Original Article

Predictors of Prostate Cancer Diagnosis at repeat Prostate Biopsy in patients initially diagnosed with Atypical Small Acinar Proliferation

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ABSTRACT

Objective: To determine the predictors of prostate cancer at repeat biopsy in patients initially diagnosed with atypical small acinar proliferation (ASAP)
Design: Retrospective study
Setting: Tepecik Training and Research Hospital, Turkey
Subjects: Among 1240 patients, only 54 patients diagnosed with ASAP on initial biopsy underwent repeat biopsy.
Intervention: Patients were classified into cancer, benign and ASAP groups according to their final pathological results after repeat biopsy.
Main outcome measure: The final pathological results of repeat biopsy were compared according to the clinico-biological features.
Results: At the repeat 24 core prostate biopsy, the diagnoses were benign prostate, prostate cancer and ASAP in 26/54 (48.2%), 20/54 (37.03%) and 8/54 (14.8%) patients, respectively. In the cancer, ASAP and benign groups, the mean age was 67.2 ± 5.4, 56.3 ± 6.7 and 61.8 ± 8.5 years, respectively. The cancer detection rate was 37.03%. Except for patient age, we found no clinical or pathological features predicting prostate cancer in patients with ASAP at repeat biopsy.
Conclusion: Only the age of the patients is a predictive factor of prostate cancer at repeat biopsy in patients diagnosed with ASAP.

KEY WORDS: acinar proliferation, biopsy, prostate

INTRODUCTION

Prostate cancer (PCa) is the most common cancer in men worldwide[1]. PCa is usually suspected on the basis of an abnormal digital rectal examination (DRE) and/or elevated prostate specific antigen (PSA) levels. The definitive diagnosis of prostate cancer depends on the histopathological confirmation of adenocarcinoma in prostate biopsy[2]. In some biopsy specimens, there are foci of small acinar structures that are highly suggestive of malignancy, but insufficient histological atypia required for the accurate diagnosis of adenocarcinoma, and hence, these structures are defined as atypical small acinar proliferation (ASAP)[3]. ASAP is observed in approximately 5% of prostate biopsies[4,5]. Patients with ASAP have a 40% risk of developing PCa in subsequent biopsies[6]. The literature recommends that all patients with an initial diagnosis of ASAP should undergo a repeat biopsy within 3 – 6 months[7]. Many researchers claim that ASAP is a condition in which the pathologist has insufficient tissue for the definitive diagnosis of PCa[8]. If inadequate tissue sampling were a prohibitive factor for the definitive diagnosis of PCa, an extended or saturation biopsy scheme should be used for repeat biopsy. The incidence of PCa is 30 - 43% in saturation prostate biopsy[9]. The cancer detection rate of saturation prostate biopsy may depend on the number of cores sampled during biopsy; therefore, obtaining more prostate tissue can increase the cancer detection rate[10]. After the diagnosis of ASAP, determining the predictors of prostate cancer is controversial in repeat biopsy[11]. We examined repeat biopsy results of patients with ASAP. The aim of the present study was to determine the predictors of prostate cancer on repeat biopsy in these patients.

MATERIALS AND METHODS

The medical records of 1240 patients who had undergone initial transrectal ultrasound (TRUS)-

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guided 12 core prostate biopsies in our institution between June 2013 and August 2016 were reviewed retrospectively. This study was conducted in accordance with the declaration of Helsinki, and approval was obtained from the institutional ethics committee. After obtaining informed consent from the patients, all biopsies were performed transrectally with ultrasonography guidance using a 25 cm 18-gauge, side-notch cutting (Tru-cut) needle. The biopsies were performed with the patient in the lateral decubitis position with periprostatic nerve blockage. The initial biopsy results of patients were classified into four categories: prostate cancer (adenocarcinoma), normal prostates or benign prostatic hyperplasia, high grade prostatic intraepithelial neoplasia (HGPIN) and ASAP.

In this study, we included 54 patients diagnosed with ASAP at the initial biopsy. These patients underwent TRUS-guided 24-core saturation biopsy for repeat biopsy. The clinico-biological features of the patients were recorded. The patients were excluded if they had a prior diagnosis of PCa or HGPIN. We also excluded patients who had undergone core prostate biopsy of under 24 for repeat biopsy.

The patients were classified into cancer, benign and ASAP groups according to the final pathological diagnosis after repeat biopsy. These groups were compared according to age, initial total PSA, total PSA, DRE findings, prostate volume, TRUS findings, and total and mean core length of biopsy. We also identified the Gleason scores of the cancer group. Patients with one or more hypoechoic lesions at TRUS were accepted as having an abnormal TRUS.

Statistical analysis

The conformity of the variables to the normal distribution was assessed with the Shapiro-Wilk test. The Student's t-test and the chi-squared test were used for inter-group analyses of continuous variables. Independent averages of more than two were compared with the analysis of variance and the Kruskal-Wallis tests. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc, Chicago, Illinois, USA) version 24.0 and a p-value <0.05 was considered significant.

RESULTS

The incidence of ASAP was 4.35% (54/1240). Of the 54 patients diagnosed with ASAP on initial biopsy and who underwent repeat biopsy, the mean age was 63 years (range: 48 - 76 years), the mean inital PSA was 8.6 ng/mL (range: 2.3 - 17.6 ng/mL), the mean total PSA was 9.5 (range: 3.2 - 28.1 ng/mL), the mean prostate volume was 52.5 ml (range: 26 - 121 mL), and the total and mean core lengths of biopsies were 26.8 cm (range: 21.4 - 32.4 cm) and 1.1 cm (range: 0.89 - 1.35 cm), respectively. The clinicopathological features of the patients have been summarized in Table 1. The mean interval between the first and the second prostate biopsies was 5.4 ± 1.3 months.

Table 1: Clinico-biological characteristics of patients undergoing saturation biopsy

Variables	Mean (SD)
Age (years)	63 ± 7.9
Inital PSA (ng/ml)[a]	8.6 ± 6.8
PSA (ng/ml)	9.5 ± 6
Prostate volume (ml)	52.5 ± 39.8
Total core length (cm)	26.8 ± 3.6
Mean core length (cm)	1.1 ± 0.2
DRE (n(%))	
Normal	42 (77.8)
Abnormal	12 (22.2)
TRUS finding (n(%))	
Normal[b]	14 (25.9)
Abnormal[c]	40 (74.1)
Gleason (n(%))	
6	10 (50)
7	10 (50)

PSA: prostate-specific antigen; DRE: digital rectal examination; TRUS: transrectal prostatic ultrasound

[a]: for only 54 patients; [b]: have no hypoechoic lesions in TRUS; [c]: have hypoechoic lesions in TRUS

At repeat 24 core prostate biopsy, the diagnoses were benign prostate, prostate cancer and ASAP in 26/54 (48.2%), 20/54 (37.03%) and 8/54 (14.8%) patients, respectively. The cancer detection rate was 37.03% (20/54). The Gleason score was determined to be 6 in 10 patients (50%), and 7 in 10 patients (50%) who had been diagnosed with PCa after repeat biopsy. In the cancer, ASAP and benign groups, the mean age was 67.2 ± 5.4, 56.3 ± 6.7 and 61.8 ± 8.5 years, respectively. The difference was determined to be statistically significant (p = 0.032). When these groups were compared with each other, there was no statistical difference in the inital total PSA, total PSA, DRE findings, prostate volume, TRUS findings, and the total and mean core lengths (Table 2).

DISCUSSION

In this study, we found only the age of patients to be a predictive factor for prostate cancer at repeat biopsy in patients diagnosed with ASAP. The cancer detection rate in patients with ASAP on repeat biopsy is approximately 40%, and the urologist should obtain additional biopsy from the zones of the prostate in which ASAP was detected in the initial biopsy[12]. Iczkowski *et al* reviewed the medical data of 6026 patients who had undergone prostate biopsy and determined the incidence of ASAP as 3.3%[13]. The incidence of ASAP varies from 0.7 - 23.4% in many studies. The average incidence of ASAP is 5% in the literature[14]. Consistent with the literature, our incidence was 4.35% and the cancer detection rate on repeat biopsy was 37.03%.

Table 2: Characteristics of patients undergoing saturation biopsy according to pathological results

Variables	Benign (n = 26)	ASAP (n = 8)	Cancer (n = 20)	p-value
Age (years)	61.8 ± 8.5	56.3 ± 6.7	67.2 ± 5.4	0.032
Inital PSA (ng/ml)[a]	9.9 ± 8.9	5.8 ± 3.6	8.1 ± 3.9	0.394
PSA (ng/ml)	10.9 ± 7.8	7.1 ± 2.5	8.6 ± 3.8	0.463
Prostate volume (ml)	61 ± 50.5	37.1 ± 14.1	47.7 ± 29.7	0.558
Total core length (cm)	26.2 ± 3.2	29.8 ± 3.9	26.3 ± 3.6	0.167
Mean core length (cm)	1.09 ± 0.1	1.24 ± 0.1	1.09 ± 0.1	0.236
DRE (n(%))				0.249
Normal	22 (84.6)	8 (100)	12 (60)	
Abnormal	4 (15.4)	0 (0)	8 (40)	
TRUS finding (n(%))				0.845
Normal[b]	8 (30.8)	2 (25)	4 (20)	
Abnormal[c]	18 (69.2)	6 (75)	16 (80)	

PSA: prostate-specific antigen; DRE: digital rectal examination; TRUS: transrectal prostatic ultrasound; ASAP: Atypical small acinar proliferation

[a]: for only 54 patients; [b]: have no hypoechoic lesions in TRUS; [c]: have hypoechoic lesions in TRUS

After the diagnosis of ASAP, determining the predictors of prostate cancer is controversial in subsequent biopsy. Iczkowski *et al* found no predictor factor for detecting PCa in patients with ASAP after the initial biopsy[13]. Epstein *et al* reported that there was no association between PCa and the clinicopathological features of patients with ASAP[15]. Park *et al* reported that age and DRE were predictors of PCa in patients with ASAP[16]. Similar to this study, we found that age was an independent predictor of cancer, but DRE was not a significant cancer detection variable in patients with ASAP at repeat biopsy. Mearini *et al* reviewed the data of 1274 patients who had undergone prostate biopsy[17]. They determined the incidence of ASAP to be 5.9% and observed that the total PSA was a predictor of PCa at subsequent biopsy. Contrary to this study, we found that the inital total PSA and total PSA levels were not significantly increased in patients with ASAP at repeat biopsy. Similar to our study, many investigators recommend a repeat biopsy within 3 - 6 months, irrespective of follow-up of the PSA values[14,18].

Levine *et al* observed that the PCa detection rate decreased with increasing prostate volume[19]. They reported that the cancer detection rates were 43%, 27% and 24% in patients with prostate volumes of lower than 30 cc, between 30 cc and 50 cc, and greater than 50 cc, respectively. Scattoni *et al* reported that 12 core biopsy may not have been sufficient for correct sampling of the prostate glands larger than 50 ml in which ASAP is present[20]. In our study, we used the 24 core saturation biopsy scheme for repeat biopsy and observed that the cancer group prostate volume was smaller than that of the benign group, but the difference was not statistically significant.

In spite of the presence of many studies on the core number and location of cores, there is a limited number of studies on the biopsy core length, which is one of the most important parameters in determining the quality of the biopsy[21,22]. Although there are studies suggesting that a greater core length increases the rates of PCa diagnosis, there have also been studies suggesting that the diagnosis of PCa is not affected by core length[19,20,23]. In our study, the total and mean core lengths were not significant variables predicting the cancer detection rate in patients with ASAP.

Warlick *et al* reported that 17.3% of patients with ASAP had high-grade (Gleason >7) PCa on repeat biopsy[24]. In another study, Raskolnikov *et al* determined that 5% of patients with ASAP had high grade PCa on subsequent prostate biopsy[18]. In this study, we observed that 18.5% of patients with ASAP were subsequently found to have high-grade (Gleason >7) PCa.

While there are studies advocating the benefit of magnetic resonance imaging (MRI) prior to repeat biopsy in determining hidden cancers that have escaped the eye, despite previously negative prostate biopsies in patients in whom the suspicion of cancer persists, there are also studies that contradict this[25]. Due to the MRI being a costly procedure, it has not been used prior to re-biopsy.

There are several limitations in our study. The first limitation of our study is its retrospective nature. The second limitation of this study is that the biopsy cores were not examined by the same pathologist. The other limitation of this study is the small number of patients with ASAP included in the study, and this limitation has affected the interpretation of the results. A larger pool of patients will provide a more accurate picture.

CONCLUSION

ASAP is associated with an approximate rate of 40% of PCa at repeat biopsy. All patients diagnosed with ASAP need repeat biopsy within 3 – 6 months. We observed that only the age of patients was a predictive

factor of prostate cancer at repeat biopsy in patients with ASAP. Large-scale, multi-center, prospective studies will provide a more accurate picture for the clinical significance of the predictors of prostate cancer at repeat biopsy in patients with ASAP.

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