ORIGINAL ARTICLE

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Frequency of Incidental Prostate Adenocarcinoma Detection in Patients with Radical Cystoprostatectomy for Bladder Urothelial Cancer and Research into the Need for PSA Monitoring for Local-systemic Recurrence

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Abstract

Objective: The incidental prostat adenocancer (PCa) detection rate in pathology material from radical cystoprostatectomy (RCP) has rates varying from 10% to 70% in the literature. Studies have blamed one of the causes for these different rates on the use of cross-section intervals with different widths during the investigation of prostate specimens. In this study was to research the incidental PCa frequency in patients undergoing operation and simultaneously to research the need for PSA follow-up in terms of local-systemic recurrence.

Methods: The pathologies of 115 patients undergoing RCP due to bladder cancer 2011 to 2017 were retrospectively investigated. A total of 26 patients,10 patients with pathology reported as non-urothelial cancer, 5 patients who were female and 11 patients who did not attend follow-up, were excluded. Eighty nine patients were included in the postoperative follow-up. Cystectomy materials were evaluated at 3 mm intervals, and prostate materials at 6 mm intervals. In addition to the evaluation of pathology results, PSA follow-up for at least 6 months was applied to all patients.

Results: In study, mean age calculated as 62.8±0.9 years. Concurrent prostate adenocarcinoma was detected in 18 (20.2%) patients. Preoperative PSA was calculated as 2.06±0.2 ng/mL. PSA follow-up was applied to all patients. PSA elevation was not observed in any patient with benign prostate pathology. PSA elevation was observed in the follow-up of the only patient in the ISUP 3 with PCa. Patients with benign and malignant prostate pathology were compared in terms of age, pre-operative PSA, bladder pathology and survey. No significant difference was found between the groups.

Conclusion: In patients whose prostate pathology was reported as benign, it was observed that there was no increase in PSA even if the cancer was missed. It was thought that these patients with clinically insignificant PCa did not affect the survey in these patients who already had morbidity in terms of bladder tumor.

Keywords: Prostate cancer, bladder cancer, radical cystoprostatectomy, PSA

INTRODUCTION

Prostate cancer (PCa) is in second place for cancer-linked deaths in men after lung cancer (1). The nearly half of PCa patients are asymptomatic. In spite of screening tests, a portion of patients continue their lives without diagnosis and may be diagnosed during postmortem biopsy and autopsy studies after death due to another cause completely (2). The incidental PCa detection rate in pathology material from radical cystoprostatectomy (RCP) operations due to bladder tumors has rates varying from 10% to

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70% in the literature (3,4). Studies have blamed one of the causes for these different rates on the use of cross-section intervals with different widths during investigation of prostate specimens (5). As the section intervals expand, PCa diagnosis may be missed. However, the effect of this missed incidental cancer on patient survival and quality of life is not fully known.

Most prostate pathologies identified by chance are small, localized, well-differentiated clinically insignificant tumors. Only 20% of all PCas is reported to be clinically significant (6).

The primary aim in this study was to research the incidental PCa frequency in patients undergoing RCP operation due to bladder urothelial cancer, and simultaneously to research the need for 3-month PSA follow-up in terms of local-systemic recurrence in the patients with PCa detected and/or not detected; in other words in the probable group with missed cancer diagnosis. The secondary aim was to report opinions about the survival and prognosis of patients.

METHODS

The pathologies of 115 patients undergoing RCP due to bladder cancer in our clinic from January 2011 to January 2017 were retrospectively investigated. A total of 26 patients, 10 patients with pathology reported as non-urothelial cancer, 5 patients who were female, and 11 patients who did not attend follow-up, were excluded from the study. Finally, a total of 89 patients undergoing RCP due to urothelial cancer was included in the postoperative follow-up. None of the patients had previous PCa diagnosis before the operation.

Preoperatively, digital rectal examination findings, PSA values and imaging methods were assessed. No patient had transrectal prostate biopsy performed before RCP. The prostate tissue was investigated at 6 mm section intervals. Patients with identified adenocarcinoma had the remaining prostate tissue included in follow-up and reviewed again. Bladder tumor pathologies were assessed according to TNM classification, while those with simultaneous PCa identified were assessed for volume, surgical margins, TNM classification and Gleason rating system according to ISUP classification.

Patients with postoperative incidental PCa identified were followed up with PSA at 3-month intervals, while other patients were followed at 6-month intervals.

Statistical Analysis

Care was taken to ensure that patients had at least two 6-month PSA checks. While making a descriptive statistical evaluation, categorical percentage (%) and frequency for variables; median minimum- for numeric variables maximum; and mean ± standard deviation values were used. Two variables Correlation analysis was used to determine the relationship between data. Groups with each other chi-square for categorical variables and Mann-Whitney U for numerical variables test was used. The study performed assessments retrospectively. The analysis of data used a statistical analysis program (SPSS, version 20.0). Statistical significance was set as $p<0.05$.

RESULTS

The study included 89 male patients with mean age calculated as 62.8±0.9 years. Patients were followed for mean 22.7 months (6-72). Urinary diversion method were orthotopic ileal pouch for 35 patients (39.3%), non-continent ileal conduit in 36 patients (40.4%) and ureterocutanostomy for 18 patients (20.2%).

When cystectomy specimens are investigated according to TNM classification, 13 patients were pT1 stage (14.6%), 18 patients were pT2 stage (20.2%), 26 patients were pT3 stage (29.2%), 20 patients were pT4 stage (22.5%), 7 patients were pTa stage (7.8%) and 5 patients were pT0 stage (5.6%). The results for cystoprostatectomy specimens identified simultaneous PCa in 18 patients (20.2%). When these 18 patients were investigated, according to ISUP classification, 15 patients were stage 1 (83.3%), 2 patients were stage 2 (11.1%) and 1 patient was stage 3 (5.6%). When all patients were considered, the mean preoperative PSA was calculated as 2.06±0.2 ng/mL (Table 1).

When the preoperative PSA values of incidental PCa patients are investigated, 3 patients were identified to have high PSA values according to age. Biopsy accompanied with transrectal ultrasound was not considered necessary for these patients as it would not change the final treatment decision. When these 18 patients were investigated, according to ISUP classification, 15 patients were stage 1 (83.3%), 2 patients were stage 2 (11.1%) and 1 patient was stage 3 (5.6%) (Table 2).

Patients with simultaneous PCa identified (n=18) and with benign prostate pathology (n=71) were divided into two groups and compared. There was an age difference between the two groups, but statistical significance was not observed (p=0.2). When preoperative PSA values were investigated in both groups, the group with adenocancer detected had values of 2.35 ng/mL, while the other group had values of 1.98 ng/mL. Again, there was a difference but it was not statistically significant (p=0.07). Similarly, group 1 and group 2 had similar features in terms of cystectomy pathologies, postoperative PSA follow-up results, simultaneous prostatic stromal invasion and survival (Table 3).

During 22-month follow-up of all patients, 37 patients died. Of these patients, only 8 had simultaneous PCa. When the causes of death of patients are investigated, none were observed to die due to prostate adenocancer. There was no statistical difference between the two groups in terms of disease-linked survival (56.6-59.2%) (p=0.6).

DISCUSSION

Globally PCa is ranked second among cancers seen in men (7). The incidence is increasing linked to the extension of mean human life expectancy and increased PSA screening. According to autopsy studies, a man of about 50 years of age has 30-50% risk of PCa, while this rate reaches 80% at the age of 80 (2).

Table 1. Patient characteristics (n=89)

Age	62.8±0.9
Preoperative PSA (ng/mL)	2.06±0.2
Incidental PCa	18/89 (20.2%)
Bladder tm. stage	
T0	5 (5.6%)
Ta	7 (7.8%)
T1	13 (14.6%)
T2	18 (20.2%)
T3	26 (29.2%)
T4	20 (22.5%)
PCa stage	
pT2a	12/18 (66.6%)
pT2c	6/18 (34.4%)
PCa ISUP	
STAGE 1 (Gleason 3+3)	15/18 (83.3%)
STAGE 2 (Gleason 3+4)	2/18 (11.1%)
STAGE 3 (Gleason 4+3)	1/18 (5.6%)

PCa: Prostate cancer

Table 2. Characteristics and histopathological findings of patients with prostate cancer detected (n=18)

PSA	Age	Gleason	PCa stage	Bladder tm stage
2.2	66	3+3	pT2a	pT1
3.3	80	3+3	pT2a	pT1
2.8	72	4+3	pT2c	pT4
2.4	77	3+3	pT2a	pT2
3.6	61	3+3	pT2a	pT1
1	60	3+3	pT2a	pT4
4.9	56	3+3	pT2c	pT3
5.9	68	3+4	pT2a	pT4
2	54	3+4	pT2c	pT3
1.6	59	3+3	pT2a	pT2
1.2	59	3+3	pT2a	pT3
1.4	71	3+3	pT2a	pT1
1.5	64	3+3	pT2c	pT4
0.6	49	3+3	pT2a	pT2
1.6	61	3+3	pT2a	pT2
0.5	66	3+3	pT2a	pT1
5.1	63	3+3	pT2c	pT3
2.9	75	3+3	pT2c	pT3

PCa: Prostate cancer

In studies investigating patients undergoing RCP due to invasive bladder cancer, the incidental PCa frequency was identified to be 10 to 70% (8-13). One of the reasons for different rates in these studies is the use of section intervals with different widths during the investigation of prostate specimens (5). Cystoprostatectomy material from 40 cases with prostate tissue sampled at 2-3 mm intervals identified PCa in 45% (14). Another series of 248 cases undergoing RCP found the incidental PCa rate was 4% in tissue samples investigated with sections at 5 mm intervals (15). The data show that as the section intervals grow larger, PCa diagnosis is missed. In our study, specimens were investigated at 6 mm intervals and the incidental PCa rate was found to be 20.2%.

When our study is compared with similar studies in the literature, mean age was younger and simultaneously PCa rates were relatively lower. Second, our clinically significant PCa rate was 16% and this was below the values in the literature (Table 4).

Androulakakis et al. (16) found the presence of PCa and bladder cancer together did not affect the prognosis for both diseases. It appears that patient prognosis is associated separately with the features of each tumor. Pritchett et al. (17) found no difference in terms of survival for patients with both cancers compared to those with only bladder cancer. Poor survival rates in most patients were associated with advanced stage bladder tumor when compared with patients with incidental PCa (18).

In our study, when patients with and without PCa identified are compared, prostate adenocancer did not affect patient survival with 100% cancer specific surveillance. There was no difference survival between the two groups. However, the low number of patients and lack of investigation of disease-specific survival prevent the discussion of this topic. According to these results, PCa accompanying bladder tumor appears not to affect the total survival of patients. The reason for this may be linked to the worse progression of bladder transitional epithelial cell carcinoma compared to PCa. In conclusion, the situation determining surveillance was determined to be the bladder tumor stage.

With the common use of PSA, a significant portion of the increasingly diagnosed PCas are in the clinically insignificant class. Treatment of a disease that will not cause death or other complications will involve unnecessary risks and complications.

The point we wish to draw attention to is that as the group with incidental PCa identified have high rates of clinically insignificant PCa, even if these patients are missed, surveillance

Table 3. Comparison of cases with comorbid prostate cancer (Group 1) and cases with only bladder tumor (Group 2) in cystoprostatectomy samples			
	Group 1 (n=18) %	**Group 2 (n=71) %**	**p value**
Age	65.1±2	62.2±1	0.2
Preop PSA ng/mL	2.35±0.3	1.98±0.2	0.07
Follow-up duration	25±4	22±1	0.9
Bladder tm stage T0 Ta T1 T2 T3 T4	 0 0% 0 0% 5 27.8% 4 22.2% 5 27.8% 4 22.8%	 4 5.6% 8 11.3% 8 11.3% 14 19.7% 21 29.6% 16 22.5%	0.23
Postop PSa mean	0.05	0.02	0.46
Stromal invasion	18/1 (5.6%)	71/14 (19.7%)	0.14
Exitus	8 (44.4%)	29 (40.8%)	0.6
Survival	10 (56.6%)	42 (59.2%)	

Table 4. Some radical cystoprostatectomy series outcomes in the literature						
Study	**Year**	**n**	**Age**	**PCa**	**Significant PCa**	**Section interval**
Pritchet	1988	165	64	45 (27%)	NA	NA
Abbas	1996	40	64	18 (45%)	NA	2-3
Revelo	2004	121	67	50 (41%)	24 (48%)	2-3
Delongchamps	2005	141	62	20 (14%)	14 (70%)	4
Nakagawa	2009	349	65	91 (26%)	68 (74%)	5
Gakis	2010	95	68	26 (27%)	7 (27%)	4-5
Aytac	2011	300	62	60 (20%)	40 (66%)	3-5
Alsinnawi	2012	110	66	35 (32%)	10 (28%)	4
Chang Cho	2013	96	66	39 (40%)	20 (51%)	4
Türk	2015	126	66	26 (20%)	8 (30%)	3
Fragkoulis	2016	64	69	22 (34%)	6 (27%)	4-5
Heidegger	2017	213	71	113 (50%)	59 (52%)	2-3
Our work	2017	89	62	18 (20%)	3 (16%)	6

will not change much. After all, these patients were operated and PCa that may emerge in the future was detected and treated while localized. Even if local or systemic recurrence foci are identified in these patients, it is considered to be low-grade PCa and surveillance will not change.

Study Limitations

Limitations of our study are that it was retrospective, had a short follow-up duration and pathologies were not assessed by the same specialist.

CONCLUSION

When literature data is investigated, in addition to differences like race and age, we see section intervals provide different results. When designing our study, we determined that different section intervals provided very different outcomes. Questions were asked whether this difference caused us to miss some cancers and whether these missed cancers were significant for the patient's clinical status and surveillance. In conclusion, it was not considered necessary to perform PSA follow-up in the group with benign incidental prostate pathology and clinically insignificant prostate cancer. It is considered that the surveillance of these patients should be determined by bladder cancer.

Ethics

Ethics Committee Approval: This study involving human participants was in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki

Declaration and its later amendments or comparable ethical standards. Institutional review board of İzmir Katip Çelebi University (date: 09.08.2017, number: 170) approved this study.

Informed Consent: Informed consents were obtained from all research participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.S.D., Y.Y., Y.A., S.Ö., Concept: A.S.D., Y.Y., Y.A., Design: A.S.D., Y.Y., Y.A., Data Collection or Processing: A.S.D., Analysis or Interpretation: A.S.D., O.K., S.Ö., Literature Search: A.S.D., O.K., Writing: A.S.D.

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