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Post-void residual urine volume: Potential recurrence risk factor for bladder cancer among the smoking male patients

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ABSTRACT

Aromatic amines and polycyclic aromatic hydrocarbons are chemical carcinogens that stimulate urothelial cell dysplasia and result in bladder cancer. Bladder outlet obstruction due to BPH may increase the contact time of any potential carcinogens in the urine to the bladder urothelium. We aimed to compare the post-void residual (PVR) urine volume between recurrent and nonrecurrent non-muscle invasive bladder cancer (NMIBC) patients with concomitant lower urinary tract symptoms (LUTS).

A total of 480 patients with NMIBC were operated at our institution between May 2014 and May 2018. Of these patients, 93 men with concomitant LUTS were identified. After excluding 40 men who quitted smoking, 53 smoker men were included in study. Patient age, smoking habits, grade and stage of tumor, risk group of the tumor were recorded along with presence of recurrence. PVR urine volume was compared between patients with recurrent and nonrecurrent NMIBC.

The mean age was similar between patients with recurrent (n=17) and nonrecurrent (n=36) NMIBC ($p = 0.475$). The amount of smoking (pack year) was not different between the two groups ($p = 0.407$). The grade and stage of tumors were also statistically insignificant in both groups. Mean PVR urine volume was higher in patients with recurrent (88 mL) compared to nonrecurrent(62 mL) group. However, these results were not statistically significant ($p = 0.548$).

We believe that the lower PVR urine volume, the lower risk for bladder cancer recurrence, although we couldn't prove this hypothesis statistically. Further clinical studies are needed to confirm the relationship between those.

Key Words: Bladder Cancer, Lower Urinary Tract Symptoms, Post-Void Residual Urine, Recurrence, Risk Factor, Smoking

Introduction

Bladder cancer is the most frequent malignancy of the urinary tract with an average standardized mortality rate of 3.2 /100,000 for men and 0.9 /100,000 for women (1). It is the sixth most commonly diagnosed cancer with 4% of cancer death rate in the United States and even the third most common cause of cancer in male population in Turkey (2, 3).

Several studies have reported the association between smoking and bladder cancer (4-7). In addition, smoking cessation has been shown to reduce the incidence of bladder cancer in 61% and 26% of males and females, respectively (5). Besides smoking, several carcinogens (e.g., aromatic amines, polycyclic aromatic hydrocarbons, and arsenic) are found to increase the risk of bladder cancer (8).

Lower urinary tract symptoms (LUTS) are a group of complaints among people, which can be defined as abnormal voiding sensations that occur with a frequency or severity affecting the quality of life (9). Approximately 15%–60% of men aged >40 years reported having LUTS, which are traditionally attributed to bladder outlet obstruction due to benign prostatic hyperplasia (BPH) (10,11). An enlarged prostate may block the urine flow during voiding and cause a substantial amount of post-void residual (PVR) urine retained in the bladder after urination. This may increase the contact time of potential carcinogens existing in the urine, which may stimulate urothelial cell dysplasia and results in bladder cancer (12). A recent study has demonstrated an association between LUTS (particularly urinary hesitancy) and development of bladder cancer in men (12).

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Table 1. The characteristics of patients with recurrent and nonrecurrent NMIBC

		Recurrence (−)		Recurrence (+)		p
Age (year)		66.69 ± 9.72		68.65 ± 8.05		0.475
Mean cigarette consumption (pack year)		33.39 ± 30.21		26.59 ± 20.96		0.407
Risk category	Low	n(3)	8.33%	n(1)	5.88%	0.951
	Intermediate	n(2)	5.56%	n(1)	5.88%	
	High	n(31)	86.11%	n(15)	88.24%	
Tumor grade	Low Grade	n(25)	69.44%	n(10)	58.82%	0.446
	High Grade	n(11)	30.56%	n(7)	41.18%	
Tumor stage	T1	n(29)	80.56%	n(13)	76.47%	0.732
	Ta	n(7)	19.44%	n(4)	23.53%	
Tumor number		2.27 ± 2.03		2.47 ± 2.39		0.396
Tumor size (cm)		3.35 ± 1.72		4.47 ± 2.03		0.057
PVR (mL)		62.78 ± 50.53		88.47 ± 77.07		0.548

The aim of this study was to compare the PVR urine volume between recurrent and nonrecurrent non-muscle invasive bladder cancer (NMIBC) among male smoker patients with concomitant LUTS.

Materials and Methods

Study Population and Design: After obtaining approval of the Institutional Review Board of a Training and Research Hospital, our patient database was retrospectively analyzed. Records of 480 patients with NMIBC who were diagnosed and operated at our institution, between Nov 2014 and May 2018, were reviewed. Of these patients, 93 men with concomitant LUTS were identified. There was no female NMIBC patient with concomitant LUTS. After excluding 40 men who did not smoke, 53 smoker men were finally included in the study. Patient age, smoking habits, grade and stage of tumor, risk group of the tumor were recorded along with the presence of recurrence. Classification of tumor stage and tumor grade was determined by using the 2009 TNM classification (8th Edn.), which was updated in 2017 (13) and 2004 WHO grading system, respectively (14). Risk group stratification was categorised according to the 2018 European Association of Urology (EAU) Guidelines (15). PVR urine volume was measured with the BladderScan BVI 9400 (Verathon, Bothell, WA) immediately after voiding and compared between patients with recurrent and nonrecurrent NMIBC.

Statistical Analysis: Statistical analyses were performed using Number Cruncher Statistical System 2007 statistical software package program (NCSS, LLC, Kaysville, UT, USA). In addition to descriptive statistics (mean, standard deviation), independent t-test and Mann–Whitney U test were used for the comparison of variables. Statistical significance level was set as $p < 0.05$.

Results

Characteristics of the patients included in this study are demonstrated in (Table 1).

The mean age was similar between patients with nonrecurrent and recurrent NMIBC (66.7 ± 9.7 vs. 68.7 ± 8.1 years, $p = 0.475$), and the amount of smoking (pack year) was not different between the two groups (33.4 ± 30.2 vs. 26.6 ± 20.0, $p = 0.407$). The grade, stage, number, and size of the tumor were not statistically different between these two groups.

The mean PVR urine volume was higher in patients with recurrent compared with the nonrecurrent group as 88 mL and 62 mL, respectively. However, this difference was not statistically significant ($p = 0.548$).

Discussion

To the best of our knowledge, the association between bladder cancer risk and LUTS has been evaluated only by Zhou et al (12). Using data from the Health Professionals Follow-up Study, the authors demonstrated that LUTS (particularly urinary hesitancy) are associated with the development of bladder cancer in 30,183 men who were followed up during 1996–2010. They reported that LUTS might be utilized as a parameter to identify men with an increased risk of bladder cancer (12). The authors also indicated that the high intravesical pressure caused by urinary hesitancy in the beginning of voiding may further increase the penetration of chemicals into the urothelium and results in higher bladder cancer rates. Moreover, they suggested that urinary hesitancy may indicate higher volume of PVR urine, which can also

increase the contact time of potential carcinogens in the urine. However, they did not assess the impact of PVR urine volume on the development of bladder cancer.

Another component of LUTS is nocturia that is defined as a complaint which the individual has to wake up at night one or more times to void (16). The findings of a recent study showed that patients who urinated more than twice per night had a 40%–50% reduction in bladder cancer risk compared to those who did not urinate at night (17). However, further studies are warranted to confirm whether increased frequency of night urination is related to a reduced risk of bladder cancer.

In this study, we found higher PVR urine volume in patients with recurrent NMIBC than that in patients with nonrecurrent NMIBC. Although this difference was not statistically significant, patients with NMIBC with higher PVR urine volumes may have higher recurrence rates due to increased exposure of chemical carcinogens existing in the urine of smoker patients. Other several studies have suggested that increased water intake (18) and alcohol consumption (beer and wine) (19, 20), which eliminate carcinogens from the bladder, may be associated with a slight reduction in bladder cancer. Considering the findings of these studies, patients with NMIBC who have significant amount of PVR urine may be advised to increase their daily water intake until the treatment of LUTS.

This study is not without limitations. First of all, the low number of patients, which may result in failure to detect a statistically significant difference in PVR urine volume between patients with recurrent and nonrecurrent NMIBC, may raise concerns regarding the reliability of our findings. However, we believe that increasing the sample size may confirm whether patients with NMIBC with higher PVR urine volume have an increased risk for bladder cancer recurrence. Not administering the International Prostate Symptom Score (IPSS) questionnaire and not measuring the uroflowmetric parameters may be considered as other limitations of the study. It is also a well-known fact that intravesical chemotherapy after transurethral resection of bladder tumor reduces recurrence of NMIBC (21), but instillation of chemotherapy and/or immunotherapy and the type and duration of those were not recorded in our study. Future trials may incorporate these assessments into their analyses, which may also have an association with the recurrence rates.

In conclusion, patients with recurrent NMIBC had higher PVR urine volume than that of patients with nonrecurrent NMIBC in our study, but the difference was statistically insignificant. We think that medical and/or surgical treatment of LUTS in male patients with NMIBC should not be postponed, and a minimum PVR urine volume must be maintained so as to decrease the risk of recurrence. Further clinical studies with larger patient population are needed to confirm the relationship between PVR urine volume and bladder cancer recurrence.

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