Prediction of Prostatic Involvement by Transitional Cell Carcinoma of the Bladder Using Pathologic Characteristics of the Bladder Tumor

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Introduction: The aim of this prospective study is to determine the relationship between the pathologic characteristics of the transitional cell carcinoma (TCC) of the bladder and prostatic involvement.

Materials and Methods: Sixty men with bladder TCC underwent standard radical cystoprostatectomy and were enrolled in this study. Vascular and perineural invasion, maximum diameter of the tumor, presence of carcinoma in situ, distance between the tumor and the bladder neck, and grade and local stage of the tumor were recorded and their relation with prostatic involvement was studied. In addition, hydronephrosis and age of the patients were included in the analysis.

Results: The mean age of the patients was 63.9 ± 11.1 years. Of 60 men included in this study, 15 patients were found to have prostatic involvement with TCC (25%). Univariate statistical analyses showed that vascular invasion and the distance between the tumor and the bladder neck were significantly related to the prostatic involvement ($P = .007$; $P < .001$). But, in the logistic regression, only the distance between the tumor and the bladder neck was significantly related to the prostatic involvement ($P = .001$).

Conclusion: This study suggests that the probability of prostatic involvement in patients with bladder TCC tumors near the bladder neck is high. Prostate-sparing or capsule-sparing cystectomy should be avoided in such patients.

Keywords: bladder, transitional cell carcinoma, prostate, prostate-sparing cystectomy

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INTRODUCTION

Transitional cell carcinoma (TCC) extending to the prostate was first reported in 1952 by Melicow and Hollowell who described carcinoma in situ (CIS) of the prostate coexistent with TCC of the bladder as the Bowen's disease.[1,2] A close relation between TCC of the prostate and TCC of the bladder has been suggested.[3] Prostatic TCC involvement has been reported in 7% to 48% of the patients undergoing radical cystoprostatectomy.[4,5] Radical cystoprostatectomy remains the standard treatment of high-risk, superficial, recurrent, muscle-invasive bladder cancer. However, it can be associated with substantial morbidity.[6] Some investigators have advocated prostate-sparing radical cystectomy. This approach obviates dissection distal to the bladder neck, leaving the neurovascular bundles and the sphincter entirely undisturbed. It has been associated with excellent functional results after neobladder reconstruction.[7,8] The vas deferens can also be spared, allowing preservation of fertility.[8] It has been

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shown that nerve-sparing modifications does not compromise the control of the cancer.[9,10] Finally, a new method of prostate capsule-sparing has also been described with similar results.[11] However, these approaches have raised the concern that the prostatic involvement may be neglected and we have to predict if cystoprostatectomy is required. In this study, we decided to find the relationship between different microscopic and macroscopic features of the TCC of the bladder and the risk of the prostatic involvement.

MATERIALS AND METHODS

Between January 2003 and November 2005, this prospective study was performed in Shaheed Labbafinejad Medical Center. The study was approved by the institutional review board of the Urology and Nephrology Research Center affiliated with Shaheed Beheshti University of Medical Sciences. All patients with proven bladder TCC who were candidates for radical cystectomy were included in this study. Patients with a history of previous surgery on the bladder or prostate, systemic chemotherapy, and prior pelvic or lower abdominal radiotherapy were excluded. Sixty patients met these criteria and entered the study. They underwent standard radical cystoprostatectomy with en bloc excision of the bladder, prostate, and seminal vesicles. On pathologic examination, mapping (macroscopic features) and microscopic characteristics of the bladder tumors were determined by a single pathologist. Characteristics of the tumors including the number of the tumors (single or multiple), maximum diameter of the tumors in centimeter, distance of the tumors from prostatovesical junction (TD), existence of CIS, tumor grade (low or high), local stage (superficial, T2, T3, and T4), and vascular and perineural invasion were also recorded. Involvement of the prostate by TCC was assessed by the same pathologist, as well. In addition, hydronephrosis was assessed by preoperative ultrasonography or CT scan and was included in the analyses.

Statistical analyses were performed by SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Ill, USA). We evaluated the relationship between each single factor and the prostatic involvement using the chi-square test. The differences in age and TD between the patients with and without prostatic involvement were analyzed by the Student *t* test and Kolmogorov-Smirnov test. All factors with a significant effect were analyzed using logistic regression (backward Wald method) afterwards. The receiver operating characteristic (ROC) curve was used to select a cutoff point with the best diagnostic accuracy for continuous variables.

RESULTS

The mean age of the patients was 63.9 ± 11.1 years at the time of surgical operation. Of 60 men enrolled in this study, 15 (25%) had TCC in their prostates (Table 1). Of 15 patients with prostatic involvement, 6 (40%) had TCC in the urethra, 6 (40%) in the stroma, and 3 (20%) in both. The characteristics of the patients and the tumors in the 2 groups of prostatic involvement positives and prostatic involvement negatives are shown in Table 2. Univariate analysis demonstrated that from the 9 factors assessed, only vascular invasion ($P = .007$; odds ratio, 5.28; 95% confidence interval, 1.48 to 18.82) and TD ($P = .007$; 95% confidence interval, 0.74 to 1.91) had significant relationships with the prostatic involvement. The results for age and TD which had been analyzed by the Student *t* test were confirmed by Kolmogorov-Smirnov test. In the second step, vascular invasion and TD in addition to multifocality of the bladder tumor were entered in the logistic regression model. We first calculated multifocality in association with the other 2 factors because of its relatively low *P* value and the fact that it had been found to be a significant factor in some previous studies.[8,12] The logistic regression analysis showed that only TD had a significant relation with the involvement of prostate by TCC ($P = .001$). The ROC curve showed high sensitivity and specificity (area under the curve, 0.92) and the odds ratio for TD was 0.021 (95% confidence interval, 0.002 to 0.219), but due to the

Table 1. Prostatic Involvement in Patients with Bladder Cancer*

Tumors in Patients	Number (%)
Evaluated cases	60
Number of involved prostates	20 (32)
Adenocarcinoma	5 (7)
TCC	15 (25)
TCC in urethra	6 (40)
TCC in stroma	6 (40)
TCC in both	3 (20)

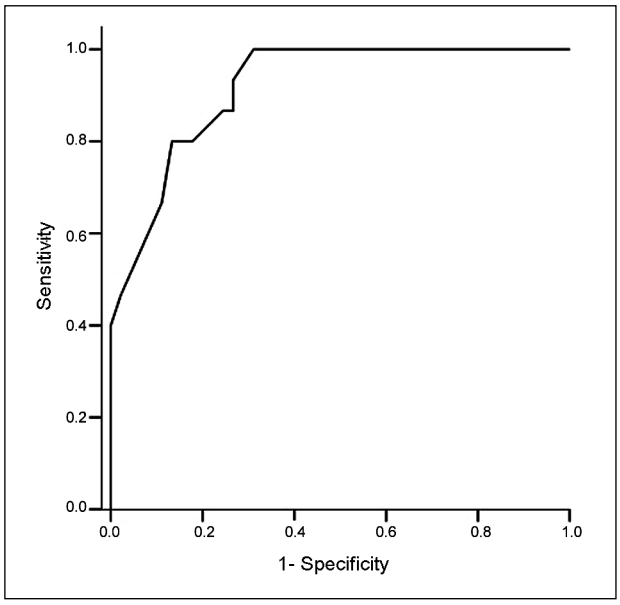
*TCC indicates transitional cell carcinoma.

Table 2. Characteristics of Patients and Bladder TCC in Relation to Involvement of Prostate*

Factors	Prostatic Involvement†		*P*	Odds Ratio	95% CI
	Positive	Negative			
Age, mean, y	63.2 ± 12.4	64.2 ± 10.8	.79	…	-8.37 to 6.46
TD, mean, cm	0.46 ± 0.35	1.79 ± 1.10	< .001	…	0.74 to 1.91
Tumor stage					
noninvasive	15 (88.2)	2 (11.8)	.37	…	…
T2	20 (71.4)	8 (28.6)			
T3	8 (72.7)	3 (27.3)			
T4	2 (50)	2 (50)			
CIS	16 (73)	6 (27)	.76	1.21	0.36 to 4.01
Present					
Vascular Invasion	8 (50)	8 (50)	.007	5.29	1.48 to 18.82
Perineural Invasion	7 (64)	4 (36)	.34	1.97	0.48 to 8.00
Multifocal disease	21 (66)	11 (34)	.07	3.14	0.87 to 11.36
High grade disease	23 (72)	9 (28)	.55	1.44	0.44 to 4.70
Hydronephrosis	17 (77)	5 (23)	.76	0.82	0.24 to 2.82
Tumor diameter ≥ 2 cm	38 (76)	12 (24)	.69	0.74	0.16 to 3.30

*TCC indicates transitional cell carcinoma; CI, confidence interval; TD, tumor distance from bladder neck; and CIS, carcinoma in situ.
†Values in parentheses are percents.

limited number of patients, we did not specify the cutoff value for TD (Figure).



Receiver operating characteristic curve shows the sensitivity and 1 - specificity of the tumor distance from the bladder neck for the prostatic involvement by transitional cell carcinoma

DISCUSSION

The incidence of primary TCC of the prostate is thought to be 1% to 4% of all prostate malignancies.[13,14] Involvement of the prostate with bladder TCC is more common (7% to 43%).[4]

Spitz and colleagues performed prostate-sparing radical cystectomy on 4 patients for the first time,[15]

Vallancien and coworkers treated a larger series of men with bladder TCC using this method.[16] They used digital rectal examination, serum prostate specific antigen, and transrectal ultrasonography of the prostate for preoperative evaluation of the patients. If each of these factors was abnormal, they performed prostatic biopsy, and if carcinoma was found, prostate-sparing operation was abandoned. Their study lacked evaluation of potential factors that may predict the involvement of the prostate by TCC.

We designed this prospective study to determine the factors that might influence prostatic involvement. The parameters we considered were vascular invasion, perineural invasion, multifocality, size, grade, local stage, tumor distance from the bladder neck, CIS, age, and hydronephrosis. The incidence of prostatic TCC involvement was 25%; similar to the results reported

in other studies (27% to 30%).[2,12] In multivariate analysis, only TD was shown to be an influential factor on the involvement of the prostate. Kefer and colleagues reported a retrospective study on the pathologic specimens of 70 men who had undergone radical cystoprostatectomy for bladder TCC.[8] They demonstrated that the existence of CIS, multifocality of the tumor, and involvement of the bladder neck influence the involvement of the prostate by TCC. In 2003, Liedberg and colleagues reported 2 factors related to the prostatic involvement in patients with TCC of the bladder: the existence of TCC or CIS in the bladder neck and multifocality of the bladder tumor.[12] As seen, multifocality of the tumor was a significant factor in both previous studies. Although this variable was not significantly related to the prostatic involvement in our study, its *P* value was reported to be .07 indicating that if assessed in a larger sample of patients, it might be more significant. Kefer and colleagues described the CIS related to prostatic involvement, but Liedberg and colleagues reported CIS to be significant only when it was present in the bladder neck. Our results did not show this relationship, either.

Finally, the only factor that is shown to be related with TCC involvement of the prostate in all reports is the presence or absence of the tumor in the bladder neck. This factor was described as the distance of the tumor from the bladder neck in our study, which was shown to be closely related to the prostatic involvement. We determined a cutoff point of 0.55 cm for this factor; however, the clinical use of such a parameter requires larger studies.

CONCLUSION

The distance of bladder tumor from the bladder neck has a potent relationship with the prostatic TCC involvement in patients with TCC of the bladder. Also, multifocality of the bladder tumor may increase the probability of prostatic involvement. Thus, it seems reasonable to avoid prostate-sparing or capsule-sparing cystectomy in patients with bladder tumors very close to the bladder neck and in those with multifocal tumors.

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CONFLICT OF INTEREST

None declared.

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