

## Factors affecting presence of detrusor muscle tissue in pathology specimen of transurethral bladder tumor resection

Transüretral mesane tümörü rezeksiyonu patoloji örneğinde detrusor kas dokusunun varlığını etkileyen faktörler

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### ÖZET

**Amaç:** Mesane tümörü patolojik incelemesinde detrusor kas dokusunun (DKD) ortaya konulması doğru evreleme ve transüretral mesane tümörü rezeksiyonu (TUR-MT) sonrası tedavi planlanmasında oldukça önem arz eder. Bu çalışmada TUR-MT sonrası patoloji spesmeninde DKD örneklenmesine etki eden faktörleri belirlemeyi amaçladık.

**Gereç ve Yöntemler:** Kliniğimizde primer mesane tümörü nedeniyle TUR-MT yapılan ve ameliyat notunda tümörün lokalizasyonunun işaretlendiği mesane diyagramı kullanılan 59 hastanın dosyaları retrospektif olarak incelendi. Patoloji spesmeninde DKD izlenmeyen 26 hasta grup I, DKD izlenen 33 hasta grup II olarak isimlendirildi. Gruplar arasında yaş, cinsiyet, tümör sayısı, tümör boyutu ve tümör lokalizasyonu açısından fark olup olmadığı incelendi.

**Bulgular:** Çalışmamızda DKD izlenme oranı %56 olarak tespit edildi. Hastaların yaş ortalamaları grup I' de  $69.5 \pm 10.2$  iken grup II' de  $68.7 \pm 9.2$  idi ( $p=0.755$ ). İki grup arasında cinsiyet dağılımı açısından istatistiksel olarak anlamlı fark saptanmadı ( $p=0.646$ ). Tümör lokalizasyonuna baktığımızda grup I de tümörlerin %11.5'i kubbeye, %11.5'i karşı duvarda ve %77' si yan duvarlarda; grup 2' de ise %6.1'i kubbeye, %27.2' si karşı duvarda ve %66.7' si de yan duvarlarda izlendi. Grup I ve grup II arasında tümör lokalizasyonu açısından anlamlı fark saptanmadı ( $p>0.05$ ). Ortalama tümör sayısının ve tümör boyutlarının her iki grupta da istatistiksel olarak benzer olduğu saptandı ( $p>0,05$ ).

**Sonuç:** Hastaların patolojik örneklerinde DKD görülmesine yaş, cinsiyet, tümör boyutu, tümör sayısı, tümörün mesane duvarındaki lokalizasyonu gibi değişkenlerin etkisinin olmadığı saptandı.

**Anahtar kelimeler:** mesane tümörü, TUR-MT, tümör lokalizasyonu, detrusor kas tabakası


*This study has been conducted retrospectively. All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.*

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## ABSTRACT

**Objective:** Sampling of detrusor muscle tissue (DMT) in the pathological examination of the bladder tumor is very important in the planning of correct staging and treatment. In the present study, we aimed to determine the factors affecting the DMT sampling in the pathology specimen after TUR-BT.

**Material and Methods:** The medical records of 59 patients who underwent TUR-BT were retrospectively analyzed. Twenty-six patients who had no DMT in the pathology specimen were classified as group I and 33 patients with DMT were classified as group II. Difference between groups in terms of age, gender, tumor number, tumor size and tumor localization were examined.

**Results:** DMT was found in 56% of pathology specimens. There was no statistically significant difference in terms of gender distribution between the two groups ( $p=0.646$ ). Tumor localizations were as follows; 11.5% is on the dome, 11.5% is on the opposite wall and 77% is on the side walls in group I; and In group 2, 6.1% were found on the dome, 27.2% on the opposite wall and 66.7% on the side walls. There was no statistically significant difference between group I and group II in terms of tumor localization ( $p>0.05$ ). The mean number of tumors and mean tumor size were found to be statistically similar in both groups ( $p>0.05$ ).

**Conclusion:** It was concluded that variables such as age, gender, tumor size, number of tumors, and localization of the tumor did not affect the presence of DMT in the pathological specimen of the patients.

**Keywords:** *bladder cancer, TUR-BT, tumor localization, detrusor muscle tissue*

## INTRODUCTION

Bladder cancer ranks seventh in males and 11th in females among the all types of cancers worldwide. In our country, bladder cancer is the third most common cancer in men following lung and prostate cancer (1, 2). Transurethral bladder tumor resection (TUR-BT) is the surgical method used for the diagnosis and treatment of bladder cancer. The pathological staging of the bladder tumor is done by the pathological examination of the tissue obtained from TUR-BT. A bladder tumor is named as non-muscle invasive bladder cancer (NMIBC) and muscle invasive bladder cancer (MIBC) based on whether or not DMT is involved in the bladder wall. The most important prognostic factor in bladder tumors is DMT invasion, in which case more aggressive methods are preferred in the treatment. In cases where DMT is not observed in samples obtained from TUR-BT, the procedure is considered to be incomplete and secondary transurethral bladder tumor resection (Re-TUR) should be performed for correct clinical staging (3). In 24-49% of cases where Re-TUR is performed, stage of the tumor is raised up and a need for change in the treatment arises (4, 5). In patients with T1 at the first resection, 4-25% MIBC is observed at the secondary resection. If DMT is not present at the first resection, this rate rises to 45% (6). Therefore, sampling of the DMT during the first resection of bladder tumor is important. In this study, we aimed to determine the factors affecting DMT sampling in pathology specimen during bladder tumor resection.

## MATERIAL AND METHODS

Medical data of 97 patients who underwent TUR-BT for bladder tumor between January 1, 2017 and July 1, 2018 were retrospectively reviewed. Patients with secondary bladder tumor, with a pathological stage of T2 and above, those with an operation note that did not describe the bladder location with a diagram, those who developed obturator reflex during resection and/or those with any degree of bladder perforation were excluded from the study. The files of 59 patients with primary MIBC, in which the localization of the tumor was marked on the bladder diagram in the operation note, were retrospectively analyzed. All resections were performed with 26 Fr Olympus resectoscope using 30° vision optics, 100 V cut with Gyrus plasma kinetic device and 80 V coagulation under 0.9% NaCl irrigation. Patients who did not have DMT in the pathology specimen were named as group I and the patients who have DMT in the pathology specimen were named as group II. The differences between the two groups in terms of age, gender, number of tumors, tumor diameter and tumor localization were investigated.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

### Statistical Analysis

The consistency of continuous variables to normal distribution was investigated with the Kolmogorov-Smirnov test. Variables with Gaussian distribution were shown as mean $\pm$ SD, and variables indicated by count (interval variable) mode (minimum-maximum). Pearson's Chi-square test or Fisher's Exact Test was used for comparison of the group frequencies. Student's test was used for comparison of variables with normal distribution. Independent variables were evaluated by logistic regression analysis for dependent variables with dichotomous characteristics. Statistical significance was evaluated at  $p < 0.05$  (two-tailed) level.

### RESULTS

The mean age of 26 patients in group I was  $69.5 \pm 10.2$ , the mean age of 33 patients in group II was  $68.7 \pm 9.2$  ( $p = 0.755$ ). In our study, the DMT was found in 56% of the pathology specimens. In both groups, number of male patients was higher, and female/male ratios were 3/23 and 2/31 in group I and group II, respectively. There was no statistically significant difference between the two groups ( $p = 0.646$ ). When tumor localization is examined, 11.5% of the tumors in group I were located in the dome, 11.5% in the opposite wall and 77% in the side walls; In group II, 6.1% were found in the dome, 27.2% in the opposite wall and 66.7% in the side walls. There was no statistically significant difference between group I and group II in terms of tumor localization ( $p > 0.05$ ). The mean number of tumors and tumor sizes were found to be statistically similar in both groups ( $p > 0.05$ ). When the tumor grade was taken into account, low grade tumors were found in 11 patients (42.3%) and high grade tumors in 15 patients (57.7%) in Group I. Patients with low grade and high grade tumors were 13 (39.4%) and 20 (60.6%) in Group II, respectively. There was no statistically significant difference between the two groups in terms of the grade of the tumor ( $p = 0.821$ ) (Table 1).

With logistic regression analysis, it was found that there was no relationship between variables such as age, gender, tumor size, number of tumors, and localization of the tumor in the bladder wall in pathological specimens (Table 2).

**Table 1.** Factors affecting detrusor muscle tissue in pathology specimen between groups

	Group I (n = 26)	Group II (n = 33)	P
<b>Age / year</b>	69.5 $\pm$ 10.2	68.7 $\pm$ 9.2	0.755
<b>Gender (female / male)</b>	3/23	2/31	0.646
<b>Tumor size</b>			
< 3mm (n, %)	7 (%26.9)	7 (%21.1)	0.760
$\geq$ 3mm (n, %)	19 (%73.1)	26 (%78.8)	
<b>The number of tumors</b>	1 (1-4)	1 (1-6)	0.469
<b>Tumor localization</b>			
<b>Dome (n,%)</b>	3 (% 11.5)	2 (% 6.1)	0.287
<b>Side wall (n,%)</b>	20 (% 76.9)	22 (% 66.7)	
<b>Opposite wall (n,%)</b>	3 (% 11.5)	9 (% 27.3)	
<b>Low grade, n (%)</b>	11 (%42,3)	13 (%39,4)	0,821
<b>High grade, n (%)</b>	15 (%57,7)	20 (%60,6)	

\* *p* value obtained with Fisher's Exact Test

**Table 2:** Comparison of the distribution of the group frequencies of the factors affecting the appearance of muscle tissue in TUR-MT pathology

Independent variables	$\beta$	p	O.R. (95% CI)
Constant	-0,790	= 0,720	-
Age	0,001	= 0,967	1,001 (0,946-1,060)
Gender	-0,655	= 0,518	0,519 (0,071-3,789)
Tumor size	0,500	= 0,462	0,606 (0,160-2,299)
Tumor localization	0,732	= 0,219	2,079 (0,648-6,670)
The number of tumors	0,157	= 0,566	1,170 (0,685-1,997)

O.R. odds ratio,  $\beta$ , regression coefficient

## DISCUSSION

The gold standard modality for the diagnosis, treatment and pathological staging in bladder tumor is TUR-BT. The presence of DMT in pathology material obtained from TUR-BT has been shown to be the determinant of resection quality, recurrence-free and progression-free survival (7-9). Sampling of the DMT in the pathology specimen is also related to the pathological stage and grade of the resected tumor. While the incidence of DMT layer in pathology specimens obtained from TUR-BT in MIBT is 41.9% for tumors of all stages and grades, this rate is 39.7%, regardless of the stage, without distinction of Ta and T1 in high grade tumors. While the rate of DMT presence in specimens in high grade Ta tumors is 45.9%, this rate is 51.8% in high grade T1 tumors (10). In our study, the incidence of DMT in pathology specimen was 56% higher compared with the literature. Furthermore, in our study, we found that there was no statistical significance between tumor grade and the presence of muscle tissue in pathology specimens. While the rate of low grade tumor was 42.3% in patients with no presence of DMT in pathology specimen, the rate of low grade tumor in patients with presence of DMT was 39.4%. High grade tumor rates were 57.7% and 60.6% in patients with and with no presence of DMT in pathology specimen ( $p=0.821$ ).

It was shown that the absence of DMT in pathology specimen was associated with tumor size and tumor morphology, However it was not significantly related to the surgeon's experience (11). While flat tumors with a wide-base are associated with alower incidence of DMT presence in the pathology specimen, increase in the tumor size is inversely proportional with presence of DMT in the pathology specimen (8, 12). Tumor morphology and surgeon experience were not evaluated in our study. It was shown that there was no statistically significant difference between tumor size and DMT sampling.

The obturator nerve originates from the L2-4 nerve roots of the lumbar plexus and contains both motor and sensory nerve fibers. It passes through the obturator canal and enters the pelvis, and travels inside the psoas major muscle and progresses close to the inferolateral wall of the bladder, bladder neck and prostatic urethra (13). During resection of the tumors localized in this area, especially in bladder lateral wall tumors, adductor muscle spasm may develop due to the electrical stimulation of the obturator nerve as its trajectory is close bladder and complications such as excessive bleeding, bladder wall perforation, vascular laceration, vascular damage, hematoma and incomplete tumor resection can occur (14). Of all superficial bladder tumors, 46.8% are located on the lateral wall, and severe adductor muscle spasms occur in 20% of the cases during transurethral resection of lateral bladder tumors (15, 16). That is why most physicians are concerned about the obturator reflex and its consequences during TUR-BT. Especially in the resection of side wall tumors, DMT sampling may be negatively affected in tumors localized in this area. In a study examining the presence of DMT in the pathology material of patients who underwent and did not undergo

obturator nerve blockade (ONB), it was shown that 26.5% of the patients in the group who did not undergo ONB and 4.2% of the patients who underwent ONB did not have any DMT in resection material. However, it has also been demonstrated that there is no statistically significant difference between the localization of the tumor in the bladder wall and presence of DMT in pathology specimen (11, 17). In our study, although the tumor was localized in the lateral walls in 77% of patients who did not have DMT in pathology specimen, it was found that tumor localization was not associated with DMT sampling compared to patients who had DMT in pathology specimen ( $P=0.287$ ). Presence of DMT in pathology specimen obtained from bladder urothelial carcinoma has been shown to be related to gender and the type of energy used. In a randomized controlled study by Teoh et al., bipolar energy use for resection has been shown to be associated with presence of DMT in pathology specimen. It is also reported that the female gender has a positive effect on the presence of DMT. This finding is explained by the thin bladder wall in women (18). In our study, although 91.1% of the patients were male, we assume that the use of bipolar energy in all resections caused a higher sampling rate of DMT in pathology specimen compared with the literature.

Different methods have been developed in order to perform proper resection and to reveal the possibility of sampling DMT in pathology specimen. One of these is establishing a pre-surgical checklist (CL) and compliance with these lists during resection. Studies have shown that the use of CL has positive effects on surgeon's attention and results in statistically significant improvements on recurrence-free survival after resection. However, it has been shown that it does not have a statistically significant effect on the likelihood of presence of DMT in resection material (12, 19).

## CONCLUSION

The presence of DMT in pathology specimen obtained from TUR-BT is very important for correct staging. In this study, the factors affecting the presence of DMT in pathology specimen obtained from TUR-BT were examined and it was shown that the variables such as age, gender, tumor number, tumor size, and localization of tumor in bladder did not have a statistically significant effect on muscle tissue sampling. The retrospective nature of the study and the low number of patients can be considered as limitations of this study. Further prospective randomized studies on this subject should be conducted in order to reveal the factors affecting the sampling of the DMT in pathology more clearly.

## Conflicts of Interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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## Authors' Contributions

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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