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Evaluation of incidental prostate cancer in patients who underwent radical cystectomy and its effect on survival

Radikal sistektomi uygulanan hastalarda insidental prostat kanserinin değerlendirilmesi ve sağkalım üzerindeki etkisi

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Abstract

Aim: Our study aimed to investigate the incidence of incidental prostate adenocarcinoma, its histopathological results and its effect on survival in patients who underwent radical cystectomy due to bladder tumor.

Materials and Methods: Patients who underwent radical cystectomy with a diagnosis of bladder tumor in our clinic in the last ten years and who had no preoperative suspicion or diagnosis of prostate cancer were included in the study. Patients were divided into two groups those with and without incidentally prostate cancer. Both groups were compared in terms of age, PSA value, histopathological features and overall survival.

Results: 15 (22.6%) of 79 patients who underwent radical cystectomy and were followed up for an average of 62 months were incidentally diagnosed with prostate adenocarcinoma. There was a significant difference between mean PSA value in patients with prostate cancer and the group without prostate cancer (p=0.004). When we evaluated it in terms of five-year overall survival, no significant difference was found between the two groups.

Conclusion: Although incidental prostate cancer does not seem to affect survival, it is necessary to follow up regularly in the presence of prostate cancer and be more careful, especially in the presence of locally advanced prostate cancer.

Keywords: Cystectomy, Survival; Incidental prostate adenocarcinoma; urotelial bladder carcinoma.

Öz

Amaç: Çalışmamızda mesane tümörü nedeniyle radikal sistektomi uygulanan hastalarda rastlantısal prostat adenokarsinomu görülme sıklığı, histopatolojik sonuçları ve sağ kalım üzerine etkisinin araştırılması amaçlandı.

Gereç ve Yöntem: Çalışmaya son 10 yıl içinde kliniğimizde mesane tümörü tanısıyla radikal sistektomi yapılan, ameliyat öncesi prostat kanseri şüphesi veya tanısı olmayan hastalar dahil edildi. Hastalar rastlantısal prostat kanseri saptanan ve saptanmayan grup olarak ikiye ayrıldı. Her iki grup yaş, PSA değeri, histopatolojik özellikler ve genel sağkalım açısından karşılaştırıldı.

Bulgular: Radikal sistektomi uygulanan ve ortalama 62 ay takip edilen 79 hastanın 15'ine (%22,6) insidental prostat adenokarsinomu tanısı konuldu. Prostat kanserli hastalar ile prostat kanseri olmayan grup arasında ortalama PSA değeri arasında anlamlı fark vardı (p=0,004). Beş yıllık genel sağkalım açısından değerlendirdiğimizde iki grup arasında anlamlı fark bulunamadı.

Sonuç: İnsidental prostat kanseri sağ kalımı etkilemiyor gibi görünse de prostat kanseri varlığında düzenli takip yapmak ve özellikle lokal ileri prostat kanseri varlığında daha dikkatli olmak gerekir.

Anahtar Kelimeler: Sistektomi; Sağkalım; Rastlantısal prostat adenokarsinomu; ürotelyal mesane karsinomu.

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Introduction

Prostate cancer is the most common cancer that causes death in men after lung cancer in the World.[1] The incidence of prostate cancer in the world is 30.6/100,000, and the incidence in Turkey is 10.9-28/100,000.[2] Bladder cancer is the ninth most common cancer worldwide and the seventh most common cancer in the male population, and there is male predominance in bladder cancer.[3] Bladder cancer and prostate cancer are genitourinary malignancies that cause serious morbidity and mortality.[4] Extended lymph node dissection along with radical cystectomy (RS) is the standard treatment for muscle-invasive bladder tumors. Some surgeons have preferred to preserve the prostate or prostate capsule apex during radical cystectomy, taking the risk of leaving cancer tissue behind, in order to avoid the urinary and sexual side effects of the operation, but as per the standard surgical procedure, all prostate tissue must be removed. The frequency of incidental prostate adenocarcinoma detected after RS varies in various series.[5] The majority of incidental prostate adenocarcinomas detected in patients undergoing RS are localized and clinically insignificant cancers.[6] In this study, the incidence, histopathological evaluation results and follow-up period of patients who underwent radical cystoprostatectomy due to bladder tumor and incidentally detected prostate adenocarcinoma were examined.

Materials and Methods

Type of the study

We planned our study as retrospective.

The sample size of the study

Patients who underwent radical cystectomy with a diagnosis of bladder tumor in our clinic between March 2013 and March 2023 and who had no preoperative suspicion or diagnosis of prostate cancer were included in the study. Patients who underwent radical cystoprostatectomy and bilateral extended pelvic lymphadenectomy were evaluated retrospectively. Patients who were histopathologically diagnosed with prostate cancer before RS, patients who underwent cystectomy for reasons other than bladder cancer, female patients were excluded from the study. Patients who received neo-adjuvant chemotherapy were also not included in our study because it would change the outcome of the article in terms of survival and affect the pathology results.

Data collection tools

Preoperative digital rectal examination (DRE), serum prostate specific antigen (PSA), chest radiography and whole abdomen imaging were performed on the patients to prove that there was no local or distant metastasis for the bladder tumor. Histopathological evaluation was performed by an experienced uropathologist. Serum PSA levels were checked in each patient every 3 months for prostate cancer follow-up in the postoperative period. Prostate cancer biochemical recurrence; It was defined as a PSA value >0.2 ng/mL measured at least twice. The patients were divided into two groups: those with incidental prostate cancer detection and those without detection. The two groups were assessed based on age, preoperative PSA value, bladder tumor stage, tumor grade, presence of concurrent carcinoma in situ, surgical margin positivity, lymph node involvement, and overall survival.

Data analysis

SPSS (IBM version 21, NY, USA) program was used in statistical analysis. Independent samples t-test was used for two-group comparisons of normally distributed quantitative variables, and Mann-Whitney U test was used for two-group comparisons of non-normally distributed quantitative variables. When comparing the tumor stages of the groups with and without prostate cancer, chi-square was performed by categorizing them. Pearson chi-square test and Fisher's exact probability test were used to compare qualitative data. Evaluation of overall survival was performed using Kaplan- Meier survival analysis. Statistical significance was accepted as $p<0.05$.

Ethics committee approval

The study protocol received scrutiny and approval from the Sivas Cumhuriyet University Clinical Research Ethics

Committee (decision no: 2023-07/02, date: 20.07.2023). Our study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent form were obtained from all patients.

Results

In the study, data of 102 patients who underwent radical cystectomy were examined. Of these patients, 9 were not included in the study because they had prostate cancer under follow-up, 8 because they received neo-adjuvant chemotherapy, 5 because metastasis was detected at the time of diagnosis, and 1 patient was female. Data from the remaining 79 patients were analyzed retrospectively. Inclusion in the study was indicated in the flow chart (Figure 1).

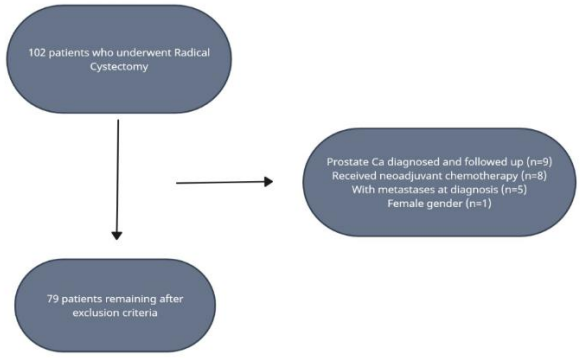

Figure 1. Study inclusion flow chart.

The remaining 79 patients after exclusion criteria were followed for an average of 62 months (4-148 months). 15 (22.6%) of the 79 patients included in the study were diagnosed with incidentally prostate adenocarcinoma. Demographic characteristics and histopathological findings of both groups are presented in Table 1. The average age of the patients with prostate cancer was 63.0±1.5, the group without prostate cancer was 65.1±1.4, there was no significant difference between the groups (p=0.312). In DRE performed on patients diagnosed with prostate cancer, it was determined that all patients had benign findings. The mean preoperative PSA value in patients with prostate cancer was 4.75 ng/ml, and the mean PSA value in the group without prostate cancer was 2.67 ng/ml (p=0.004). There was a significant difference between the groups (Table1).

In the histopathological examination of cysto-prostatectomy specimens of patients with prostate cancer, organ-confined tumor (≤ pT2) was detected in 8 (53.4%) patients, advanced stage (≥pT3) urothelial carcinoma was detected in 7 patients (46.6%), and there was no patient with no urothelial carcinoma detected and evaluated as T0. When we evaluated in terms of surgical margin positivity, surgical margin positivity was detected in 3 (20%) patients in the group with prostate cancer and in 11 (17.2%) patients in the group without prostate cancer (p=0.52). When evaluated in terms of lymph node metastasis, lymph node positivity was detected in 4 (26.7%) patients in the group with prostate cancer detected and in 16 (25%) patients in the group without prostate cancer, and this rate was similar between both groups (p=0.56) (Table 1).

The predominant histological stage for prostate cancer was observed to be T2 (46.7%). When patients with incidental prostate cancer were evaluated, 6 (40%) patients were found to have clinically significant prostate cancer (ISUP≥2), and when we analyzed these patients, the number of patients with Gleason score ≥ 7 was 6 (40%). There were no patients locally advanced stage (≥pT3a) (table 2). The average follow-up period in patients diagnosed with prostate cancer was 47 months (3-74) and biochemical recurrence was detected in 3 patients during this follow-up period. Pelvic radiotherapy was applied to two patients with biochemical recurrence, and one patient received hormonotherapy. No death was observed in any patient due to prostate adenocarcinoma, but in the group without prostate cancer, death occurred in 8 (12.5%) patients due to bladder tumor during an average follow-up period of 65 months (3-84).

Upon analyzing the five-year overall survival, we observed that patients with prostate cancer had an overall survival rate of 84%, while those without prostate cancer had a rate of 87.4%. The statistical analysis revealed no significant difference between the two groups, with a p-value of 0.691.

Table 1. Statistical comparison of patient groups.

	Prostate Cancer (+)	Prostate Cancer (-)	*p*
N	15 (23.4%)	64 (76.6%)	-
Age (years)	63.0 ± 1.5	65.1 ± 1.4	0.312
PSA (ng/ml)	4.75 ± 1.05	2.67 ± 0.29	0.004
Follow-up (month)	47.8 ± 8.6	65.3 ± 5.0	0.220
Bladder tm Stage			
pTa	1(6.7%)	3(4.7%)	0.767
pT1	0	8(12.5%)	
pT2	7(46.7%)	23(35.9%)	
pT3	4(26.7%)	18(28.1%)	
pT4	3(20%)	12(18.7%)	
CIS			
No	15	63	0.810
Yes	0	1	
Surgical Margin Positivity			
No	12	53	0.520
Yes	3	11	
Lymph Node Involvement			
No	11	48	0.560
Yes	4	16	
Metastasis			
No	13	59	0.390
Yes	2	5	
Ex	2 (13.3%)	8 (12.5%)	0.680

CIS: Carcinoma in situ.

Table 2. Pathological results and follow-up of prostate cancer patients.

Age	Bladder tm Stage	Psa	Surgical margin	Lymph node	Metastasis	Prostate Ca Stage	Gleason	ISUP	Follw-up	Ex
62	T2b	9.24	-	-	-	T2a	3+3	1	118	-
64	T4a	14.21	+	-	Lung	T2c	5+4	5	6	+
73	T3a	3.37	-	+	-	T2a	3+3	1	52	-
60	T4a	1.65	-	-	-	T2a	3+3	1	28	-
66	T3a	4.78	-	-	-	T2b	3+4	2	50	-
58	T3a	2.12	+	+	Lung	T2a	3+3	1	108	-
68	T2a	2.59	-	-	-	T2a	3+3	1	65	-
64	T2a	6.3	-	-	-	T2a	3+3	1	44	-
58	T2b	4.52	-	-	-	T2a	3+3	1	36	-
69	T4a	11.76	+	+	-	T2a	4+4	4	13	+
63	T2b	6.08	-	+	-	T2a	3+3	1	70	-
71	T3a	11.23	-	-	-	T2c	3+4	2	56	-
64	T2a	3.12	-	-	-	T2b	3+4	2	15	-
54	T2a	0.537	-	-	-	T2a	3+3	1	6	-
51	Ta	4.77	-	-	-	T2c	3+4	2	50	-

Discussion

The detection rates of simultaneous prostate cancer in patients who underwent radical cystectomy are seen between 4% and 61% in various series.[7-12] In our study, prostate cancer was detected in 15 (23.4%) of 79 male patients who underwent RS. On the other hand, rates reaching 60% have been reported in some studies.[13] The reason for this difference in prevalence may be epidemiological and racial differences in studies and differences in evaluation of pathology specimens. There are studies in the literature demonstrating that advanced age is an important independent marker in detecting prostate cancer concurrent with radical cystectomy.[11,13,14] Bladder cancer and prostate cancer reach their highest incidence rate over the age of 70.[15] Similarly, Bell et al. reported in an autopsy series that the incidence of prostate cancer increased with age.[16] Contrary to the literature, in our study,

the age of the group with incidental prostate cancer was found to be lower, and there was no significant difference between the group with and without prostate cancer. In their large-scale study, Fahmy et al. found that while advanced age was associated with the incidence of incidental prostate cancer, there was no age difference between clinically significant or clinically insignificant prostate cancer subgroups.[9] In our study, when the histopathological results of bladder cancer were evaluated between the groups with and without prostate cancer, no difference was detected in terms of tumor stage, presence of carcinoma in situ, lymph node metastasis and surgical margin positivity.

Although some previous studies on incidental prostate cancer stated that PSA could not be used as a predictor of prostate cancer, in our study, the PSA value was found to be statistically significantly higher in the prostate cancer group.[14] The clinical importance of PSA values should not be ignored in the preoperative evaluation of patients.

It was observed that the 3 patients with biochemical recurrence had high Gleason scores and/or locally advanced stage (pT3a) prostate cancer. In our study, no death due to prostate cancer was observed in any patient with biochemical recurrence. In their study, Pignot et al. observed biochemical recurrence in only 16 (1.9%) of the 931 incidental prostate cancer patients. Furthermore, no prostate cancer-related death was observed in any patient during the average follow-up period of 23 months.[15]

In patients with localized prostate cancer, the 5-year prostate cancer-specific survival after surgery is 100% and the 10-year survival rate is 99%.[16] Even in patients with pT3b disease who underwent radical prostatectomy, disease-related death may not occur within 6 years.[17] With these results, much longer follow-up periods will be required for incidental prostate adenocarcinoma in radical cystectomy to have a negative impact on cancer-related and overall survival. For muscle-invasive bladder cancer, the 5-year cancer-related survival rate is 55% in patients who undergo radical cystectomy without neoadjuvant chemotherapy. Recurrence may develop in these patients after a median follow-up of 12.5 months.[17] Cancer-related death rates in the older age group are lower than age and comorbidities-related death rates. If the prognosis is to be determined after cancer diagnosis in this age group, age and comorbidities should be taken into consideration as major causes of deat.

There are studies in the literature reporting that incidental prostate cancer has no effect on overall and cancer-related survival.[20,21] In contrast, Heidegger et al. observed that six of the 15 patients who developed biochemical recurrence died as a result of prostate cancer within a relatively short period, ranging from nine months to four years.[10] In a large series study, Fahmy et al. observed that the group with incidental prostate cancer had a relatively low 5-year overall survival rate (p=0.03).[9] In our study, the presence of prostate cancer did not have a negative effect on overall survival. Despite tumor aggressiveness remains high as age and tumor stage increases, these inconsistencies in studies indicate the need for prospective studies with larger and standardized study groups.

When we search in Urology literature in Turkey, we come across 8 articles on this subject. In these studies; The incidence of incidental prostate cancer in patients being treated RS has been reported to be between 9% and 30.2%.[19-26] When our study is compared to other studies, it is seen that there is an acceptable number of patients, a longer follow-up period, and a longer-term survival analysis (Table 3).

Previous multicenter studies have shown that the majority of prostate cancer accompanying bladder cancer is organ-confined (≤pT2) and non-aggressive, well-differentiated prostate cancer. The probability of developing non-aggressive prostate cancer has been found to be higher, especially in young age group men (under 60 and 70 years of age). For such reasons, it has been stated in studies that accompanying prostate cancer has no effect on the patient's survival.[18] The decrease in survival rates due to incidental prostate cancer may not be seen in the short-term follow-up due to reasons such as shorter

survival due to the pathological stage of bladder cancer, rapid recurrence, and older age of patients. However, the presence of locally advanced prostate cancer requires regular follow-up after surgery. The shortcomings of the study are that it has a retrospective evaluation and that the follow-up period is relatively short in terms of prostate cancer follow-up.

Table 3. Data from studies conducted on this subject.

Outhor	n	Follow-up (month)	Prostate Cancer(+). n (%)	Mean Age		Mean PSA ng/ml	
				Prostate Cancer (+)	Prostate Cancer (-)	Prostate Cancer (+)	Prostate Cancer (-)
Türk et al.[19] 2015	126	20	26 (20.6%)	67.1	65.8	4.2	3.9
Ceylan et al.[20] 2016	119	27.1	16 (13.4%)	62.3	-	2.13	-
Uğurlu et al.[21] 2010	149	22.8	14 (9.3%)	64.2	57.7	3.26	-
Sarı et al.[22] 2007	178	-	16 (9%)	-	-	-	-
Hızlı et al.[23] 2005	50	-	5 (10%)	70.2	62	-	-
Başpınar et al.[24] 2013	59	-	9 (15.3%)	71	65	-	-
Turan et al.[25] 2018	190	33	43 (22.6%)	70	63.7	5.38	2.72
Özer et al.[26] 2020	197	-	51 (30.2%)	62.9	66.4	3.5	2.6
Our Study	102	62	15 (23.4%)	63.0	65.1	5.75	2.67

Study limitation

The main limitation of our study is the small number of patients participating in the study. This can be explained by the fact that recent surgeries could not be included in the study in order to establish a 5-year follow-up rate. Although not specifying tumor volumes represents a classification in terms of survival, its absence in our study is among the limitations of the study.

Conclusion

As a result, it is common to detect prostate cancer in patients who underwent radical cystoprostatectomy, and in our study, this rate was found to be 23.4% and was consistent with the literature. Therefore, the pathologies of patients who underwent radical cystoprostatectomy should be evaluated carefully and in detail. Although prostate adenocarcinoma is limited to the organ in most patients, it is also important to follow up the patients in terms of this disease.

Ethics Committee Approval

The study protocol received scrutiny and approval from the Sivas Cumhuriyet University Clinical Research Ethics Committee (decision no: 2023-07/02, date: 20.07.2023). Our study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent form were obtained from all patients.

Informed Consent

All participants provided informed consent upon enrollment.

Authors Contrubituons

A.Ö.: Idea/Concept, Design, Audit/Consultancy, Materials, Data collectıon and/or processing, Analysis and/or comment, Literature review, Writing, Critical review. İ.E.E.: Idea/Concept, Design, Audit/Consultancy, Resources, Analysis and/or comment, Literature review, Writing. H.S.: Idea/Concept, Design, Audit/Consultancy, Resources, Materials, Data collectıon and/or processing, Critical review. A.A.: Idea/Concept, Design, Audit/Consultancy, Resources, Materials, Data collectıon and/or processing, Critical review.

Conflict of Interests

There is no conflict of interest to declare.

Financial Disclosure

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Statements

These research results have yet to be presented anywhere previously. Data related to the study is available on request.

Peer-review

Externally peer-reviewed.

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