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The Effect of Sex and Age Differences on Pathology Results in Primary Bladder Cancer Patients

Primer Mesane Kanseri Tanısı Alan Hastaların Cinsiyet ve Yaş Farklılığının Patolojik Sonuçlara Etkisi

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Abstract

Objective: Bladder cancer is more frequently seen in males, whereas prognosis is usually worse in female patients. Although many factors affect the prognosis of urothelial carcinoma of bladder have been proposed, the effect of female gender on the prognosis of bladder urothelial carcinoma is controversial. Several factors have been suggested regarding the effect of gender difference on the prognosis of bladder urothelial carcinoma.

Materials and Methods: A retrospective study of 589 patients who underwent transurethral resection for the first time between January 2011 and January 2017 with preliminary diagnosis of bladder cancer was performed. Age, sex, tumor stage, histological subtype and tumor grade were evaluated in the study.

Results: No significant difference was found between the sexes in terms of tumor stage (p=0.663). The rate of high-grade tumors was 48.6% (n=235) in males and 63% (n=41) in females and statistically significantly higher in females than males (p<0.041). As the age progressed, it was found that tumor stage and extend increased (p<0.0001). Tumor grade and histological subtype were not statistically significant in terms of age groups.

Conclusion: In this study, newly diagnosed bladder tumor patients evaluated and revealed more in male gender. Furthermore, when evaluated in terms of age groups, it was shown that the stage and degree of the tumor increased as the age increased.

Keywords: Bladder cancer, gender, age, tumor grade, prognosis

Öz

Amaç: Mesane kanseri, erkeklerde daha fazla görülmesine rağmen kadınlarda prognozu daha kötüdür. Mesanenin üretelyal karsinomu prognozunda etkili birçok faktör ortaya konulmuş olup, kadın cinsiyetinin mesanenin üretelyal karsinomu prognozuna etkisi tartışmalıdır. Cinsiyet farklılığının mesanenin üretelyal karsinomu prognozuna etkisi ile ilgili çeşitli faktörler öne sürülmektedir.

Gereç ve Yöntem: Ocak 2011 ile Ocak 2017 tarihleri arasında mesane tümörü ön tanısı ile ilk defa transüretral rezeksiyon yapılan 589 hasta geriye dönük olarak incelendi. Çalışmada yaş, cinsiyet, tümör evresi, histolojik alt tip ve tümör derecesi değerlendirildi.

Bulgular: Tümör evresine göre her iki cinsiyette istatistiksel fark görülmedi (p=0,663). Yüksek dereceli tümör görülme oranı erkeklerde %48,6 (n=235) ve kadınlarda %63 (n=41) olup, istatistiksel olarak anlamlı olarak kadınlarda daha fazla idi (p<0,041). Yaş ilerledikçe tümör evresi ve derecesinin arttığı tespit edildi (p<0,0001). Yaş grupları açısından tümör derecesi ve histolojik alt tipin istatistiksel anlamlı olmadığı görüldü.

Sonuç: Bu çalışmamızda yeni tanı alan mesane tümörü hastaları değerlendirilmiş ve erkek cinsiyette daha fazla görüldüğü ortaya konmuştur. Ayrıca yaş grupları açısından değerlendirildiğinde yaş arttıkça tümör evre ve derecesinin arttığı gösterilmiştir.

Anahtar Kelimeler: Mesane kanseri, cinsiyet, yaş, tümör derecesi, prognoz

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Introduction

Urothelial carcinoma of the bladder (UCB) is the 7th most frequently diagnosed malignancy in males and 17th most frequently diagnosed malignancy in females globally (1). Moreover, UCB has the highest treatment costs per case among other cancer types from diagnosis to death of the patient (2). Although it is more frequently diagnosed in males, female patients show worse prognosis (3,4). There are several factors which are thought to affect UCB prognosis, whereas the effect of female gender on UCB is still debated.

Many factors about the effect of the difference in sex on UCB prognosis were shown in the literature. Some of the most commonly accepted factors are the difference in exposure to the environmental carcinogens, genetic differences, differences in hormonal balance, anatomical differences, social life differences and different tumor biology (1). In addition, the possibility of misdiagnosing vaginal bleeding in female patients as hematuria can cause a delay in UCB diagnosis and diagnosis in advanced tumor stages (5,6) when sexes are compared. In contrast to higher incidence rates seen in males, female patients usually have worse outcomes during early and invasive tumor stages. The exact association and influence of gender on UCB incidence rates, staging, prognosis and survival rates are still not clear to this day.

Materials and Methods

Data from 589 patients who went under transurethral resection for the first time with a pre-diagnosis of bladder tumor between January 2011 and January 2017 were retrospectively reviewed. The study data reviewed age, sex, tumor stage, histological subtype and tumor grade of the patients. Eight patients with tumors other than urothelial carcinoma and 12 patients with insufficient data were excluded from the study.

After initial transurethral resection was performed in all patients, second transurethral resection was indicated in patients with leftover tumors or patients under medium-to-high bladder cancer risk according to the guidelines of European Urology Association. Following these transurethral resections, the highest tumor stage and grade were included in the assessment. All specimens were sent to pathology for routine examination. Tumor staging was done using 2010 American Joint Committee on Cancer Tumor-Node-Metastasis Classification whereas tumor grading was done using 2004 World Health Organization classification. The assessed variables in the study were age, sex, tumor stage and grade.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences 20.0 (SPSS Inc, Chicago, USA). Kolmogorov-Smirnov test was used for the normal spread of continuous variables and expressed as mean value and standard deviation. Chi-square test and Fisher's exact test were used to compare categorical variables. Significance level was determined as $p<0.05$.

Results

Out of 569 patients included in the study, 497 (87.3%) patients were male and 72 (12.7%) were female (p=0.001). Mean age of the patients was calculated as 72.5±8.3 (44-82) in males and 76.5±7.7 (52-75) in females (p=0.02). Tumor staging spread was 125 (25.8%) pTa stage patients in males and 16 (25.3%) in females. Tumor stage pT1 was seen in 45.5% (n=220) of male and 44% (n=28) of female patients. Stage pT2 tumors were more frequently seen in females with 30.7% (n=20) vs. 27.1% (n=131) in males. No significant difference was detected between the sexes in terms of tumor stage (p=0.663). High-grade tumors were seen in 48.6% (n=235) of males and 63% (n=41) in females, with female patients significantly higher (p<0.041). In addition, it was found out that the age during the time of diagnosis was significantly higher in female patients compared to males (p=0.02). When histological subtypes were reviewed, non-transitional cell carcinoma (TCC) pathologies were seen more frequently in females as opposed to males (Table 1).

When patients were classified to age groups, the majority of the patients were found to be between 65-80 years of age (n=284, 49.9%). The most frequently diagnosed tumor stage in those patients were found to be pT1 and tumor stage and grade were shown to increase with the age (p<0.0001). No significant relationships were seen between age groups and tumor grade and histological subtypes (Table 2).

Discussion

Bladder tumors are the 4th most frequently diagnosed cancer type in males and 9th in females (7). It is estimated that there are over 500.000 bladder tumor cases in USA alone today (7). In addition, UCB treatments have the highest treatment costs per patient from the initial diagnosis to the death of the patient (2). Several studies showed that males are more frequently diagnosed compared to females and the incidence rate of the

Table 1. Tumor properties according to sex

	Male	Female	p
Number of patients (n)	497 (87.3)	72 (12.7)	**0.001**
Mean age (year)	72.5	76.5	**0.02**
Histological subtype (n) (%)			**0.009**
TCC	483 (97.1)	65 (90.2)	
Non-TCC	14 (2.9)	7 (9.8)	
Tumor stage (n) (%)			**0.663**
pTa	125 (25.8)	16 (25.3)	
pT1	220 (45.5)	28 (44)	
pT2	131 (27.1)	20 (30.7)	
Papilloma	6 (1.6)	0	
Tumor grade (n) (%)			**0.041**
High	235 (48.6)	41 (63)	
Low	247 (51.4)	24 (37)	

TCC: Transitional cell carcinoma

disease increase with age. However, there are also a few other studies that tell the opposite. In this study, our primary objective was to assess the pathology results of the patients with newly diagnosed bladder tumors in terms of age and sex differences.

UCB incidence and disease severity show differences between the sexes. The possible causes for those differences are thought to be different exposure levels to environmental carcinogens, genetic differences, differences in hormonal balance, anatomical differences, social life differences and different tumor biology between the sexes (1,8). Although UCB is more frequent in males, they usually have a better prognosis in comparison with female patients. This is further evidenced by the fact that although bladder tumor is diagnosed 3-4 times more in males, the death rates associated with bladder tumors are only 2 times more than the female patients (9). Likewise, in our study, we saw a significantly increased diagnosis rate in male patients.

A retrospective study which included 20514 patients reported male-to-female ratio as 4:1 and said that female patients were diagnosed in advanced stages of the disease (10,11). Another study showed that female patients tend to get diagnosed in a later age compared to males (12). However, there are other studies which argue that the UCB is more frequently seen in elder male patients (13,14,15). In our study, we saw a significant increase in mean age at the time of UCB diagnosis in female patients (76.5) as opposed to males (72.5).

Another retrospective study done in Netherlands between 1989 and 1994 also reported that female patients were diagnosed in advanced stages compared to male patients in general (10,11). Other studies with larger volumes also reported that the female patients were likely to be diagnosed in advanced tumor stages and those patients usually have a worse prognosis than men (16,17,18,19,20). In our study, we also saw that female patients have a significantly higher tumor grade at the time of diagnosis in accordance with the previous results reported in the literature. Although female patients also had advanced stage tumors in majority as well, it was not deemed as statistically significant.

Mungan et al.'s (11) study reported that female patients have a higher non-TCC tumor diagnosis rate compared to males. In our study, we also found out that female patients had a higher non-TCC tumor rates as compared to males.

There are a number of studies about the disease aggression and prognosis in young and old patients. However, the results of these studies are still debated and contradictory. Today, age is deemed as the most important risk factor in the prognosis of UCB development. Mean age of UCB development is 70 (21). About 12% of the male and females over 65 are diagnosed with bladder tumors today and it is thought to increase twofold until 2030 (22,23,24,25,26).

Many demographic studies reported an increase in UCB outcomes in patients over 65 compared to younger patients, with incidence rates 11 times and mortality rates 15 times higher than average (7,21). A study performed in California reported that the incidence rate of UCB peaks at 85 (27).

It is reported that the tumor is more differentiated and less aggressive in bladder tumor patients younger than 40 years of age (28,29). In addition, other studies reported decreased recurrence and progression rates in younger patients as well (28,29,30,31,32). As opposed to this, there are also other studies that showed no significant difference between age

Table 2. Tumor properties according to age groups

	<65	**65-80**	**>80**	**p**
Number of patients (n) (%)	114 (20)	284 (49.9)	171 (30.1)	
Sex (n) (%)				**0.148**
Male	104 (91.2)	250 (88)	143 (83.6)	
Female	10 (8.8)	34 (12)	28 (16.4)	
Histological subtype (n) (%)				**0.727**
TCC	111 (97.3)	275 (96.8)	163 (95.3)	
Non-TCC	3 (2.7)	9 (3.2)	8 (4.7)	
Tumor stage (n) (%)				**<0.0001**
pTa	26 (23.4)	71 (25.8)	42 (25.8)	
pT1	64 (57.6)	118 (42.9)	66 (40.4)	
pT2	16 (14.4)	84 (30.5)	55 (33.8)	
Papillom	4 (4.6)	2 (0.8)	0	
Tumor grade (n) (%)				**<0.0001**
High	43 (38.7)	159 (57.8)	104 (63.8)	
Low	68 (61.3)	116 (42.2)	59 (36.2)	

TCC: Transitional cell carcinoma

groups in terms of disease progression and severity (33,34,35). In our study, percentage of stage T2 patients were found to be significantly higher in age group 65-80 and over 80. Likewise, tumor grade also seemed to increase significantly with age. When age groups were compared, there was no significant difference between the sexes. Again, no significant difference was detected in histological subtypes between the age groups. However, this might be due to the low number of non-TCC patients.

Study Limitations

The main limitations of our study are the retrospective design, a relatively small number of patients and inability to review the data on recurrence, progression and survival rates of the patients.

Conclusion

In this study, we reviewed the newly diagnosed bladder tumor patients and saw that the diagnosis rates were significantly higher in male patients. However, we also saw that although the incidence rate is lower in female patients, they usually had higher tumor stage and grades. In addition, when age groups were compared, the tumor grade and stage increased with the age. The effect of sex on incidence rate and disease stage should be supported with survival rate data.

Ethics

Ethics Committee Approval: The study was retrospectively reviewed by examining patient files. For this reason, ethical approval was not received.
Informed Consent: Retrospective study.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.T., S.Ü., Concept: H.T., Design: H.T., Data Collection or Processing: H.T., S.Ü., B.E., Analysis or Interpretation: H.T., S.Ü., Literature Search: H.T., B.E., Writing: H.T., B.E.
Conflict of Interest: No conflict of interest was declared by the authors.
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