostate cancer. The patients with sustained high PSA levels underwent repeat biopsies.

Results: The median age of the 75 men was 33 years (range, 26-40 years) and the mean PSA level was 6.57 ng/ml (range, 4.32-13.45 ng/ml). The results of the primary biopsy was 1 (1.3%) case of prostate cancer, 70 cases (93%) with benign tissue, 2 cases (2.6%) with inflammation, and 1 case each (1.3%) with high grade intraepithelial neoplasia (HGPIN) and atypical small acinar proliferation (ASAP). Of the 10 men who underwent a second biopsy, all had benign findings. Three of the men who underwent a third biopsy all had benign tissue findings.

Conclusions: The prostate cancer detection rate in young men less than 40 years of age with high PSA levels and normal DREs was very low. Repeat biopsy for sustained high PSA levels in young men less than 40 years of age may not be indicated.

Key Words: *Prostate-specific antigen, Digital rectal examination, Biopsy, Young adult, Prostatic neoplasms*

Article History:
received 23 June, 2009
accepted 19 October, 2009

Corresponding Author:
Hyun Moo Lee
Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50, Ilwon-dong, Gangnam-gu, Seoul 135-710, Korea
TEL: +82-2-3410-6543
FAX: +82-2-3410-3027
E-mail: besthml@medimail.co.kr

INTRODUCTION

Prostate-specific antigen (PSA), a single-chain 33 kDa glycoprotein serine protease, is produced by the human prostate epithelium only [1,2]. It is the most widely used tumor marker for the diagnosis of prostate cancer, which is common in aging men. More than 80 percent of prostate cancers are found in men more than 65 years of age [3]. However, due to the broad application of PSA testing, the use of PSA screening in younger men has been increasing. According to the American Urological Association guidelines of 2009, prostate cancer screening is recommended to begin at age 40 or older in men with a life expectancy of at least 10 years [4]. Early prostate cancer screening is especially recommended in cases with high risk, such as African-American men and men with a family history [5]. The incidence of prostate cancer in men younger than 50 years of age has been reported to be approximately 3-4% of the total number of prostate cancers [6,7]. The prevalence of prostate cancer in 40-59-year-old Korean men is reported to be 0.6% [8]. Few studies have evaluated the incidence of prostate cancer in young men less than 40 years of age. In our Health Care Promotion Center, PSA screening is routinely performed in all men, regardless of age, and prostate biopsy is performed in cases with a high PSA level. From this screening, men younger than 40 years of age with high PSA levels are occasionally detected. The purpose of this study was to evaluate the results of the prostate biopsy findings in these young men and to determine the clinical significance of sustained high PSA levels.

MATERIALS AND METHODS

We retrospectively reviewed data from men with high PSA levels (higher than 4.0 ng/ml) who visited the Health Promotion Center during the period of October 1997 through August 2008. We selected samples from men younger than 40 years of age with no lower urinary tract or prostatitis symptoms. The eligible men underwent a routine exam including urine analysis, serum PSA testing, and digital rectal examination at our urology department. Those who required antibiotic treatment were excluded. In the rest of the cases, those with high PSA levels underwent transrectal ultrasonography (TRUS) and TRUS-guided prostate biopsy. TRUS examination was performed with the patients lying on their left side, using BoK 3535 ultrasound equipment with a 7 MHz biplane-probe model 8551 (BoK Medical A/S, Naerum, Denmark). Ultrasound-guided biopsies were performed with a 1.2 mm core biopsy needle mounted on a spring-loaded Biopsy Gun (Bard Ltd.) in two-dimensional planes (sagittal and axial). Ten core biopsies were obtained: 2 cores were taken from each side of the lateral and medial part of the base and midpoint, and 1 core from each side of the apex. All biopsies were confirmed by the pathology department. When the initial biopsy was negative, PSA testing was monitored every 6 months. Repeat biopsy and magnetic resonance imaging (MRI) of the prostate were performed in patients with persistently high PSA levels (higher than 4.0 ng/ml).

RESULTS

Seventy-five samples from the 81 men were initially biopsied to rule out prostate cancer. The median (range) age of the men among the 75 samples was 33 years (range, 26-40 years), and the mean PSA level of the samples was 6.57 ng/ml (range, 4.32-13.45 ng/ml). The baseline patient characteristics are shown in Table 1. Seventy-five patients had normal findings on a digital rectal examination. After the initial biopsy, among the 75 patients, 44 men had follow-up PSA testing. The mean period of follow-up was 43 months (range, 7-127 months). During the follow-up period, 15 patients had increased PSA levels (mean, 6.38 ng/ml), whereas 29 men had decreased PSA levels (mean, 5.42 ng/ml). Of 44 men, 38 men had a PSA level above 4.0 ng/ml. Ten men with sustained high levels of PSA had a second biopsy performed by use of the same method as the initial biopsy. Eight men with sustained high levels of PSA had a prostate MRI, and three of them had a finding of cancer suspicion. A third biopsy was performed in the three men.

Table 2 shows the outcome of the prostate biopsies. For the initial biopsy, prostate cancer was detected in one patient (1.3%). Men with benign prostate tissue accounted for 93% of the sample (70 men). In addition, there were two cases with inflammation (2.6%), and one each with high grade intraepithelial neoplasia (HGPIN) and atypical small acinar proliferation (ASAP) (1.3%). The age of the patient with cancer was 30 years, and his PSA level before the biopsy was 7.05 ng/ml. The Gleason score from the biopsy was 3+4. Due to the localized nature of the prostate cancer, he was treated with a radical prostatectomy. Ten men including the cases with HGPIN and ASAP underwent a second biopsy, and the histological findings showed benign tissue in all cases. In the patients with HGPIN and ASAP, the MRI findings showed no cancer. Three men underwent a third biopsy after a prostate MRI and they were confirmed to have benign tissue in all cases.

TABLE 1. Baseline characteristics of the study

Total No. of patients	75
Mean age (years)	27.5 (26-40)
Mean PSA (ng/ml)	6.57 (4.32-13.45)
No. of follow-up patients	44
No. of patients with PSA increase	15
No. of 2nd biopsy patients	10
No. of 3rd biopsy patients	3

PSA: prostate-specific antigen

TABLE 2. Outcome of TRUS-guided prostate biopsy

Pathology	1st biopsy (%) (n=75)	2nd biopsy (%) (n=10)	3rd biopsy (%) (n=3)
Benign	70 (93)	10 (100)	10 (100)
Inflammation	2 (2.6)		
HGPIN	1 (1.3)		
ASAP	1 (1.3)		
Prostate cancer	1 (1.3)		

TRUS: transrectal ultrasound, HGPIN: high grade prostatic intraepithelial neoplasia, ASAP: atypical small acinar proliferation

DISCUSSION

The results of our study showed that the PSA levels of most of the samples remained high after the initial PSA testing period. Preston et al reported that the mean serum PSA levels of Caucasian males 20-29 and 30-39 years of age were 0.47 ng/ml and 0.55 ng/ml, respectively [9]. Among African Americans, the mean serum PSA levels of the same two age groups were 0.51 ng/ml and 0.57 ng/ml. Ku et al reported that the median serum PSA levels of Korean young men were 0.90 ng/ml for the 20-29-year-old age group and 0.89 ng/ml for the 30-39-year-old age group [10]. In these two studies, there were no young men with high PSA levels who underwent prostate biopsy.

The factors causing an increase in PSA levels among men in young age groups are not well defined. Several investigations have reported PSA levels in relation to age, diet manipulation, obesity, and ethnicity [11-15]. However, the risks associated with all such factors remain controversial. Increased PSA levels are considered to be a premalignant finding or to signify the presence of a small infiltrating carcinoma that has not yet become clinically evident [16,17]. Alternatively, an initially increased PSA level

may be associated with elevated androgen secretion, which causes an increased PSA level that might influence the subsequent development of prostate cancer [17]. At present, there are no guidelines for cancer detection in men less than 40 years of age on the basis of increased PSA levels.

The results of our retrospective study on increased PSA levels in men less than 40 years of age showed that only 1.3% of the patients had prostate cancer. Ruska et al reported data on 87 men younger than 40 years of age who underwent prostate needle biopsy; 23 of them were found to have prostate cancer [18]. The most common reason for a biopsy was an abnormal digital rectal examination. However, confirmation of prostate cancer in younger men is difficult because PSA testing is not routinely performed in young men.

In our study, the 75 men studied were asymptomatic; they only had high PSA levels, and their digital rectal examination (DRE) examinations were normal. The results of our study suggest that PSA alone, in this age group, was not effective for detecting prostate cancer. According to our findings, the cancer detection rate from PSA screening was very low. In an effort to optimize the ability of serum PSA to perform as an ideal marker for the detection of cancer among young men, the characteristics of serum PSA values in young men require further study.

Histology examinations were also performed. HGPIN and ASAP were detected in 1.3% of our initial biopsy results. Roscigno et al reported on the incidence of HGPIN (0.6-24.6%) and ASAP (0.7-23.4%) in initial biopsy results [19]. The risk of developing cancer from HGPIN is 31.5% and the risk from ASAP is 40% after repeat biopsies [19]. In our two cases of HGPIN and ASAP, the results of a second biopsy confirmed only benign tissue. The multifocality of HGPIN and ASAP has been associated with a greater risk of prostate adenocarcinoma [20]. However, the results of our cases showed only unifocality in both HGPIN and ASAP samples. The MRI evaluation of HGPIN and ASAP was not suspicious for cancer. The clinical significance of HGPIN and ASAP in young men is unclear.

Performance of repeat biopsy and prostate MRI on patients with persistently high PSA levels has both risks and benefits for the early detection of prostate cancer. Consideration of the invasiveness, pain, and high cost of these procedures is important. The possibility of false-negative findings for cancer detection has been reported to be 82% in the age group less than 60 and 65% for men more than 60. The likelihood of detecting cancer on repeat biopsy is reported to be 10% [21]. Prostate cancer detection by MRI shows a wide range (from 50% to 92%) of accuracy [22]. Despite the high specificity of MRI, the routine use of MRI for prostate cancer detection remains controversial because of its low sensitivity and substantial interobserver variability [23]. In our study, the MRI findings did not match the results of the prostate biopsy. Based on the negative results of our repeat biopsies and prostate MRIs, performance of repeat biopsies in young men with persistently high PSA levels may not provide any benefit for the early detection of prostate cancer.

The limitations of this study include the following. Not all of the men with PSA elevation were followed up after the initial biopsy. In addition, the number of cases available for repeat biopsy and prostate MRI was very small. Finally, this was a retrospective study.

CONCLUSIONS

The results of this study show that prostate cancer detection in young men less than 40 years of age with high PSA levels and normal DREs was very low. The role of repeat biopsy and diagnostic MRI for persistently high levels of PSA in this age group is uncertain given the negative pathology results in all cases. Accordingly, repeat biopsy for persistently high PSA levels with normal DRE findings in men younger than 40 years of age may not be indicated. Additional large, prospective randomized trials are needed to confirm our findings.

REFERENCES

1. Wang MC, Valenzuela LA, Murphy GP, Chu TM. Purification of a human prostate specific antigen. Invest Urol 1979;17:159-63.
2. Sensabaugh GF. Isolation and characterization of a semen-specific protein from human seminal plasma: a potential new marker for semen identification. J Forensic Sci 1978;23:106-15.
3. Boyle P, Severi G, Giles GG. The epidemiology of prostate cancer. Urol Clin North Am 2003;30:209-17.
4. Greene KL, Albertsen PC, Babaian RJ, Carter HB, Gann PH, Han M, et al. Prostate specific antigen best practice statement: 2009 update. J Urol 2009;182:2232-41.
5. Smith RA, Cokkinides V, von Eschenbach AC, Levin B, Cohen C, Runowicz CD, et al. American Cancer Society guidelines for the early detection of cancer. CA Cancer J Clin 2002;52:8-22.
6. Sacco E, Prayer-Galetti T, Pinto F, Ciaccia M, Fracalanza S, Betto G, et al. Familial and hereditary prostate cancer by definition in an Italian surgical series: clinical features and outcome. Eur Urol 2005;47:761-8.
7. Azzouzi AR, Valeri A, Cormier L, Fournier G, Mangin P, Cussenot O. Familial prostate cancer cases before and after radical prostatectomy do not show any aggressiveness compared with sporadic cases. Urology 2003;61:1193-7.
8. Lee HW, Kwak KW, Choi YH, Choi HY, Lee HM. New thresholds for prostate-specific antigen velocity for prostate cancer screening in Korean patients younger than 60 years old. Korean J Urol 2008;49:113-7.
9. Preston DM, Levin LI, Jacobson DJ, Jacobsen SJ, Rubertone M, Holmes E, et al. Prostate-specific antigen levels in young white and black men 20 to 45 years old. Urology 2000;56:812-6.
10. Ku JH, Ahn JO, Lee CH, Lee NK, Park YH, Byun SS, et al. Distribution of serum prostate-specific antigen in healthy Korean men: influence of ethnicity. Urology 2002;60:475-9.
11. Oesterling JE, Kumamoto Y, Tsukamoto T, Girman CJ, Guess HA, Masumori N, et al. Serum prostate-specific antigen in a community-based population of healthy Japanese men: lower values than for similarly aged white men. Br J Urol 1995;75:347-53.
12. Freedland SJ, Terris MK, Platz EA, Presti JC Jr. Body mass index as a predictor of prostate cancer: development versus detection

on biopsy. Urology 2005;66:108-13.
13. Chung BH, Hong SJ, Cho JS, Seong DH. Relationship between serum prostate-specific antigen and prostate volume in Korean men with benign prostatic hyperplasia: a multicentre study. BJU Int 2006;97:742-6.
14. Kobayashi T, Kinoshita H, Nishizawa K, Mitsumori K, Ogawa O, Kamoto T. Age-associated increase of prostate-specific antigen in a high level of men visiting urological clinics. Int J Urol 2005; 12:733-8.
15. Bray GA. The underlying basis for obesity: relationship to cancer. J Nutr 2002;132(11 Suppl):3451S-5.
16. Antenor JA, Han M, Roehl KA, Nadler RB, Catalona WJ. Relationship between initial prostate specific antigen level and subsequent prostate cancer detection in a longitudinal screening study. J Urol 2004;172:90-3.
17. Fang J, Metter EJ, Landis P, Chan DW, Morrell CH, Carter HB. Low levels of prostate-specific antigen predict long-term risk of prostate cancer: results from the Baltimore Longitudinal Study of Aging. Urology 2001;58:411-6.
18. Ruska KM, Partin AW, Epstein JI, Kahane H. Adenocarcinoma of the prostate in men younger than 40 years of age: diagnosis and treatment with emphasis on radical prostatectomy findings. Urology 1999;53:1179-83.
19. Roscigno M, Scattoni V, Freschi M, Raber M, Colombo R, Bertini R, et al. Monofocal and plurifocal high-grade prostatic intraepithelial neoplasia on extended prostate biopsies: factors predicting cancer detection on extended repeat biopsy. Urology 2004;63:1105-10.
20. Epstein Jl, Herawi M. Prostate needle biopsies containing prostatic intraepithelial neoplasia or atypical foci suspicious for carcinoma: implications for patient care. J Urol 2006;175:820-34.
21. Djavan B, Zlotta A, Remzi M, Ghawidel K, Basharkhah A, Schulman CC, et al. Optimal predictors of prostate cancer on repeat prostate biopsy: a prospective study of 1,051 men. J Urol 2000;163:1144-8.
22. Engelbrecht MR, Jager GJ, Laheij RJ, Verbeek AL, van Lier HJ, Barentsz JO. Local staging of prostate cancer using magnetic resonance imaging: a meta-analysis. Eur Radiol 2002;12:2294-302.
23. Hricak H. MR imaging and MR spectroscopic imaging in the pre-treatment evaluation of prostate cancer. Br J Radiol 2005; 78:S103-11.