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Original Research / Özgün Araştırma

Incidental prostate cancer diagnosed after surgical treatment of benign prostatic hyperplasia

Benign prostat hiperplazisinin cerrahi tedavisi sonrası tanı konulan insidental prostat kanseri

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Özet

Amaç: İnsidental prostat kanseri (PCa) klinik belirti vermeyen, ameliyat öncesi rektal tuşe, prostat spesifik antijen (PSA) ve görüntülemeleri normal hastalarda transüretral prostat rezeksiyonu (TURP) veya açık prostatektomi sonrası tespit edilen kanser olarak tanımlanır. Bu çalışmanın amacı kliniğimizdeki insidental PCa insidansını ve klinik anlamlılığını belirlemektir.

Gereç ve Yöntemler: Merkezimizde 2014-2019 yılları arasında benign prostat hiperplazisi ön tanısı ile TURP veya transvezikal prostatektomi (TVP) uygulanan 1020 hasta retrospektif olarak incelendi. Hastanın yaşı, prostat hacmi, preoperatif PSA değeri, Gleason skoru, ISUP skoru, evresi ve ameliyat öncesi prostat biyopsisinin varlığı not edildi. Prostat kanseri için uygulanan tedavi yöntemleri değerlendirildi.

Bulgular: Ocak 2014 ile Aralık 2019 arasında toplam 1020 hasta BPH için cerrahi olarak tedavi edildi. 57 (%5.6) hastaya insidental PCa tanısı kondu. Hastaların 51'i (% 89) TURP ve 6'sı (%11) TVP olmuştu. Ortalama yaş 69.9±7.1 yıl ve ortalama PSA değeri 5.3±4.8 ng/ml idi. Hastaların çoğunluğu (%82.4) Gleason skor 6 (3+3) ve 37'si (%64.9) evre 1a olarak rapor edildi. Preoperatif prostat biyopsisi yapılan hastaların prostat hacmi ve PSA değerleri biyopsi yapılmayanlara göre anlamlı olarak daha yüksekti (p<0.01). Toplam 42 hastada aktif izlem yapıldı, 2 hastaya radikal prostatektomi, 6 hastaya radyoterapi ve 7 hastaya androjen blokajı uygulandı.

Sonuç: Kliniğimizdeki insidental PCa oranı literatürde bildirilen oranlara benzer bulunmuş-

Abstract

Objective: Incidental prostate cancer (PCa) is defined as the clinically inapparent tumor detected after transurethral resection of prostate (TURP) or open prostatectomy with benign preoperative rectal examination, prostate specific antigen (PSA) and imaging. The aim of this study is to determine the incidence and clinical significance of incidental prostate cancer in our clinic.

Material and Methods: A retrospective analysis was performed in patients who were treated with TURP or transvesical open prostatectomy (TVP) between January 2014 and December 2019. Age, prostate volume, preoperative PSA value, Gleason score, ISUP score, stage and presence of previous prostate biopsy were noted. Treatment performed for incidental PCA was determined.

Results: A total of 1020 patients were surgically treated for benign prostate hyperplasia between January 2014 and December 2019. Incidental PCa was diagnosed in 57 (5.6%) patients. 51 (89%) of the patients had TURP and 6 (11%) had TVP. Mean age was 69.9±7.1 years and mean PSA value was 5.3±4.8 ng/ml. Majority of the patients (82.4%) had a Gleason score of 6 (3+3) and 37 (64.9%) patients were reported as stage 1a. Patients with preoperative prostate biopsy have significantly higher prostate volume and PSA values compared to the patients without biopsy (p<0.01). Active surveillance was performed in 42 patients, 2 patients underwent radical prostatectomy, 6 patients had radiotherapy and 7 patients had androgen blockade.

Conclusion: We have an incidental PCa rate similar to the literature. Majority of the patients

The study was approved by the Clinical Researches Ethic Committee of Bezmialem Vakif University (Approval number: 03/60) (Date:2021.02.16).
All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

tur. Hastaların çoğunda evre 1a hastalık ve Gleason 6 skoru tespit edilmiştir. İnsidental prostat kanserinin tedavisinde konservatif tedavi seçenekleri ön planda yer almaktadır.

Anahtar Kelimeler: insidental prostat kanseri, benign prostat hiperplazisi, transüretral prostat rezeksiyonu.

have stage 1a disease and a Gleason score of 6. Most of the patients were managed conservatively.

Keywords: incidental prostate cancer, benign prostate hyperplasia, transurethral resection of prostate

INTRODUCTION

Prostate cancer (PCa) is the second most common malignancy diagnosed in the male population accounting for 15% of all cancers diagnosed (1). Patients who are planned to undergo surgery for benign prostatic hyperplasia (BPH) are usually screened for PCa before surgery to exclude the presence of coexisting PCa that could change the treatment strategy (2). Incidental PCa is defined as the clinically inapparent tumor detected after pathological examination of transurethral resection of prostate (TURP) or open prostatectomy specimens in patients with benign preoperative rectal examination, prostate specific antigen (PSA) and imaging (3). Also, there is a group of patients who had one or more transrectal prostate biopsies but no cancer was detected and referred to BPH surgery. Before PSA, the diagnosis rate of incidental PCa was 12.9% but this rate decreased to 8% after the introduction of PSA (4).

TURP is the standard treatment of BPH in patients with prostate volume under 80 gr and open prostatectomy is mostly carried out in cases with prostate volume > 80 gr (5). Central and transitional zones of the prostate are removed in TURP but prostate cancer mostly originates from the peripheral zone (6). Whereas, there are studies in the literature reporting that up to 30% of prostate cancers originate from central and transitional zones and It is difficult to diagnose these cases as cancer in the transitional zone is mostly located anteriorly and this location is hard to reach with transrectal biopsy (7).

According to the TNM staging system, if the tumor constitutes < 5% of the resected tissue it is classified as stage T1a and if the tumor is found in > 5% of resected tissue, it is classified as T1b (8). Generally, incidental PCa is accepted to be clinically insignificant but there are studies in the literature reporting that patients with increased tumor volume (T1b cancers) and Gleason score may have an unfavorable prognosis (9–11). The aim of this study is to determine the incidence and clinical significance of incidental prostate cancer in patients who had TURP or transvesical open prostatectomy (TVP) with the preoperative diagnosis of BPH in our clinic.

MATERIAL AND METHODS

A retrospective analysis was performed in patients who were treated with TURP or TVP with the diagnosis of benign prostate hyperplasia between January 2014 and December 2020. Patients who had prostate cancer after pathological assessment were determined. Age of the patient, prostate volume, preoperative PSA value, Gleason score, ISUP score, stage and presence of previous prostate biopsy were noted. Treatment method for incidental PCa was determined. Pathological assessment was performed by an experienced uropathologist. If the incidental tumor was in less than 5% of the resected tissue it was reported as stage T1a and incidental tumor detected in more than 5% of resected tissue was reported as T1b. In our clinic prostate biopsy is performed in patients whose PSA value is higher than the age-specific reference range or in patients with abnormal digital rectal examination. Some patients with high PSA and normal digital rectal examination did not go biopsy because of their old age and comorbidities. Patients with histologically confirmed prostate cancer on preoperative prostate biopsy and patients with PSA higher than 20 ng/ml were excluded from the study.

Statistical Analysis

Data storage and statistical analyses were performed using the SPSS 17.0 statistical program (SPSS Inc., Chicago, IL, USA). Normal distribution was test-

ed by Shapiro-Wilk test. Fisher's exact test and T-test were used for categorical and continuous variables in case of normal distribution and Mann-Whitney U test was used in case of non-normal distribution. Statistical significance was defined as a P value < 0.05. In the post-hoc power analysis performed with the data obtained from the study, the power was found to be 82% at 95% confidence level and 0.05 significance level.

RESULTS

A total of 1020 patients were surgically treated for BPH between January 2014 and December 2019. TURP and TVP were performed in 924 and 96 patients respectively. Incidental PCa was diagnosed on histopathological assessment in 57 (5.6%) patients. Fifty-one (89%) of the patients with incidental PCa had TURP and 6 (11%) had TVP. Baseline characteristics of the patients with incidental PCa were given in Table 1. All patients had benign digital rectal examination. The mean age of the patients was 69.9±7.1 years and the mean PSA value was 5.3±4.8 ng/ml. The majority of the patients (82.4%) had a Gleason score of 6(3+3), only 10 (17.6%) patients had Gleason score ≥7. A total of 37 (64.9%) patients were reported as stage 1a and 20 (35.1%) patients were reported as stage 1b. Eighteen (31.5%) patients had preoperative prostate biopsies reported as BPH. Biopsy was not performed in 3 patients, although their PSA levels were elevated (Figure 1). One of these patients was 68 years old with a PSA level of 6.19 ng/ml and had several additional comorbidities. This patient underwent TURP and pathology was reported as Gleason 6(3+3) stage T1b PCa. The other 2 patients were 79 and 85 years old, and their PSA values were 8.39 ng/ml and 8 ng/ml, respectively. Patient with the PSA of 8.39 ng/ml underwent TVP and postoperative pathology was stage T1a, Gleason 6(3+3) PCa. The other patient had TURP and the postoperative pathology was Gleason 7(4+3), stage T1b PCa. When the patients with preoperative prostate biopsy were compared to those who had no history of biopsy, it was seen that prostate volume and PSA values were significantly higher in patients with prostate biopsy (p=0.002 and p<0.01, respectively). No statistically significant difference was detected between the two groups in terms of stage, tumor percentage and ISUP score (Table 2).

Twenty-three patients were catheterized before the operation because of urinary retention. Most of the time, catheterized patients want to be operated on as soon as possible to get rid of the catheter. It may take 1-2 stressful months in catheterized patients with elevated PSA to see a second PSA value, provide sterile urine, perform the biopsy and obtain the pathological result. This psychological distress may be transmitted to the physician and patients who need to be biopsied first may undergo surgery instead. We thought that this situation may have an effect on incidental prostate cancer rate and to test this hypothesis patients with preoperative catheterization were compared with patients with no catheterization. It was found that there was no clinically significant difference in age, prostate volume, stage, tumor percentage and ISUP score but PSA value was significantly higher in patients with retention (Table 3). No additional treatment was given in 42 patients and active surveillance was performed. Radical Prostatectomy was performed in 2 patients, 6 patients had radiotherapy and 7 patients had androgen blockade. Patients who underwent radical prostatectomy had stage 1a prostate cancer with a Gleason score of 6 (3+3) after TURP. Transrectal prostate biopsy was recommended to these patients before radical prostatectomy but one patient refused it. In 12-core prostate biopsy, Gleason 6 (3+3) prostate cancer was detected in 3 cores and Gleason 7 (3+4) cancer was detected İn one core; pathological examination of radical prostatectomy specimen revealed Gleason score 7 (3+4) prostate cancer, pT2 stage, tumor involving 5% of the prostate. In the other patient, pT2 stage, Gleason score 6 (3+3) prostate cancer involving 2% of the prostate was detected. Prostate biopsy was only recommended to the patients who accepted radical prostatectomy, we didn't perform prostate biopsy after TURP/TVP in other patients as they were treated with conservative modalities (radiotherapy, active surveillance and androgen blockade). Androgen blockade was preferred in patients who do not accept other treatment options, who are incompatible with treatment, and cannot come for regular follow-up.

Table 1. Baseline Patient Characteristics.

No of Patients	57
Mean Age	69.9±7.1
Mean Prostate Volume	70.4±58
Mean PSA	5.3±4.8
Type of surgery (%)	
TURP	51 (89)
TVP	6 (11)
Gleason score (%)	
6(3+3)	47 (82.4)
7(3+4)	5 (8.8)
7(4+3)	4 (7)
8(4+4)	0
9(4+5)	1(1.8)
10(5+5)	0
ISUP	
1 (%)	47 (82.4)
2(%)	5 (8.8)
3(%)	4 (7)
4(%)	0
5(%)	1 (1.8)

PSA: *Prostate specific antigen,* ***TURP:*** *Transurethral resection of prostate*

TVP: *Transvesical prostatectomy,* ***ISUP:*** *International society of urological pathology score*

Table 2. Comparison of patients with preoperative prostate biopsy and without biopsy.

	Patients without Biopsy (n=39)	**Patients with Biopsy (n=18)**	**p**
Mean Age (min-max)	70.1±6.9 (56-85)	69.72±7.6 (57-85)	0.872
Median Prostate Volume (IQR)	50 (35.75-80.75)	81.5 (66.25-110.75)	0.002
Median PSA (IQR)	2.1 (1.63-6.92)	10.8 (6.88-14.66)	<0.01
Stage 1a (%)	23 (59)	13 (72)	0.432
Stage 1b (%)	16 (41)	5 (28)	0.432
Median Tumor percentage (IQR)	3 (2-5)	2.5 (2-5.25)	0.426
ISUP			1
1 (%)	31 (79.48)	16 (88.88)	
2 (%)	4 (10.27)	1(5.56)	
3 (%)	3 (7.69)	1 (5.56)	
4 (%)	0	0	
5 (%)	1 (2.56)	0	

Min: *Minimum,* ***Max:*** *Maximum,* ***IQR:*** *Interquartile range,*

PSA: *Prostate specific antigen,* ***ISUP:*** *International society of urological pathology score.*

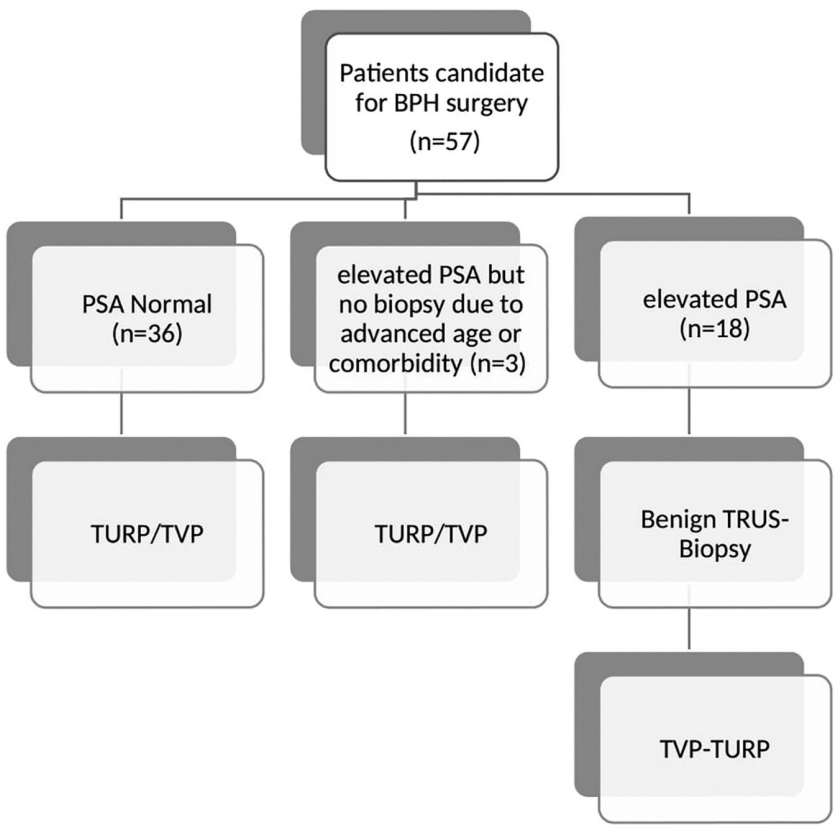
Table 3. Comparison of patients with urethral catheter and without urethral catheter.

	Patients without Catheter (n:34)	Patients with Catheter (n:23)	p
Mean Age (min-max)	69.1±7 (57-85)	71.2±7.3 (60-85)	0.274
Median Prostate Volume (IQR)	53.5 (33.5-81.75)	60 (37.5-81.5)	0.51
Median PSA (IQR)	2.43 (1.61-5.01)	4.61 (2.23-11.2)	0.011
Stage 1a (%)	19 (56)	18 (77)	0.082
Stage 1b (%)	15 (44)	5 (23)	0.082
Median Tumor percentage (IQR)	3.5 (2-6.75)	2 (1-4.5)	0.274
ISUP			0.15
1 (%)	26 (74.29)	21 (91.3)	
2 (%)	4 (11.43)	1(4.35)	
3 (%)	3 (8.57)	1 (4.35)	
4 (%)	0	0	
5 (%)	1 (2.86)	0	

Min: *Minimum,* ***Max:*** *Maximum,* ***IQR:*** *Interquartile range,* ***PSA:*** *Prostate specific antigen,*

ISUP: *International society of urological pathology score.*

Figure 1. Diagram showing the stages that patients with incidental prostate cancer go through until surgery.



DISCUSSION

Various incidence rates for incidental PCa are reported in the literature. Capogrosso et al. reported that PCa was found in 6.4% of patients after BPH surgery (12). Abedi et al. retrospectively evaluated the patients who had TURP or open prostatectomy and reported that incidental PCa was detected in 19.9 % of the cases, rate of PCa was especially high (40%) in patients who had open prostatectomy (13). In another study, all patients with PSA ≥4 ng/ml or abnormal digital rectal examination findings underwent prostate biopsy before surgery and incidental PCa was found in 15.6% of the patients (14). In this study, our detection rate of incidental cancer was 5.6% which is an acceptable rate compared to the values reported by other authors. The reason for this low rate could be that we did not avoid prostate biopsy in patients with elevated PSA. There were only 3 (5.2%) patients with elevated PSA values who had no prostate biopsy.

The introduction of PSA testing significantly decreased the detection rate of incidental prostate cancer after BPH surgery. Jones et al. compared the rate of incidental PCa in patients who underwent TURP in the era before the introduction of PSA screening to those who had TURP after PSA screening and reported a decrease in the diagnosis rate of prostate cancer from 14.9% to 5.2% (15). In a study performed in Tanzania where PSA is not readily available due to limited resources and only done in selected cases if there is a strong suspicion of malignant prostatic enlargement, incidental PCa was diagnosed in 21.6% of patients who had TURP with the presumption of BPH (16). This study may give an idea about the detection rate of incidental PCa before the introduction of PSA.

Although TURP still maintains its feature of being the gold standard treatment modality, with the development of technology, new surgical methods such as laser vaporization of prostate and prostatic lift have emerged in which no histological sampling is performed. Incidental prostate cancer can be missed in patients with such techniques. Therefore, various studies have been conducted to predict the presence of incidental PCa. Sakamoto et al. defined the independent risk factors for incidental PCa as age ≥ 75 years, prostate volume ≤ 50 cc and the absence of preoperative prostate biopsy despite PSA ≥ 4 ng/ml (17). Thirty-nine (12%) of the patients in that study did not have a prostate biopsy because of older age or patient preference although they had elevated PSA which was quite high compared to our study. In another study, older patient age and PSA density ≥ 15 ng/ml/cc were found to be independently associated with incidental Pca (14). These results show that patients with advanced age and elevated PSA should be told before the surgery that prostate cancer can be detected in histopathological examination of the surgical specimen. Prostate biopsy might reduce the risk, but in some patients, prostate cancer can still be detected postoperatively even though preoperative biopsy is benign, as in our study. There is no study in literature investigating whether there is any difference in characteristics of incidental PCa patients catheterized before surgery and patients without a catheter. We found a significant difference only in preoperative PSA value which was significantly higher in catheterized patients as expected. There was no clinically significant difference in age, prostate volume, stage, tumor percentage and ISUP score.

Most of the patients with incidental PCa have Gleason score 6 cancer. It is important to differentiate whether cancer detected is clinically significant or not. Incidental cancers with higher Gleason scores and larger volume of cancer can be clinically significant (17). Herden et al. evaluated the long-term outcome of active surveillance in patients with stage 1a and 1b prostate cancer in 68 men and reported that only 1 patient developed metastasis and no prostate cancer-specific death was observed (11). Melchior et al. performed radical prostatectomy in 17 T1a and 9 T1b patients with incidental PCa and residual tumor was detected in 11 (65%) patients with T1a and 7 (78%) patients with T1b on the other hand no extraprostatic cancer was found in any patient (18). Chung et al. performed radical prostatectomy in 95 incidental prostate cancer patients and reported that 67 (70.53%) of the patients had residual tumor and extracapsular extension was detected in 10 (10.5%) cases (19). However, in both studies, a significant number of patients had no residual tumor (pT0) after radical prostatectomy. In our

series, only 2 (3.5%) patients underwent radical prostatectomy. These patients had stage 1a prostate cancer with Gleason score of 6 (3+3) after TURP. Pathological examination of radical prostatectomy specimens revealed that one patient had pT2 stage, Gleason score 7 (3+4) tumor involving 5% of the prostate. In the other patient, pT2 stage, Gleason score 6 (3+3) prostate cancer involving 2% of the prostate was detected. None of the patients had an extraprostatic extension. Melchior et al. reported that in 30% of the patients there was an upgrade in Gleason score after radical prostatectomy (18). In another study, an upgrade in Gleason score was detected in 17% of the cases after radical prostatectomy (20). In the current study, one of the two patients who underwent radical prostatectomy had an upgrade in the Gleason score compared to the pathology of TURP, but it is not possible to make any comment about this issue as the number of patients was very low.

The majority of the patients in our study had conservative treatment. Radiotherapy was performed in 6 (10.5%) patients. Metanhalia et al. reported that of the 72 patients with incidental PCa, 46 (33%) were managed with watchful waiting, 1 (1.4%) patient underwent radical prostatectomy and 6 (8.3) underwent radiotherapy (21). Radical prostatectomy can be troublesome in patients who had TURP, complication rates are higher in this group of patients (22,23). This might be the reason why most of the patients are either managed expectantly or treated with radiotherapy. Also, there is a concern that radical prostatectomy can be overtreatment as some patients will be reported as pT0. Radiotherapy is an effective treatment method with acceptable toxicity in patients who underwent TURP, incontinence rates are slightly higher compared to the patients without TURP (24,25). In this study, data on the continence status of patients who underwent radical prostatectomy and radiotherapy are lacking. However, information obtained from the literature shows that patients who undergo radical prostatectomy and radiotherapy have a higher risk of incontinence compared to patients with no such history. This study has several limitations. First of all, it is a retrospective study with a small number of patients. The low number of patients in the biopsy group limits the results of the statistical analysis. We also do not have the follow-up data of the patients so we couldn't report about the parameters such as PSA progression and cancer-specific survival. In a multicenter study including 63 patients, it was reported that transrectal prostate biopsy after TURP in patients with incidental prostate cancer did not give additional information and the rate of upgrading in Gleason score was very low (20). They concluded that prostate biopsy after TURP could be considered in patients with low grade cancer who were planned to have active surveillance and it was not indicated in patients who would have radical prostatectomy as exact pathology would be revealed after surgery. Unfortunately, we did not perform prostate biopsy after BPH surgery in any patient who had conservative treatment. Biopsy was performed only in one patient who underwent radical prostatectomy.

CONCLUSION

The current study shows that although the incidence of prostate cancer detected after BPH surgery significantly decreased after the introduction of PSA, it can still be incidentally diagnosed on pathological specimens after BPH surgery. The majority of the patients have stage 1a disease and a Gleason score of 6 but patients with higher Gleason scores can be encountered. The treatment method should be determined together with the patient in an individualized way. Studies in literature show that patients with stage 1a disease and low Gleason score can be managed conservatively whereas in patients with stage 1b and high Gleason score curative treatments can be performed with good oncologic results.

Conflict of Interest

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Ethical Approval

The study was approved by the Clinical Research Ethics Committee of Bezmialem Vakif University (Approval number: 03/60) (Date:2021.02.16). The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

Author Contributions

Conception and design; Aİ, CE, Data acquisition; Aİ, CE, BD, MA, PY, Data analysis and interpretation; Aİ, CE, BD, MA, PY, GÇ, HA, Drafting the manuscript; Aİ, BD, MA, PY, GÇ, HA, Critical revision of the manuscript for scientific and factual content; Aİ, GÇ, HA, Statistical analysis; Aİ, CE, Supervision; HA.

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